Electronic Supplementary Material (ESI) for RSC Advances.

`Facile synthesis of 3-amino-5-aryl -1,2,4-oxadiazoles via PIDA-mediated intramolecular oxidative cyclization

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Supplementary Information

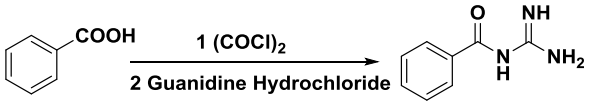
Contents.....Page

I. General Information

All reagents and solvents were obtained from commercial sources and used without further purification. All solvents were dried with 4A molecular sieve before use. Reactions were monitored by thin-layer chromatography (TLC) on silica plates (F-254) and visualized under UV light. Melting points were obtained on a Büchi Melting Point B-540 apparatus and were uncorrected. All ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker ARX-400, 400 MHz spectrometers with TMS as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, J, are reported in hertz (Hz). HRMS analysis was performed on a Q-TOF mass analyzer using the ESI ionization method.

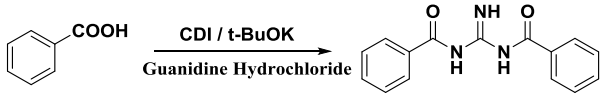
II. Synthesis of Substrates

Substrates **(1a-u, 1x)** were synthesized according to the literature methods with minor modifications.[1]
A representative procedure (synthesis of *N*-carbamimidoylbenzamide **(1a)**) is shown below.



benzoic acid (8 mmol) was dissolved in 10 ml of dichloromethane and two drops of DMF were added. Then, oxalyl chloride (21.6 mmol) were pipetted to this mixture. This mixture was stirred for 2h at room temperature and then refluxed for 3h After cooling, the solution was concentrated to dryness in vacuum and the residue was taken up in 10 ml of tetrahydrofuran. The solution obtained was slowly added dropwise to a solution of guanidine hydrochloride (36.0 mmol) in 25 ml of sodium hydroxide solution (c = 2 mol/L). The mixture was stirred for 1h at room temperature, the organic phase was separated and the aqueous phase was extracted three times with 30 ml ethyl acetate. The combined organic phases were washed with 50 ml of NaOH (c = 1 mol/L) and subsequently with 100 ml of water. Thereafter, the combined extracts were dried over Na_2SO_4, filtered and concentrated to give a crude residue. This was purified by flash column chromatography by using a system of dichloromethane /methanol and the desired product **1a** was obtained.

Substrate *N, N'*-(iminomethylene)dibenzamide **(1v)** was synthesized according to the literature method with minor modifications.[2]



A solution of guanidine hydrochloride 0.2g (2 mmol) in DMF: dioxane (1:1; 10mL) was added Potassium *tert*-butoxide 0.45g (4 mmol) and the reaction mixture was heated at 50-55℃ for 30 min. The mixture was cooled to room temperature, the solid sodium chloride was filtered and the filtrate was added to the 1-h stirred solution of benzoic acid 0.5g (4.1 mmol) and *N,N'*-Carbonyldiimidazole 1.3g (8.2 mmol) in DMF (10mL) at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, water (10mL) was added, the solid was collected by filtration and washed with cold water to obtain the product **1v**, which was further purified by flash chromatography (silica gel, methanol / dichloromethane 1:10, v/v) Yield:73% (0.4g).white solid, m.p. 160-161℃.^{1}H NMR (400 MHz, DMSO-d_6) δ_H 12.67 (1 H, s), 9.37 (2 H, s), 8.10 (4 H, d, *J*= 7.5 Hz), 7.63 (2 H, t, *J*= 7.2 Hz), 7.54 (4 H, t, *J*= 7.5 Hz).^{13}C NMR (100 MHz, DMSO-d_6) δ_C 174.35, 165.23, 164.24, 133.71, 132.99, 132.91, 129.95, 128.88, 128.58, 128.03, 123.68. HRMS (ESI-Q-TOF, m/z) calcd for $C_{15}H_{13}N_3O_2$ $[M + H]^+$: 268.1008, found $[M + H]^+$: 268.1010.

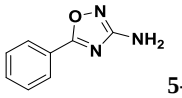
Substrates **(1y, 1z)** were synthesized according to the **reference 3**

III. General Procedure and Product Characterization

1 General procedure for the preparation of 2a-2y

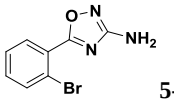
To a stirring solution of **1a** (0.6 mmol) in DMF (3 mL), PIDA (0.9 mmol) was added at 0℃.The resulting reaction mixture was stirred at room temperature for 5-6 h. After completion of the reaction (monitored by TLC), the residue was diluted with ethyl acetate (5 mL). The organic layer was washed with saturated sodium bicarbonate (2×3 mL), water (2×3 mL) and brine (2×3 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated to yield the crude product, which was further purified by flash chromatography (silica gel, ethyl acetate /petroleum ether /triethylamine 1:5:0.1, v/v), affording the desired product **2a**

2. Product Characterization



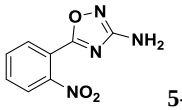
5-Phenyl-1,2,4-oxadiazol-3-amine (2a):

Yield: 69% (68 mg), white solid, m.p.:164-165 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 8.02–7.97 (2 H, m), 7.67 (1 H, t, J= 7.4 Hz), 7.60 (2 H, t, J= 7.4 Hz), 6.43 (2 H, s). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 173.45, 169.47, 133.12, 129.85, 127.81, 124.55. HRMS (ESI-Q-TOF, m/z) calcd for $C_8H_7N_3O$ [M + H]+: 162.0589, found [M + H]+: 162.0576.



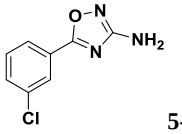
5-(2-Bromophenyl)-1,2,4-oxadiazol-3-amine (2b):

Yield: 74% (73 mg), white solid, m.p. 168-169 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.91 (1 H, dd, J =7.4, 2.1 Hz), 7.87 (1 H, dd, J= 7.6, 1.5 Hz), 7.61–7.54 (2 H, m), 6.51 (2 H, s).^{13}C NMR (100 MHz, DMSO-d_6) δ_C 170.31, 169.38, 148.81, 134.12, 133.93, 131.35, 125.03, 118.37. HRMS (ESI-Q-TOF, m/z) calcd for $C_8H_6BrN_3O$ [M + H]$^+$: 239.9694, found [M + H]$^+$: 239.9687.



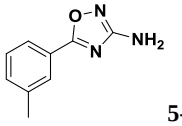
5-(2-Nitrophenyl)-1,2,4-oxadiazol-3-amine (2c):

Yield: 77% (76 mg), pale yellow solid, m.p. 199-201 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 8.14 (1 H, dd, J= 5.9, 3.3Hz), 8.04 (1 H, dd, J= 5.5, 3.6 Hz), 7.95–7.89 (2 H, m), 6.59 (2 H, s).^{13}C NMR (100 MHz, DMSO-d_6): δ_C 161.96, 158.39, 149.32, 132.37, 130.60, 127.69, 117.51, 106.35, 55.53. HRMS (ESI-Q-TOF, m/z) calcd for $C_8H_6N_4O_3$ [M + H]$^+$: 207.0440, found [M + H]$^+$: 207.0451



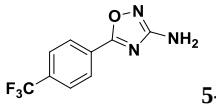
5-(3-Chlorophenyl)-1,2,4-oxadiazol-3-amine (2d):

Yield: 75% (74 mg), pale yellow solid, m.p. 159-162 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 8.00–7.93 (2 H, m), 7.75 (1 H, d, J= 8.3Hz), 7.64 (1 H, t, J= 7.9 Hz), 6.50 (2 H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 171.80, 169.08, 134.03, 132.52, 131.51, 126.89, 126.11, 125.98. HRMS (ESI-Q-TOF, m/z) calcd for $C_8H_6ClN_3O$ [M + H]$^+$: 196.0199, found [M + H]$^+$: 196.0194.



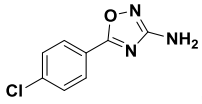
5-(M-tolyl)-1,2,4-oxadiazol-3-amine (2e):

Yield: 67% (66 mg), white solid, m.p. 146-148 ℃. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.81 (1 H, s), 7.80 – 7.76 (1 H, m), 7.48 (2 H, d, J= 5.0 Hz), 6.40 (2 H, s), 2.40 (3 H, s). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 173.55, 169.44, 139.32, 133.75, 129.75, 128.15, 124.99, 124.49, 21.28. HRMS (ESI-Q-TOF, m/z) calcd for $C_9H_9N_3O$ [M + H]$^+$: 176.0746, found [M + H]$^+$: 176.0757



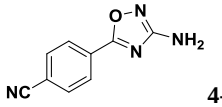
5-(4-(Trifluoromethyl) phenyl)-1,2,4-oxadiazol-3-amine (2f):

Yield: 78% (77 mg), pale yellow solid, m.p. 186-188 ℃. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.20 (2 H, d, J= 8.2 Hz), 7.98 (2 H, d, J= 8.2 Hz), 6.55 (2 H, s).^{13}C NMR (100MHz, DMSO-d_6): δ_C 172.24, 169.59, 132.40, 128.74, 128.13, 126.85, 126.82. HRMS (ESI-Q-TOF, m/z) calcd for $C_9H_6F_3N_3O$ [M + H]$^+$: 230.0463, found [M + H]$^+$: 230.0458.



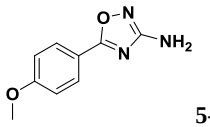
5-(4-Chlorophenyl)-1,2,4-oxadiazol-3-amine (2g):

Yield: 72% (71 mg), pale yellow solid, m.p. 224-226 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.00 (2 H, d, J= 8.6 Hz), 7.67 (2 H, d, J= 8.6 Hz), 6.46 (2 H, s).^{13}C NMR (100 MHz, DMSO-d_6): δ_C 172.36, 169.26, 137.69, 129.81, 129.41, 123.14. HRMS (ESI-Q-TOF, m/z) calcd for $C_8H_6ClN_3O$ [M + H]$^+$: 196.0199, found [M + H]$^+$: 196.0187



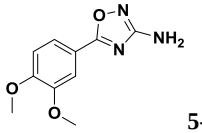
4-(3-Amino-1,2,4-oxadiazol-5-yl)benzonitrile (2h):

Yield: 76% (75 mg), white solid, m.p. 195-197 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.15 (2 H, d, J= 8.1 Hz), 8.07 (2 H, d, J= 8.1 Hz), 6.56 (2 H, s).^{13}C NMR (100 MHz, DMSO-d_6): δ_C 172.00, 169.54, 133.74, 128.47, 128.20, 118.43, 115.10. HRMS (ESI-Q-TOF, m/z) calcd for $C_9H_6N_4O$ [M + H]$^+$: 187.0542, found [M +H]$^+$: 187.0539.



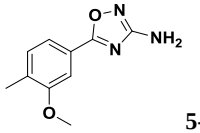
5-(4-Methoxyphenyl)-1,2,4-oxadiazol-3-amine (2i):

Yield: 62% (61 mg), pale yellow solid, m.p. 155-158 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.93 (2 H, d, J= 8.9 Hz), 7.13 (2 H, d, J= 8.9 Hz), 6.33 (2 H, s), 3.85 (3 H, s).^{13}C NMR (100 MHz DMSO-d_6): δ_C 173.00, 169.05, 162.68, 129.44, 116.66, 114.93, 55.75. HRMS (ESI-Q-TOF, m/z) calcd for $C_9H_9N_3O_2$ [M + H]$^+$: 192.0695, found [M + H]$^+$: 192.0691.



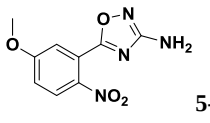
5-(3,4-Dimethoxyphenyl)-1,2,4-oxadiazol-3-amine (2j):

Yield: 57% (56 mg), yellow solid, m.p. 163-165 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.56 (1 H, d, J= 8.4 Hz), 7.43 (1 H, s), 7.12 (1 H, d, J= 8.4 Hz), 6.31 (2 H, s), 3.81 (6 H, s).^{13}C NMR (100 MHz, DMSO-d_6): δ_C 173.44, 169.36, 152.80, 149.37, 121.50, 116.85, 112.36, 110.32, 56.21, 56.02. HRMS (ESI-Q-TOF, m/z) calcd for $C_{10}H_{11}N_3O_3$ [M + H]$^+$: 222.0800, found [M + H]$^+$: 222.0809.



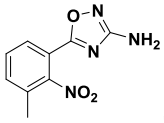
5-(3-Methoxy-4-methylphenyl)-1,2,4-oxadiazol-3-amine (2k):

Yield: 66% (65 mg), pale yellow solid, m.p. 133-136 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.50 (1 H, d, J= 7.8 Hz), 7.45 (1 H, s), 7.36 (1 H, d, J= 7.8 Hz), 6.40 (2 H, s), 3.88 (3 H, s), 2.23 (3 H, s).^{13}C NMR (100 MHz, DMSO-d_6): δ_C 173.50, 169.35, 157.99, 131.60, 131.57, 123.30, 119.90, 108.83, 55.84, 16.62. HRMS (ESI-Q-TOF, m/z) calcd for $C_{10}H_{11}N_3O_2$ [M + H]$^+$: 206.0851, found [M + H]$^+$: 206.0846



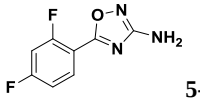
5-(5-Methoxy-2-nitrophenyl)-1,2,4-oxadiazol-3-amine (2l):

Yield: 73% (72 mg), yellow solid, m.p. 140-143 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.20 (1 H, d, J= 9.1 Hz), 7.44 (1 H, d, J= 2.8 Hz), 7.39 (1 H, dd, J= 9.1, 2.8 Hz), 6.55 (2 H, s), 3.95 (3 H, s).^{13}C NMR (100 MHz, DMSO-d_6): δ_C 170.90, 169.24, 163.21, 141.32, 128.00, 122.16, 118.16, 116.79, 57.12. HRMS (ESI-Q-TOF, m/z) calcd for $C_9H_8N_4O_4$ [M + H]$^+$: 237.0546, found [M + H]$^+$: 237.0538.



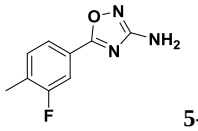
5-(3-Methyl-2-nitrophenyl)-1,2,4-oxadiazol-3-amine (2m):

Yield: 75% (74 mg), white solid, m.p. 172-175 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.98 (1 H, d, *J*= 7.5 Hz), 7.80 (1 H, d, *J*= 7.4 Hz), 7.73 (1 H, t, *J*= 7.7 Hz), 6.58 (1 H, s), 4.14 (1 H, s), 2.34 (3 H, s).^{13}C NMR (100MHz, DMSO-d_6): δ_C 169.41, 148.95, 136.33, 131.75, 131.10, 128.21, 116.27, 16.92. HRMS (ESI-Q-TOF, m/z) calcd for $C_9H_8N_4O_3$ [M + H]$^+$: 221.0596, found [M +H]$^+$: 221.0606



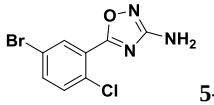
5-(2,4-Difluorophenyl)-1,2,4-oxadiazol-3-amine (2n):

Yield: 77% (76 mg), pale yellow solid, m.p. 163-165 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.09 (1 H, dd, *J*= 15.1, 8.6 Hz), 7.62 – 7.54 (1 H, m), 7.34 (1 H, dd, *J*= 10.5, 8.6 Hz), 6.52 (2 H, s).^{13}C NMR (100MHz, DMSO-d_6): δ_C 169.45, 169.02, 164.99, 160.74, 132.42, 113.23, 109.62, 106.06. HRMS (ESI-Q-TOF, m/z) calcd for $C_8H_5F_2N_3O$ [M + H]$^+$: 198.0401, found [M + H]$^+$: 198.0400.



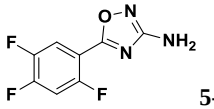
5-(3-Fluoro-4-methylphenyl)-1,2,4-oxadiazol-3-amine (2o):

Yield: 75% (74 mg), pale grey solid, m.p. 170-173 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.71 (1 H, d, *J*= 7.9 Hz), 7.66 (1 H, d, *J* =10.0 Hz), 7.51 (1 H, t, *J*= 7.8 Hz), 6.43 (2 H, s), 2.31 (3 H, s).^{13}C NMR (100 MHz, DMSO-d_6): δ_C 172.50, 169.45, 162.25, 159.82, 133.25, 130.22, 123.84, 114.20, 14.86. HRMS (ESI-Q-TOF, m/z) calcd for $C_9H_8FN_3O$ [M + H]$^+$: 194.0651, found [M + H]$^+$: 194.0646.



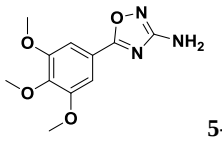
5-(5-Bromo-2-chlorophenyl)-1,2,4-oxadiazol-3-amine (2p):

Yield: 72% (71 mg), white solid, m.p., 174-177 °C.^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.13 (1 H, d, *J*= 2.4 Hz), 7.86 (1 H, dd, *J*= 8.6, 2.4 Hz), 7.66 (1 H, d, *J*= 8.6 Hz), 6.57 (2 H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 170.79, 169.20, 136.64, 134.13, 133.60, 131.82, 125.70, 120.75. HRMS (ESI-Q-TOF, m/z) calcd for $C_8H_5BrClN_3O$ [M + H]$^+$: 273.9305, found [M + H]$^+$: 273.9314.



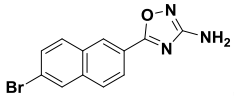
5-(2,4,5-Trifluorophenyl)-1,2,4-oxadiazol-3-amine (2q):

Yield: 79% (78 mg), pale yellow solid, m.p. 165-167 °C.^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.08 (1 H, dd, *J*= 15.5, 10.4 Hz), 7.90 (1 H, dd, *J*= 17.2, 10.6 Hz), 6.56 (2 H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 169.32, 168.78, 118.57, 118.47, 108.85, 108.63, 108.57, 108.35. HRMS (ESI-Q-TOF, m/z) calcd for $C_8H_4F_3N_3O$ [M + H]$^+$: 216.0306, found [M + H]$^+$: 216.0308.



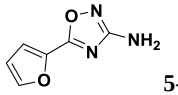
5-(3,4,5-Trimethoxyphenyl)-1,2,4-oxadiazol-3-amine (2r):

Yield: 52% (51 mg), pale yellow solid, m.p. 201-203 °C.^{1}H NMR (400 MHz, DMSO-d_6): δ_H .25 (2 H, s), 6.40 (2 H, s), 3.86 (6 H, s), 3.74 (3 H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 173.29, 169.43, 153.76, 141.67, 119.66, 105.09, 60.68, 56.53. HRMS (ESI-Q-TOF, m/z) calcd for $C_{11}H_{13}N_3O_4$ [M + H]$^{+:}$ 252.0906, found [M + H]$^+$: 252.0914.



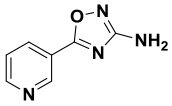
5-(6-Bromonaphthalen-2-yl)-1,2,4-oxadiazol-3-amine (2s):

Yield: 55% (54 mg), white solid, m.p. 235-238 ℃. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.69 (1 H, s), 8.36 (1 H, s), 8.14 (1 H, d, *J*= 8.9 Hz), 8.12 – 8.05 (2 H, m), 7.79 (1 H, dd, *J*= 8.7, 2.0 Hz), 6.48 (2 H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 173.45, 169.73, 136.18, 131.90, 131.55, 130.97, 130.48, 129.02, 128.81, 125.18, 122.56, 122.49. HRMS (ESI-Q-TOF, m/z) calcd for $C_{12}H_8BrN_3O$ [M + H]$^+$: 289.9851, found [M + H]$^+$: 289.9856.



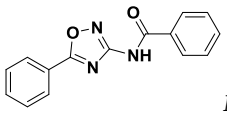
5-(Furan-2-yl)-1,2,4-oxadiazol-3-amine (2t):

Yield: 59% (58 mg), white solid, m.p. 147-150 ℃ ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.07 (1 H, d, *J*= 1.8 Hz), 7.38 (1 H, d, *J*= 3.5 Hz), 6.79 (1 H, dd, *J*= 3.5, 1.8 Hz), 6.44 (2 H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 169.32, 165.77, 148.12, 140.22, 116.69, 113.34. HRMS (ESI-Q-TOF, m/z) calcd for $C_6H_5N_3O_2$ [M + H]$^+$: 152.0382, found [M + H]$^+$: 152.0378.



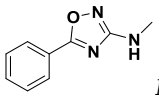
5-(Pyridin-3-yl)-1,2,4-oxadiazol-3-amine (2u):

Yield: 62% (61 mg), pale yellow solid, m.p. 176-179 ℃.^{1}H NMR (400 MHz, DMSO-d_6): δ_H 9.13 (1 H, s), 8.81 (1 H, d, *J*= 4.8 Hz), 8.33 (1 H, d, *J*= 8.0 Hz), 7.62 (1 H, dd, *J*= 8.0 , 4.8 Hz), 6.51 (2 H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 171.76, 169.47, 153.53, 148.45, 135.44, 124.85, 120.99. HRMS (ESI-Q-TOF, m/z) calcd for $C_7H_6N_4O$ [M + H]$^+$: 163.0542, found [M + H]$^+$: 163.0547.



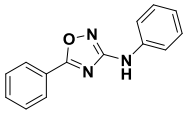
***N*-(5-phenyl-1,2,4-oxadiazol-3-yl)benzamide (2v):**

Yield: 78% (77 mg), white solid, m.p. 205-206 ℃.^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.69 (1 H, s), 8.15 – 8.10 (2 H, m), 8.08 – 8.03 (2 H, m), 7.75 (1 H, t, *J*= 7.4 Hz), 7.66 (3 H, dd, *J*= 15.3, 7.6 Hz), 7.55 (2 H, t, *J*= 7.6 Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 173.94, 164.82, 163.84, 133.30, 132.58, 132.50, 129.55, 128.47, 128.17, 127.62, 123.28. HRMS (ESI-Q-TOF, m/z) calcd for $C_{15}H_{11}N_3O_2$ [M + H]$^+$: 266.0851, found [M + H]$^{+:}$ 266.0849.



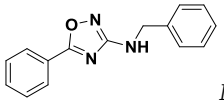
***N*-methyl-5-phenyl-1,2,4-oxadiazol-3-amine (2w)**

Yield: 57% (56 mg), white solid, m.p. 111-112 ℃.^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.00 (2 H, d, *J*= 7.3 Hz), 7.67 (1 H, t, *J*= 7.3 Hz), 7.60 (2 H, t, *J*= 7.3 Hz), 6.89 (1 H, q, *J*= 4.7 Hz), 2.76 (3 H, d, *J*= 4.7 Hz) ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 173.48, 170.09, 133.12, 129.79, 127.82, 124.49, 29.54. HRMS (ESI-Q-TOF, m/z) calcd for $C_9H_9N_3O$ [M + H]$^+$: 176.0746 found [M + H]$^{+:}$ 176.0783



***N*,5-diphenyl-1,2,4-oxadiazol-3-amine (2x)**

Yield: 42% (41 mg), white solid, m.p. 129-130 ℃.^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.06 (1 H, s), 8.08 (2 H, d, J= 8.5 Hz), 7.72 (1 H, t, J=7.4 Hz), 7.65 (2 H, t, J=8.0 Hz), 7.52 (2 H, d, J=8.5 Hz), 7.34 (2 H, t, J=8.0 Hz), 6.97 (1 H, t, J=7.3 Hz).^{13}C NMR (100 MHz, DMSO-d_6): δ_C 172.58, 165.46, 139.84, 133.03, 129.43, 128.90, 127.53, 123.51, 121.01, 116.93. HRMS (ESI-Q-TOF, m/z) calcd for $C_{14}H_{11}N_3O$ [M + H]+: 238.0902 found [M + H]$^{+:}$ 238.0945



***N*-benzyl-5-phenyl-1,2,4-oxadiazol-3-amine (2y)**

Yield: 63% (62 mg), white solid, m.p. 111-112 ℃.^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.02 – 7.97 (2 H, m), 7.67 (1 H, t, *J*=7.4 Hz), 7.63 – 7.57 (3 H, m), 7.39 – 7.31 (4 H, m), 7.25 (1 H, t, J= 6.9 Hz), 4.35 (2 H, d, J= 6.9 Hz) ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 173.57, 169.43, 139.69, 133.17, 129.80, 128.66, 127.83, 127.70,127.29, 124.40, 46.48. HRMS (ESI-Q-TOF, m/z) calcd for $C_{15}H_{13}N_3O$ $[M + H]^+$: 252.1059 found $[M + H]^{+:}$ 252.1068

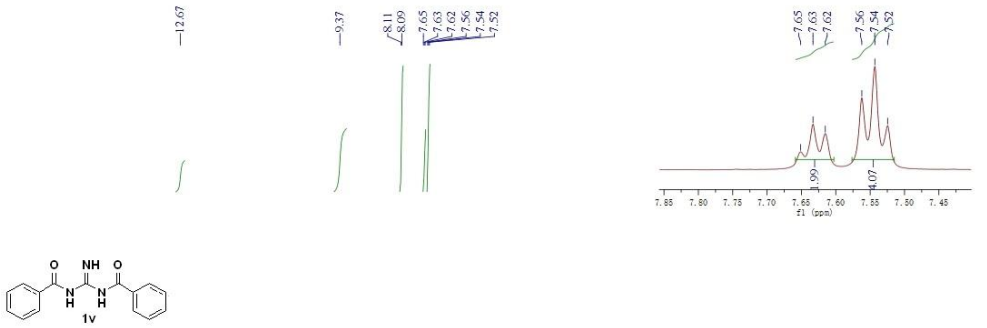
IV. References

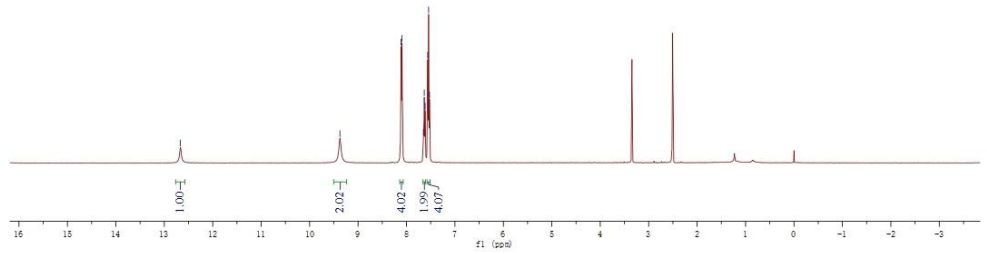
1 (a) E. G. Dinneen, L. C. Anne, and M. Michelle *US Pat.* 20150023921.(b) D. Andreas, H. Thomas, S. Alexander, M. Wolfgang, S. Frauke, L. J. Peter, and B. Michael, *DE Pat* 102011085136.

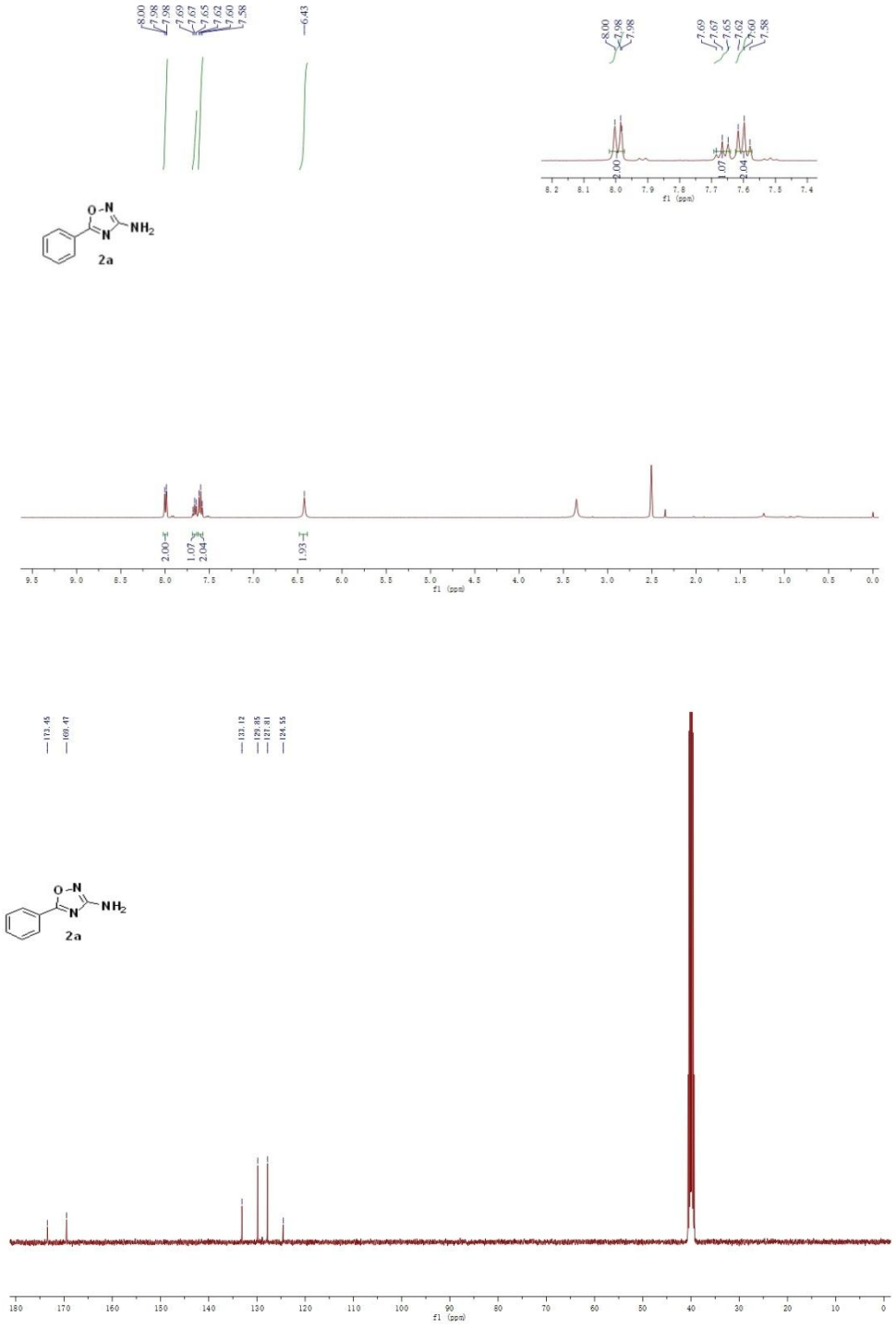
2 B. C. Das, S. M. Mahalingam, and P. Mohapatra, *Tetrahedron. Lett.*, 2009, **50**, 5860-5863.

3 T. Shinada, T. Umezawa, T. Ando, H. Kozuma, and Y. Ohfune, *Tetrahedron. Lett.*, 2006, **47** 1945-1947.

V. Copies of ^{1}H NMR and ^{13}C NMR Spectra



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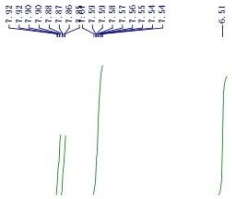

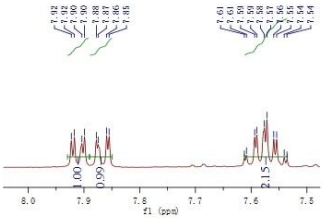

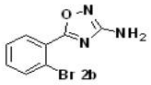

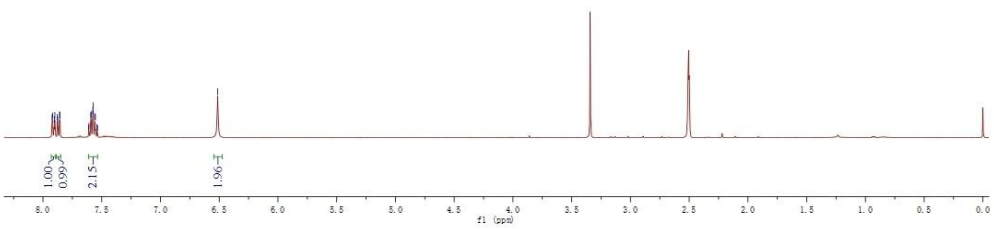

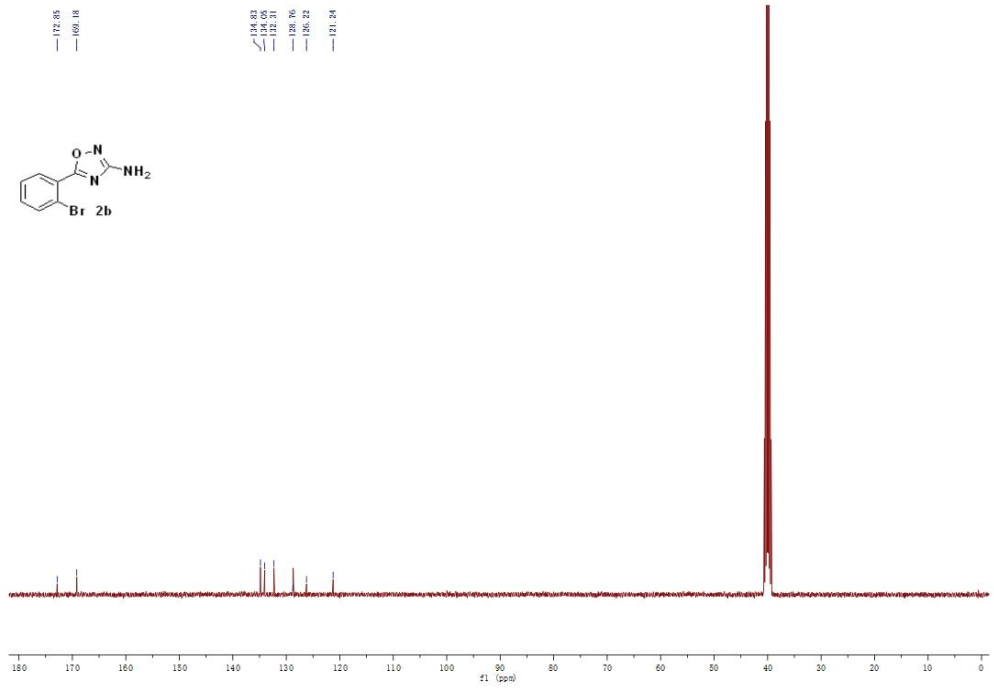

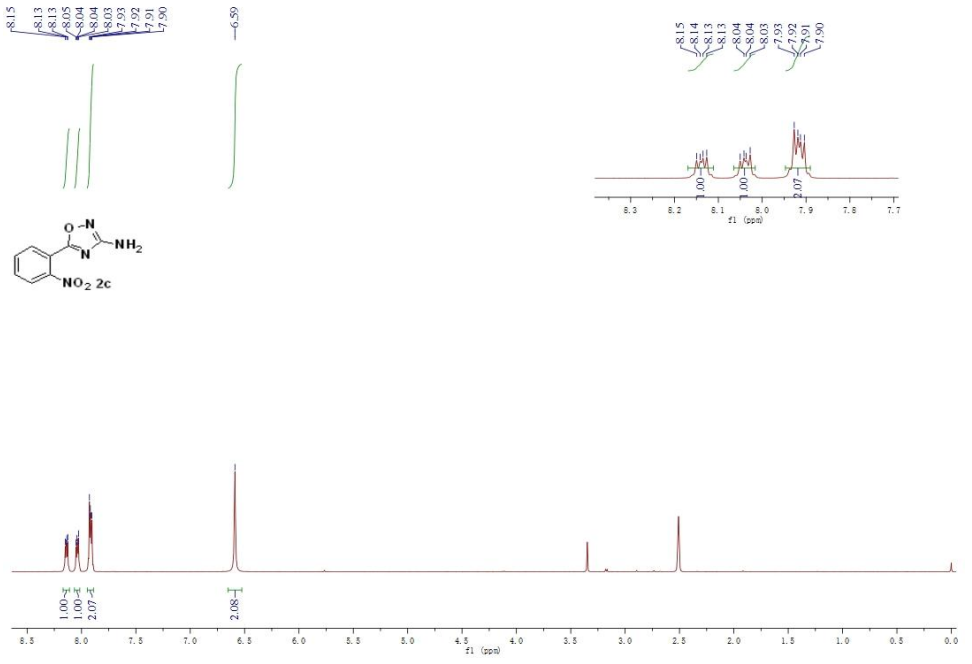
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8.05
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8.04
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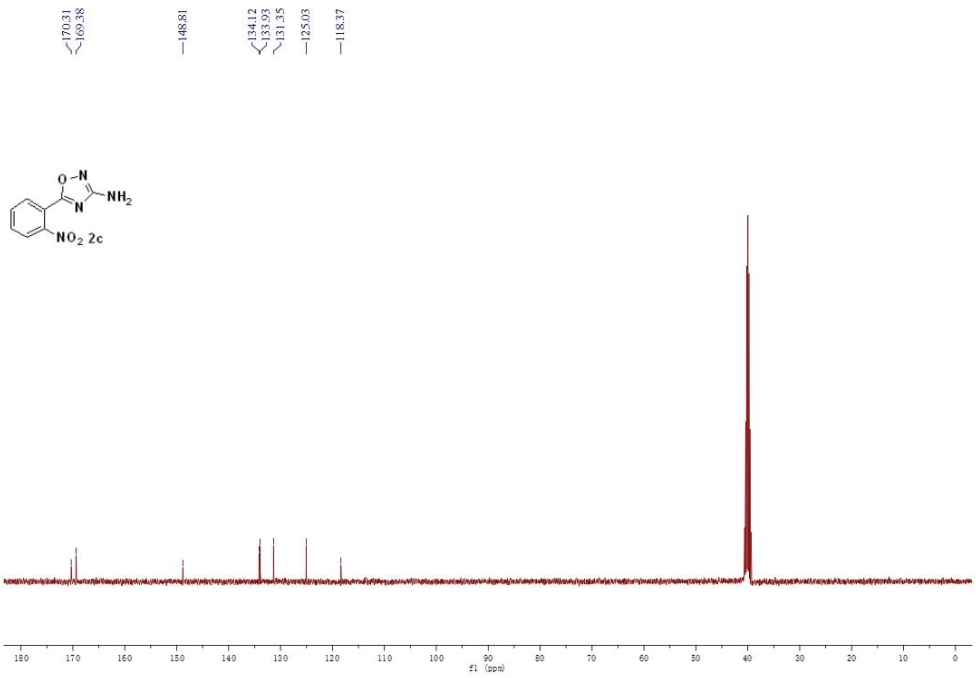
f1 (ppm)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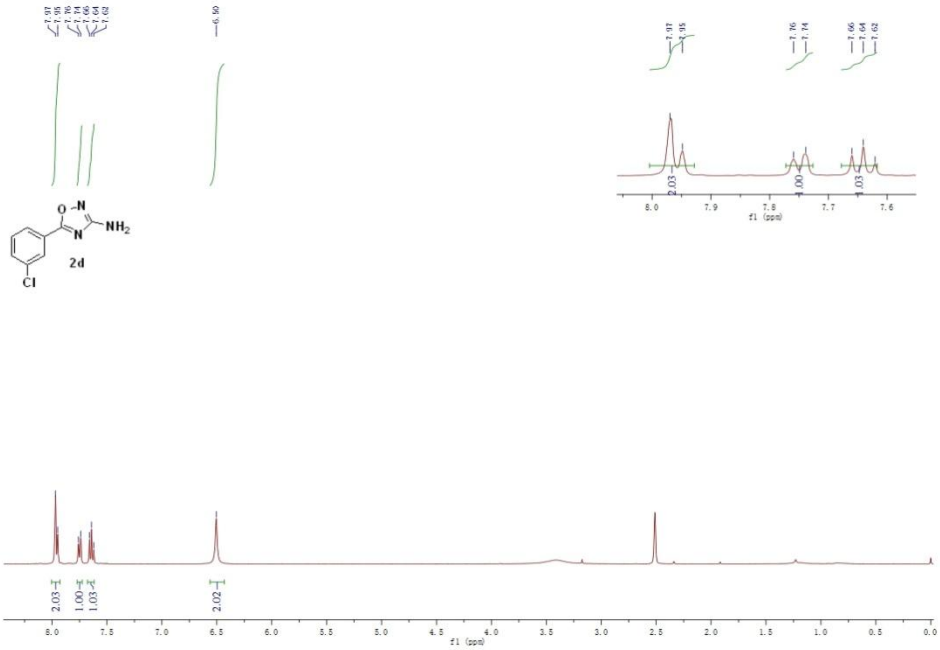
NO2 2c
f1 (ppm)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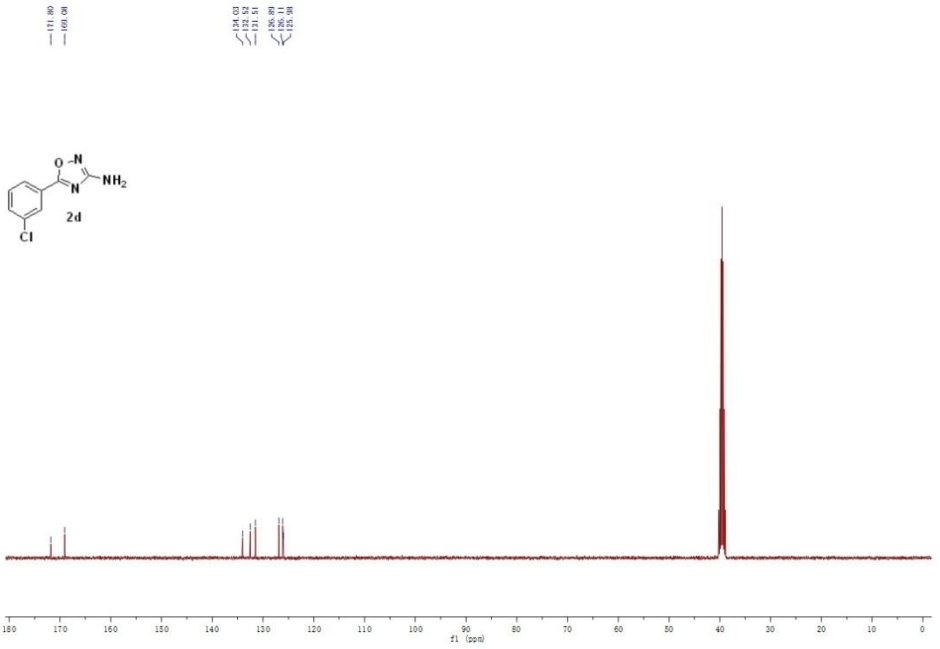
f1 (ppm)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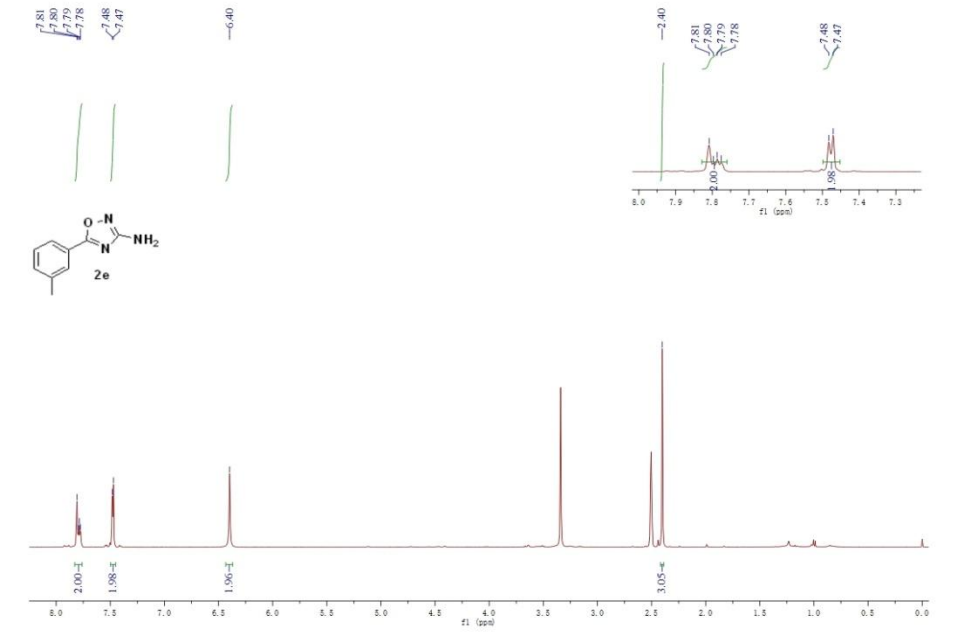
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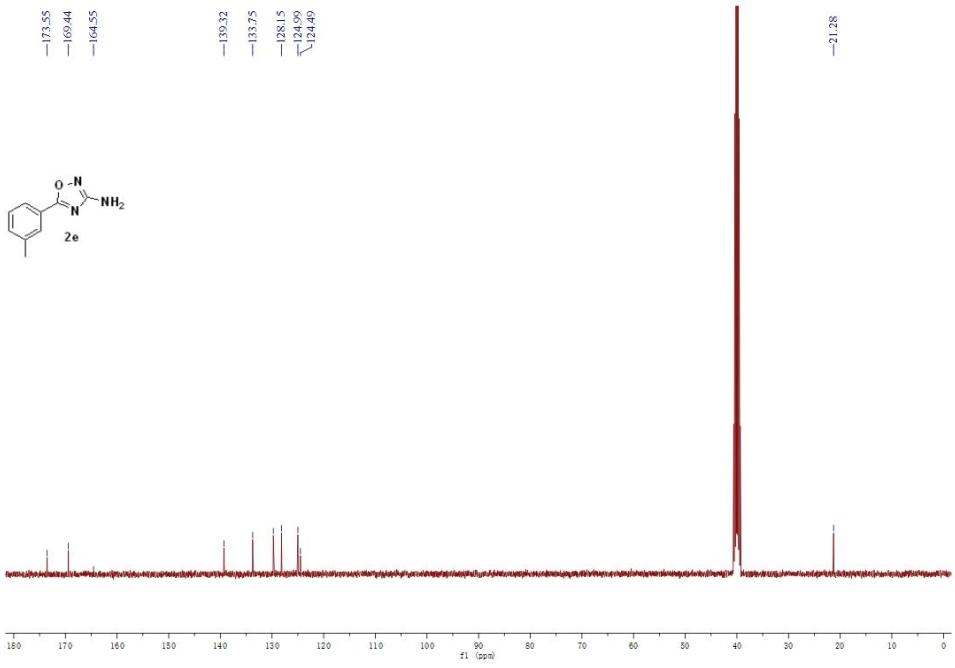
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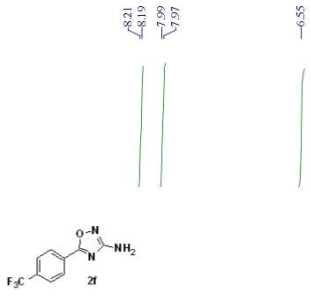
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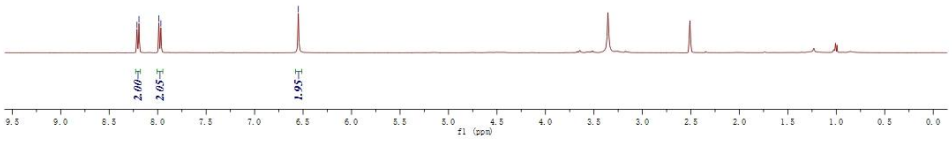
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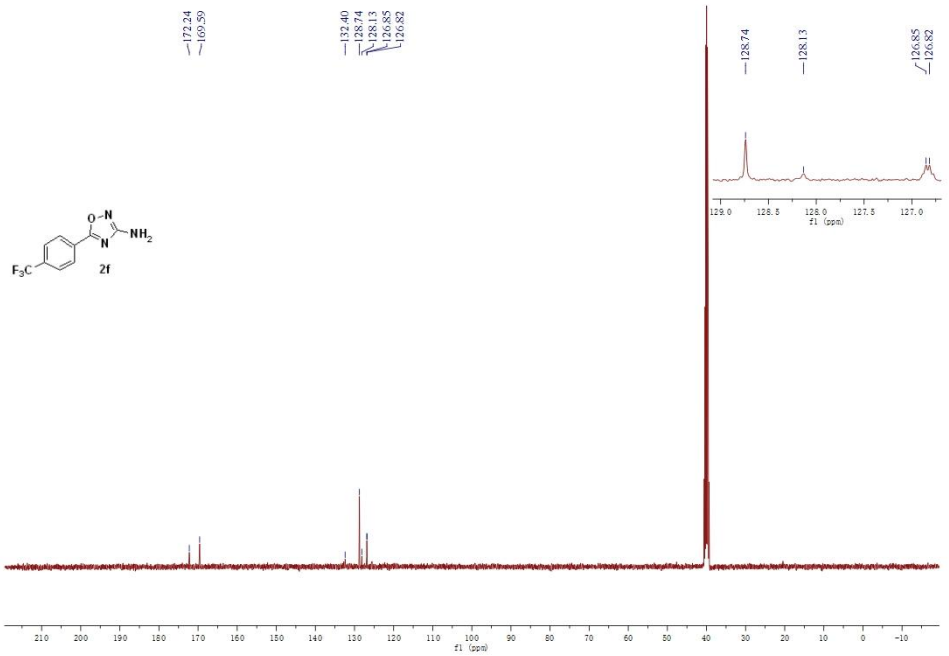
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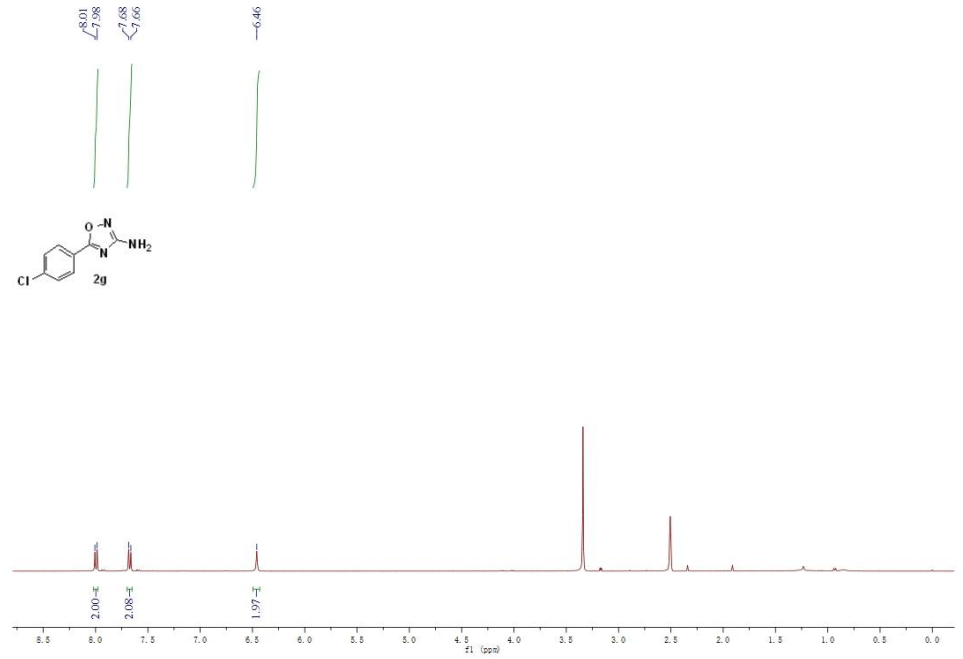
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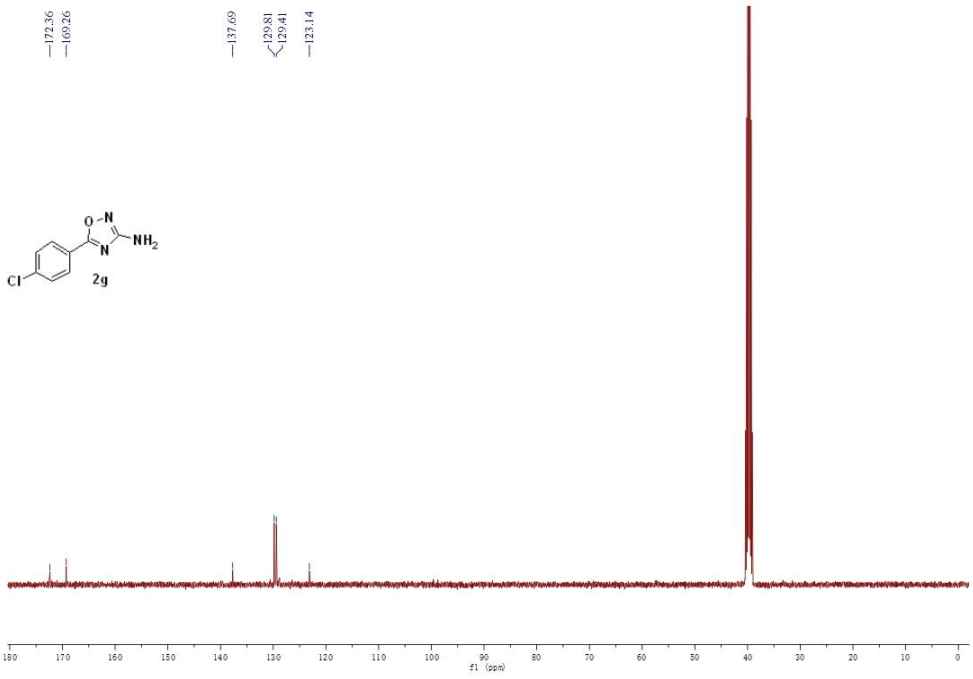
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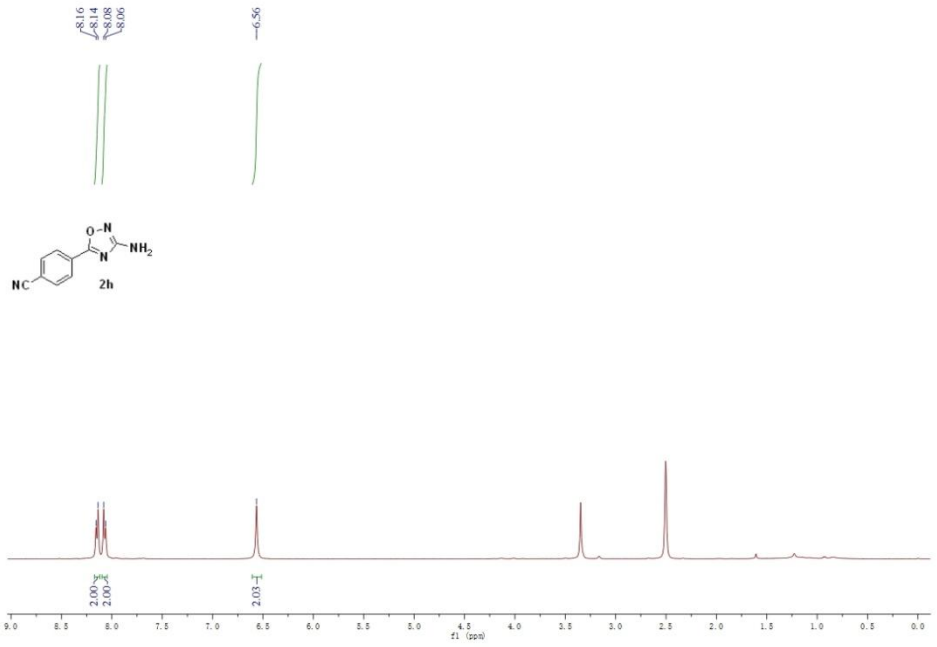
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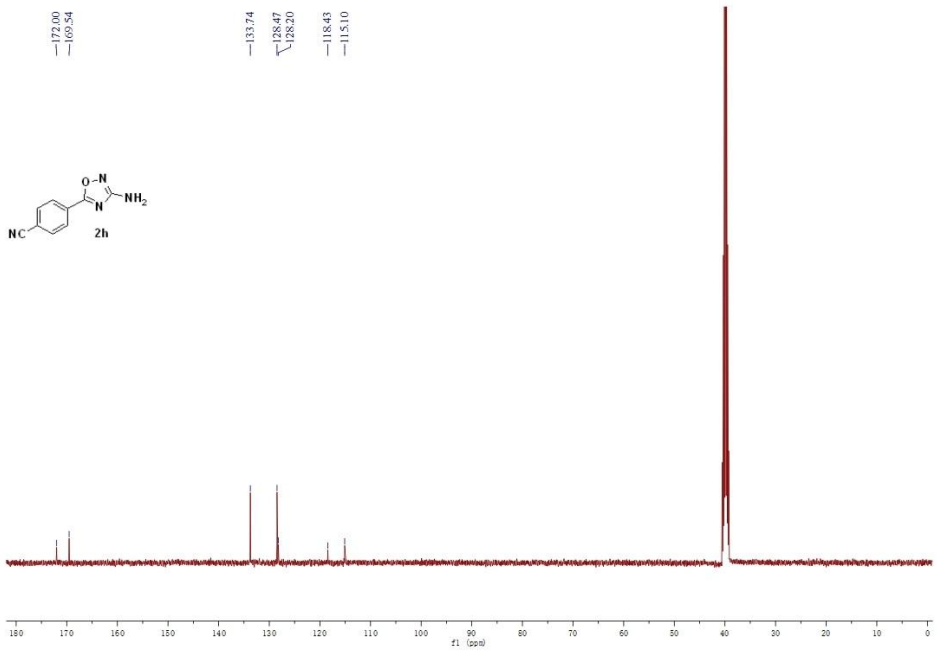
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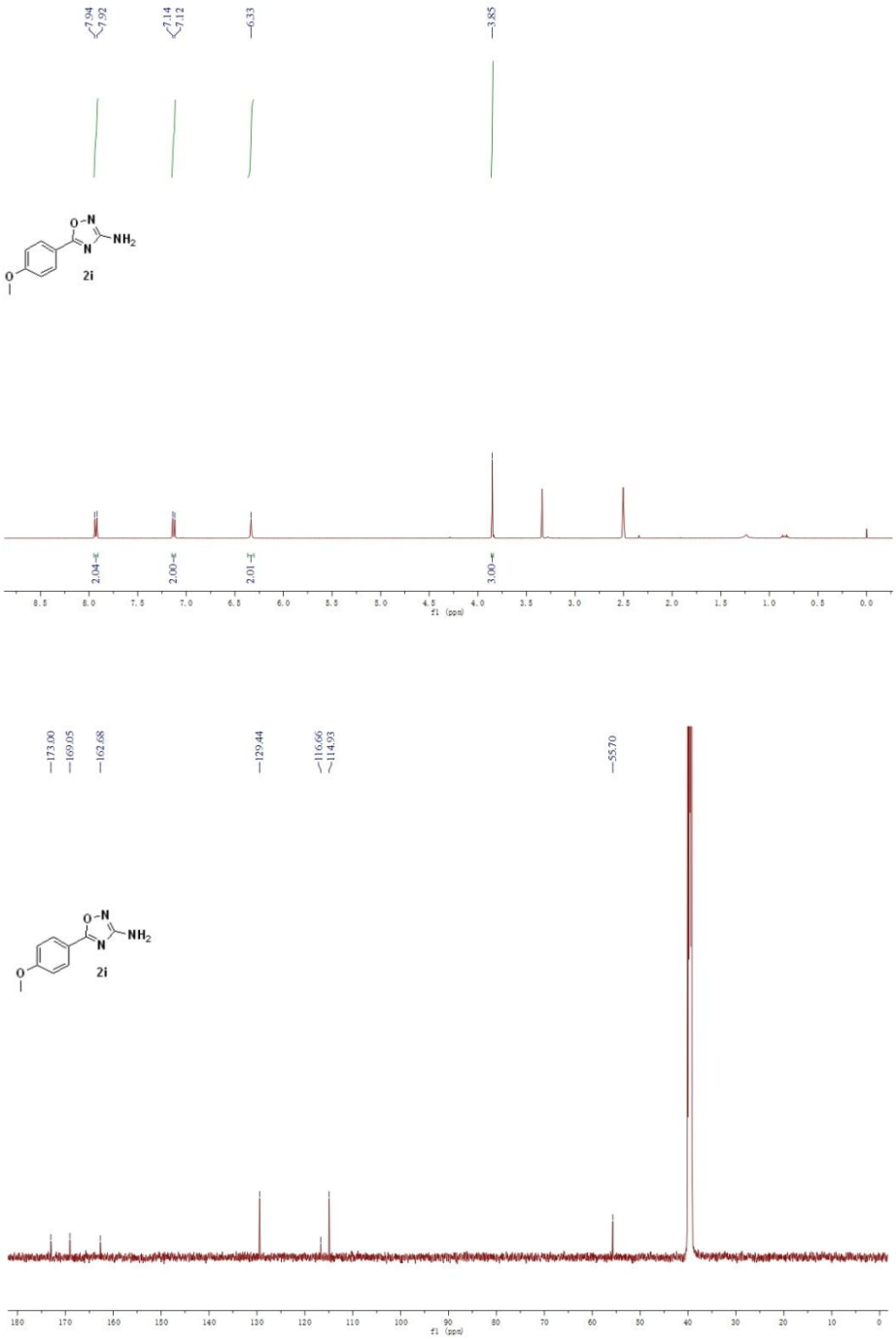
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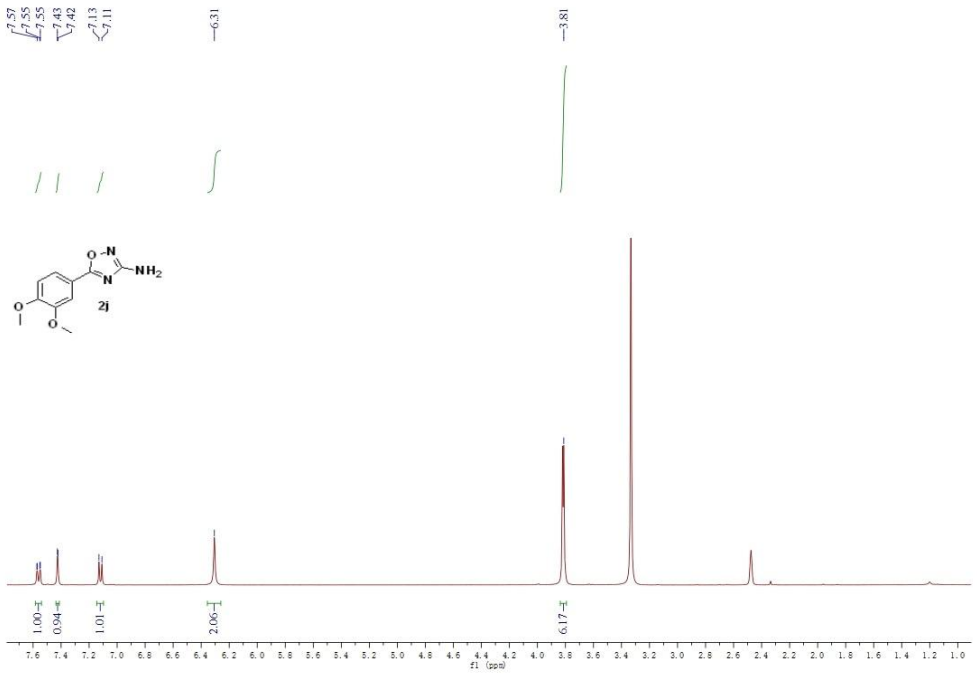
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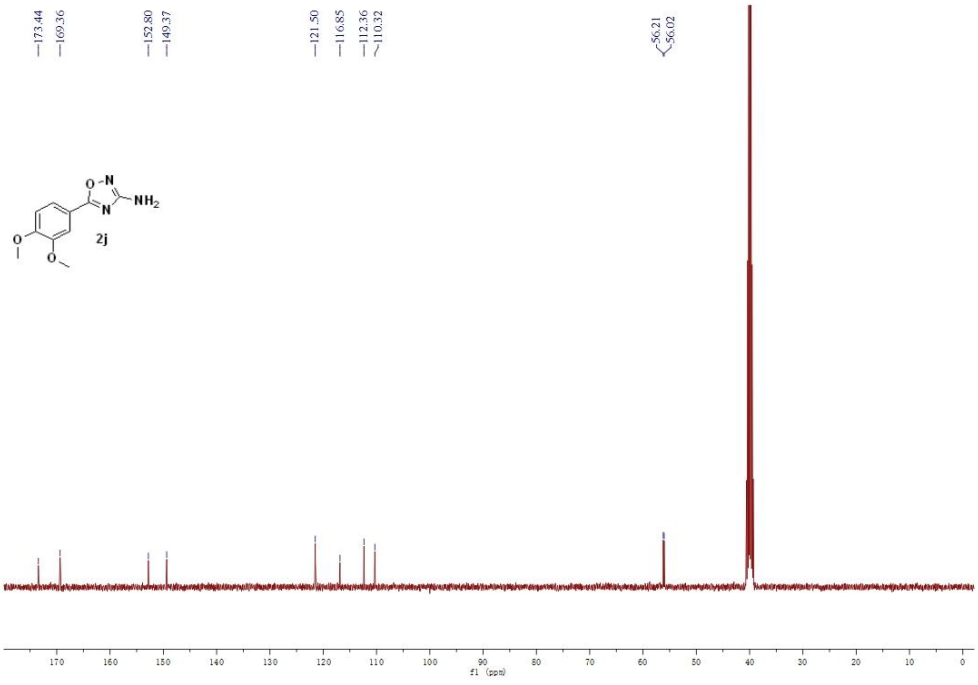
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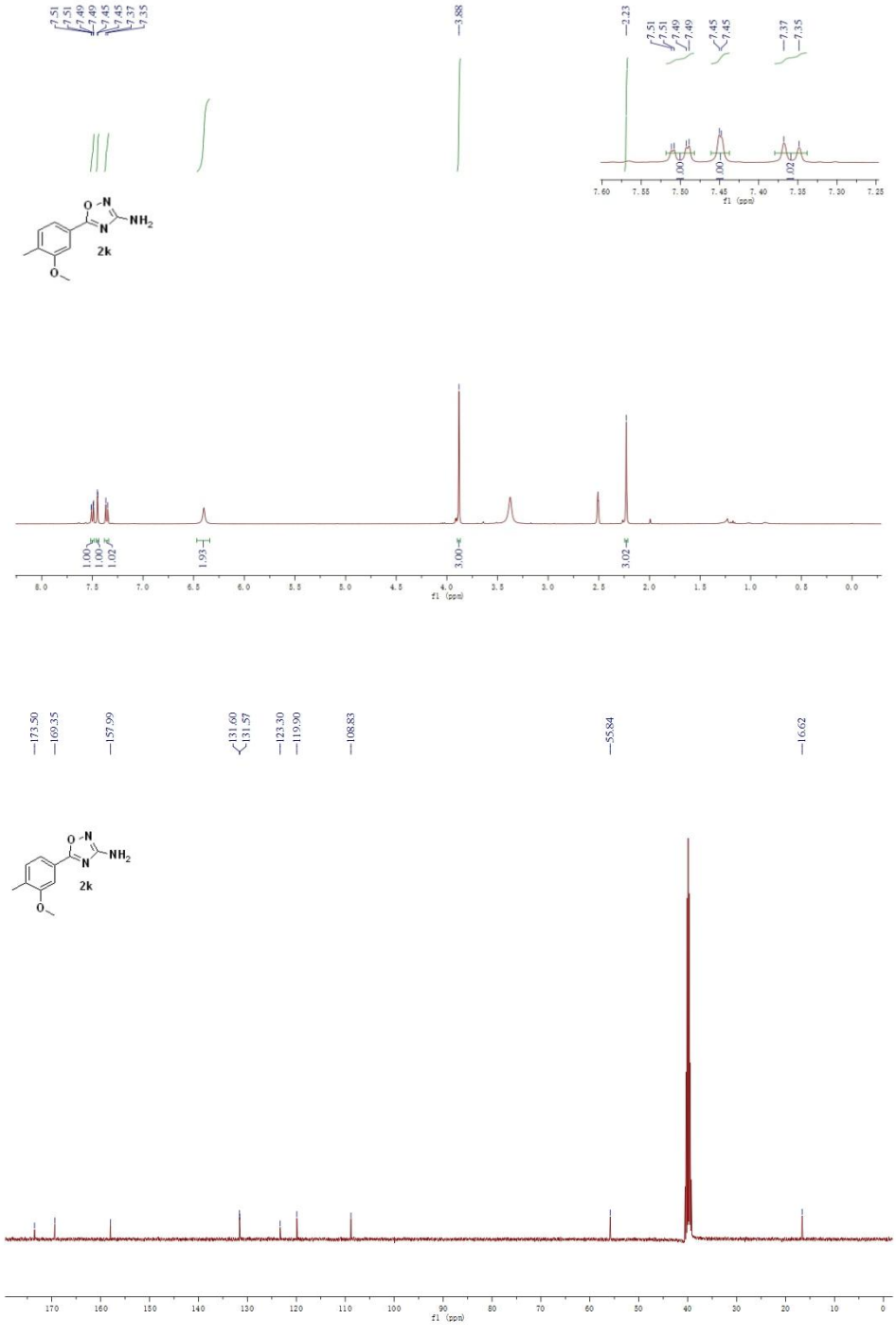
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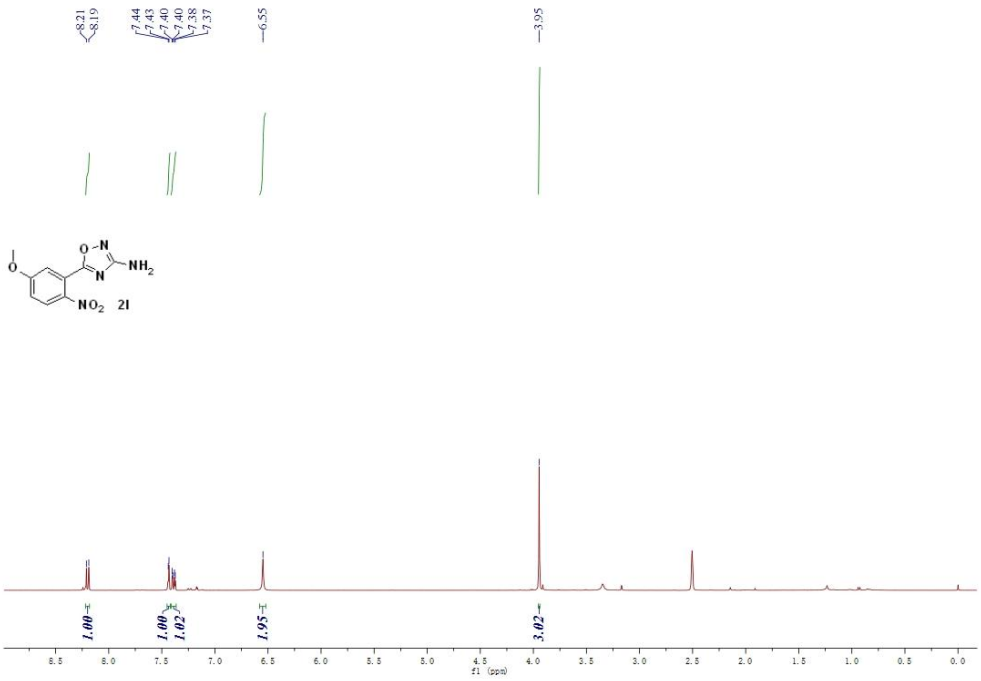
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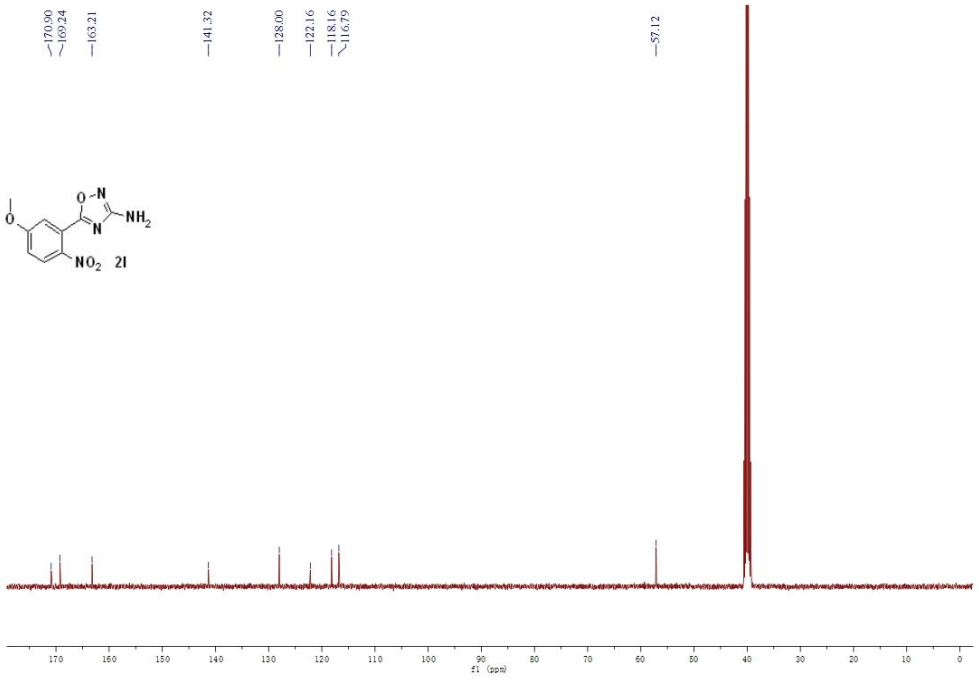
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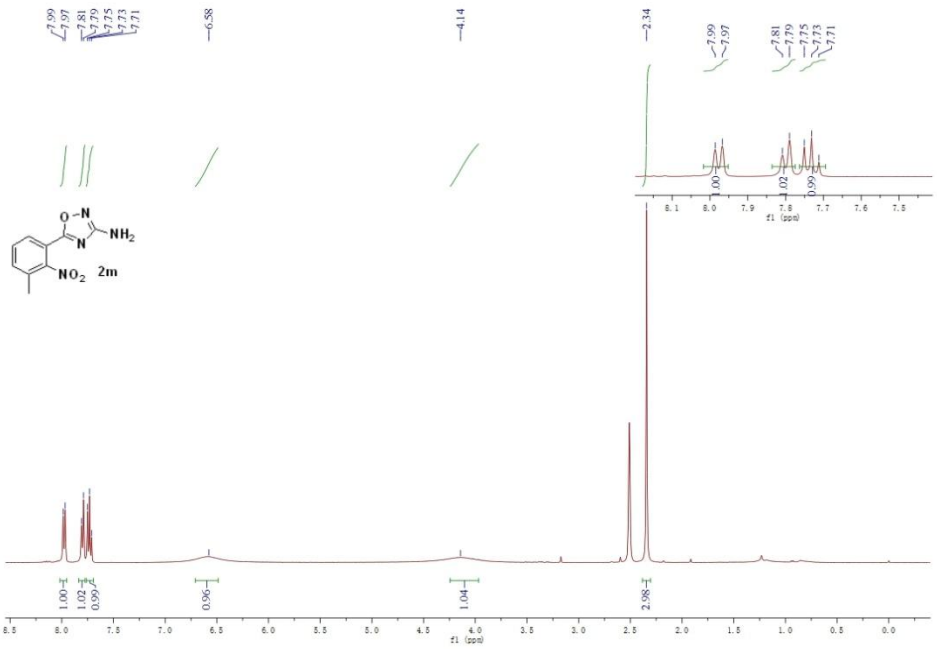
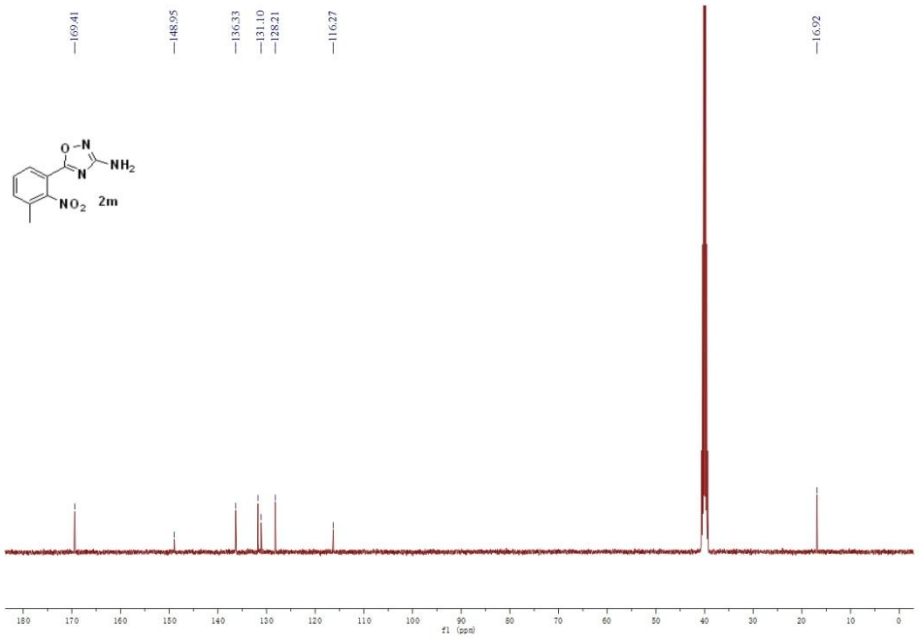
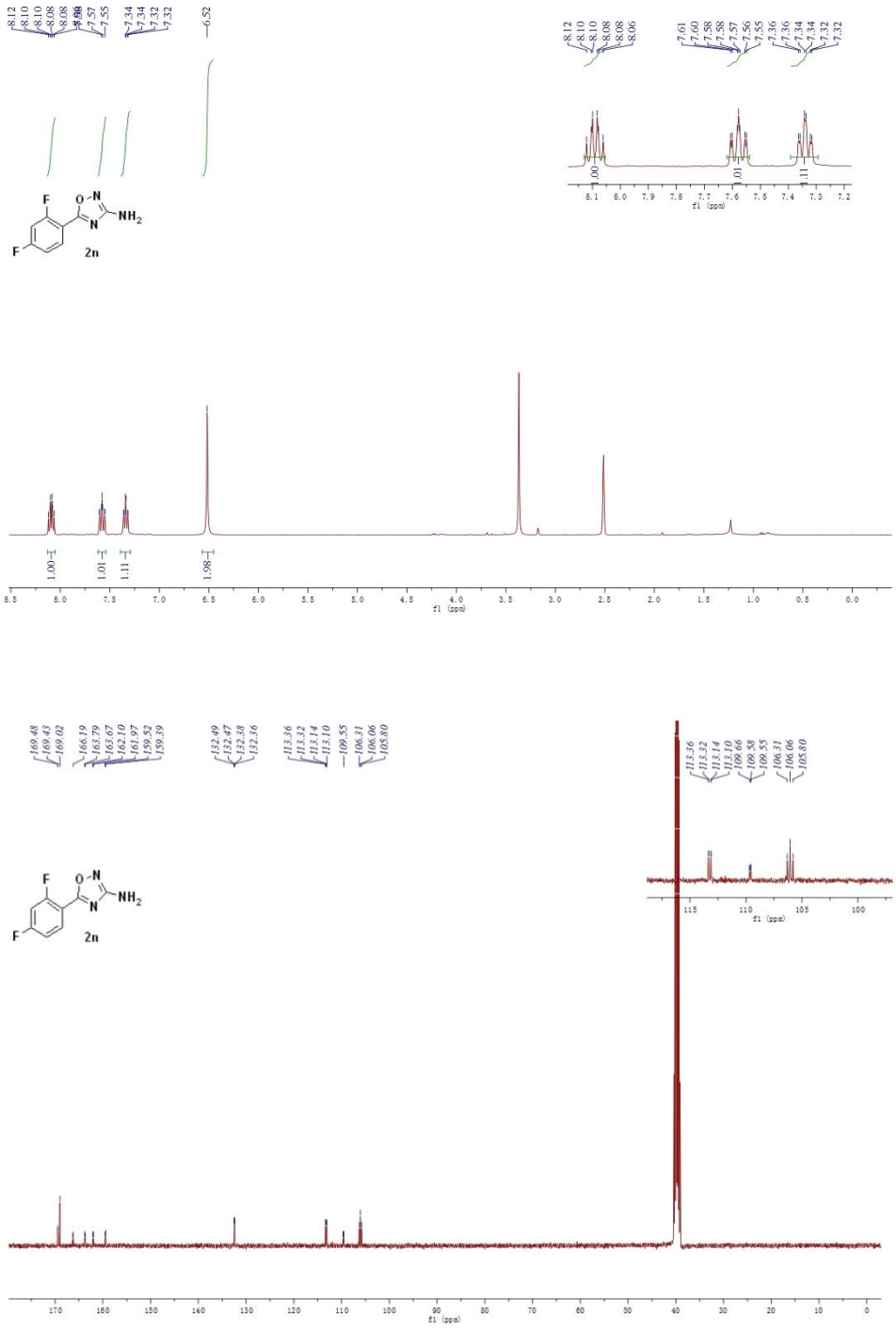
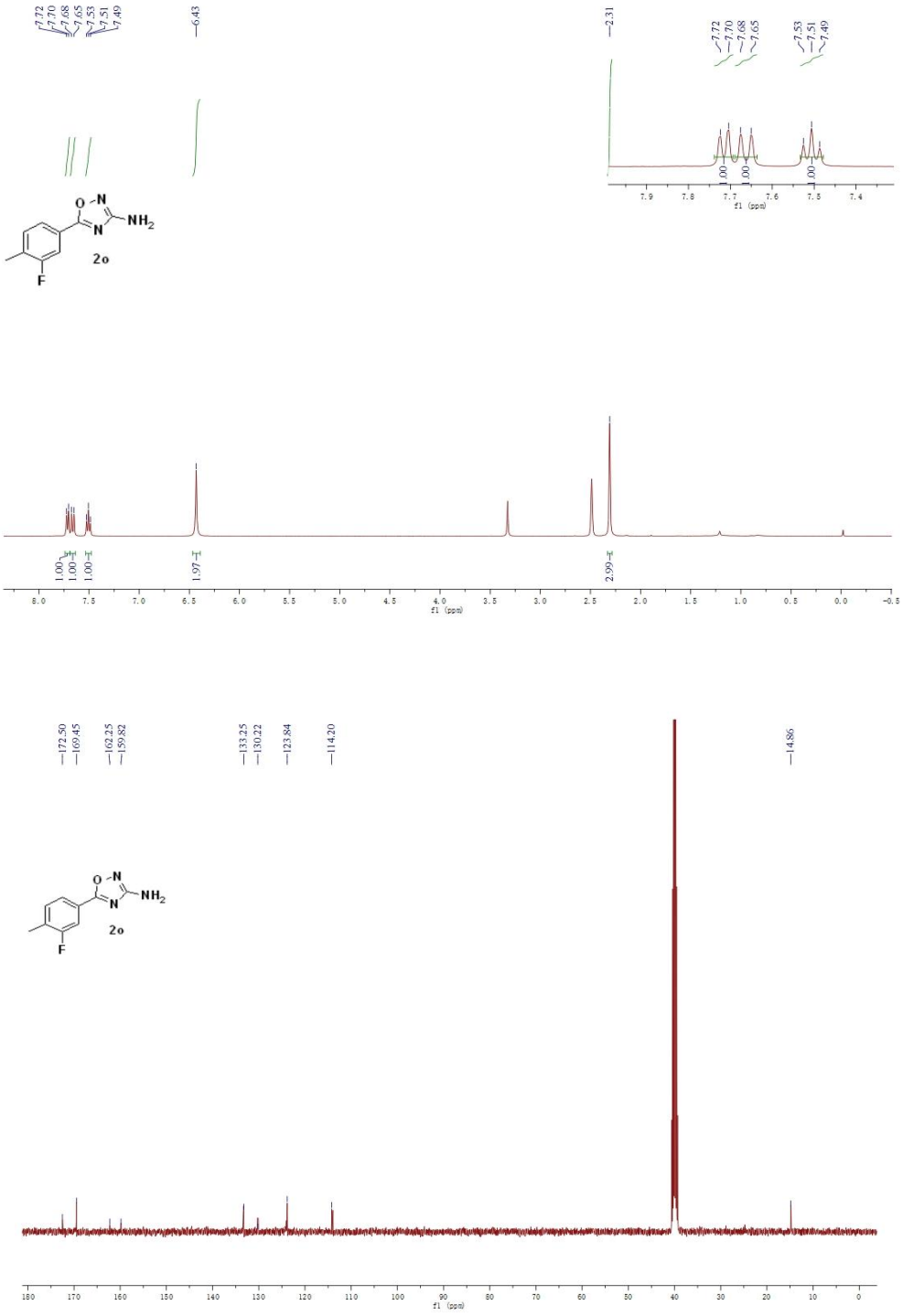
128.00
122.16
118.16
116.79
57.12
NH2
NO2
2l
f1 (ppm)

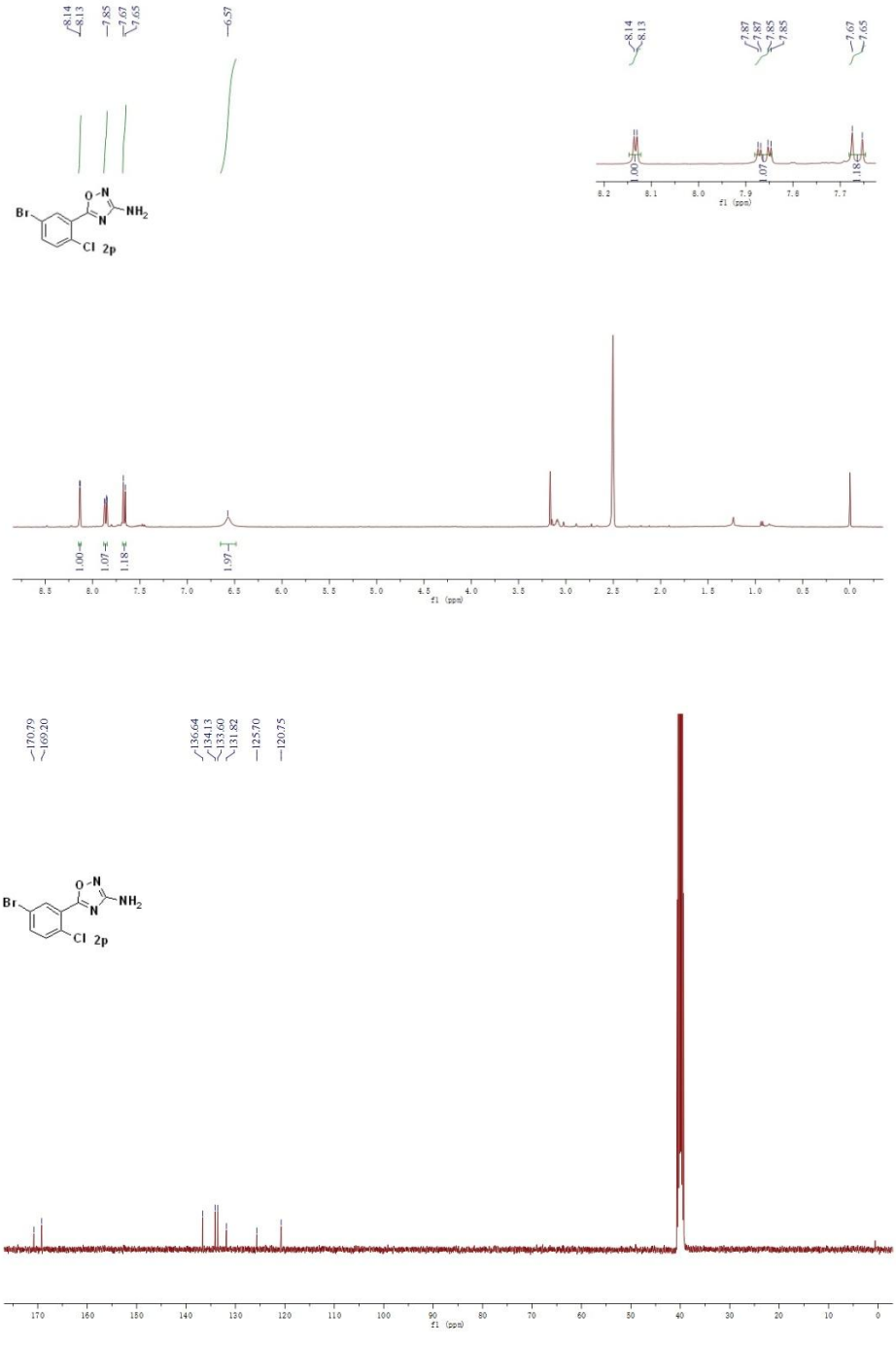

7.99
7.97
7.81
7.79
7.75
7.73
7.71
6.58
4.14
2.34
NH2
NO2
2m
1.00
1.02
0.99
0.96
1.04
2.98
f1 (ppm)

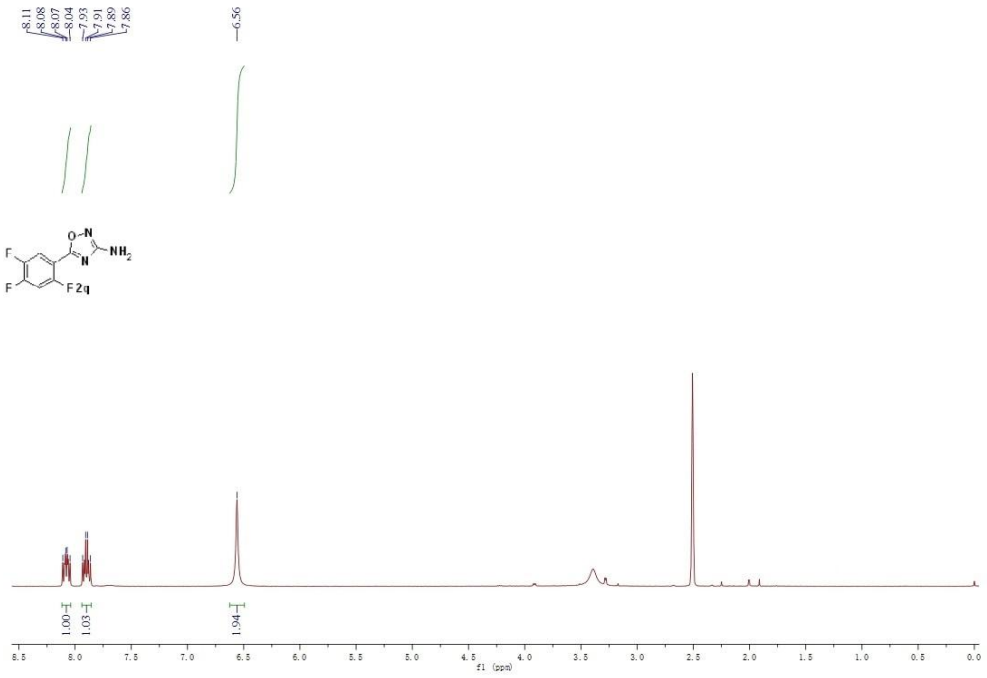

169.41
148.95
136.33
131.10
128.21
116.27
16.92
NH2
NO2
2m
f1 (ppm)

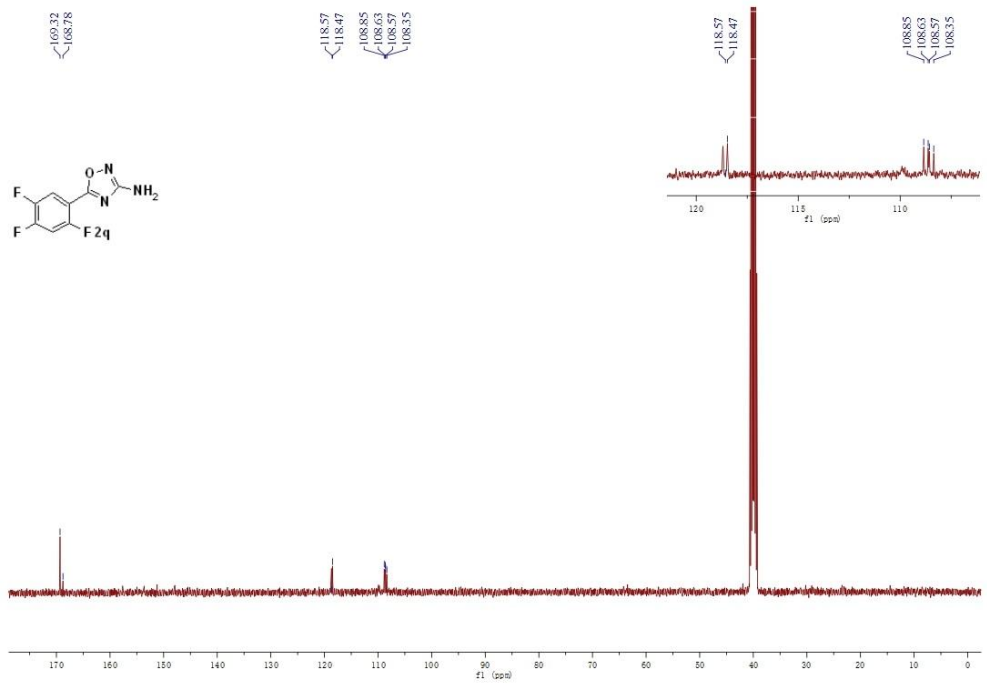

2n
f1 (ppm)

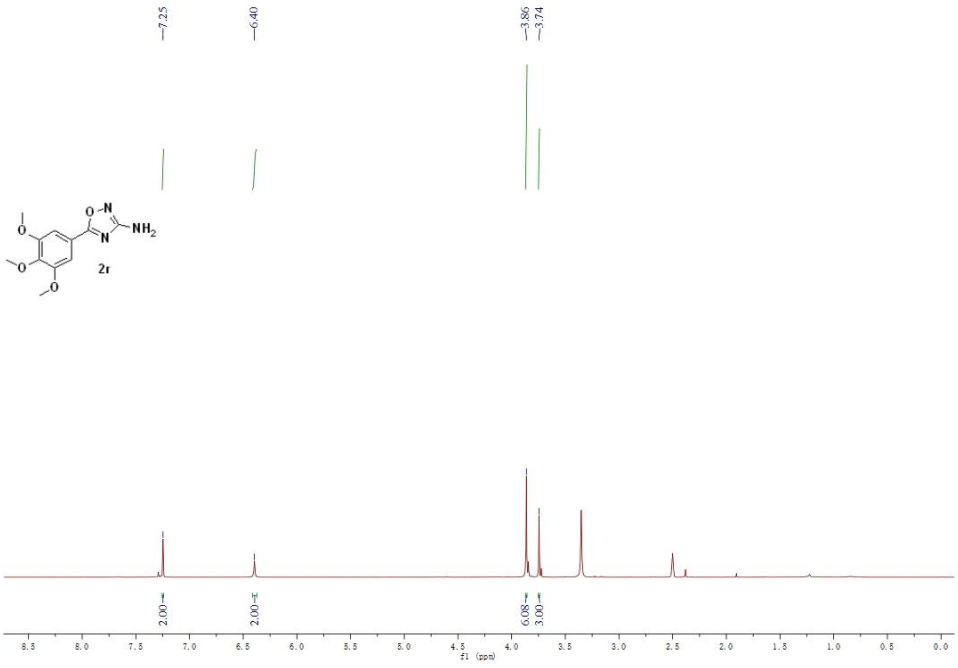

7.72
7.70
7.68
7.65
7.53
7.51
7.49
6.43
2.31
NH2
2o
F
1.00
1.00
1.00
1.97
2.99
f1 (ppm)

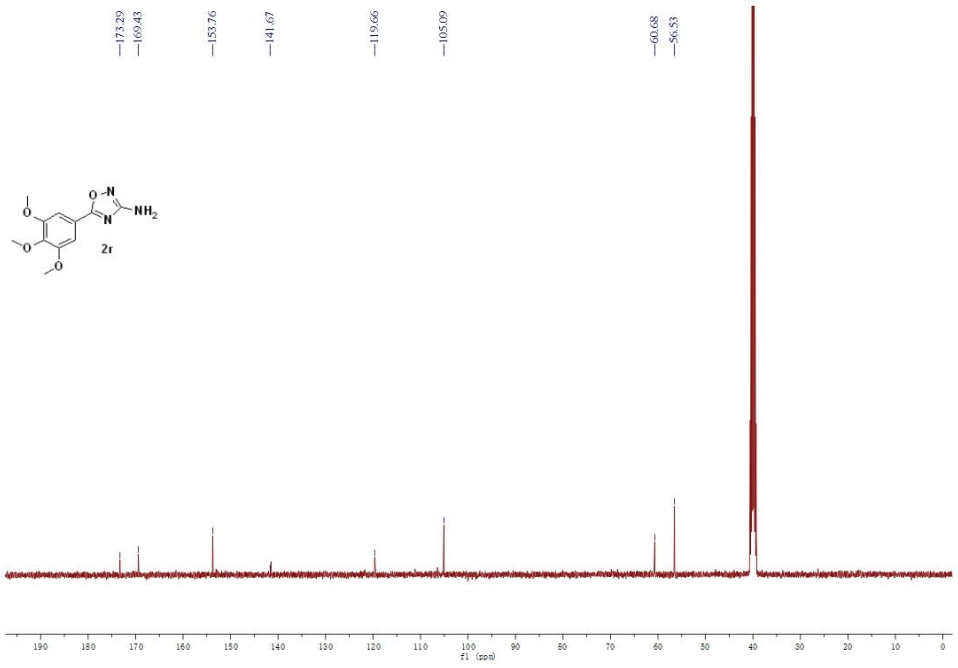
172.50
169.45
162.25
159.82
133.25
130.22
123.84
114.20
14.86
NH2
2o
F
f1 (ppm)

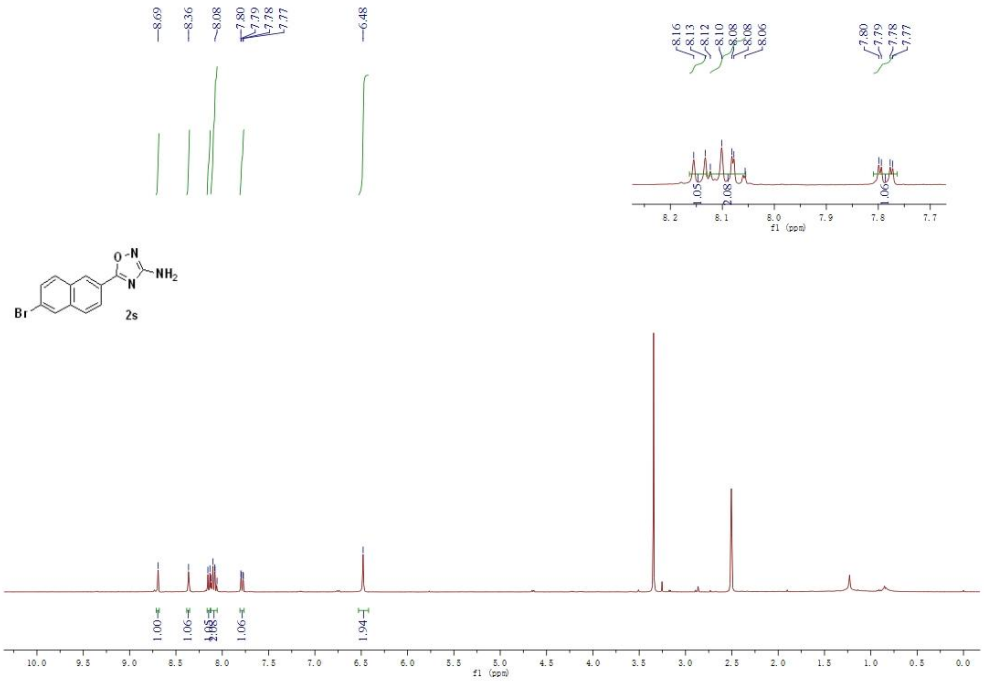

8.14
8.13
7.85
7.67
7.65
6.57
Br
Cl
NH2
2p
1.00
1.07
1.18
1.97
f1 (ppm)
170.79
169.20
136.64
134.13
133.60
131.82
125.70
120.75

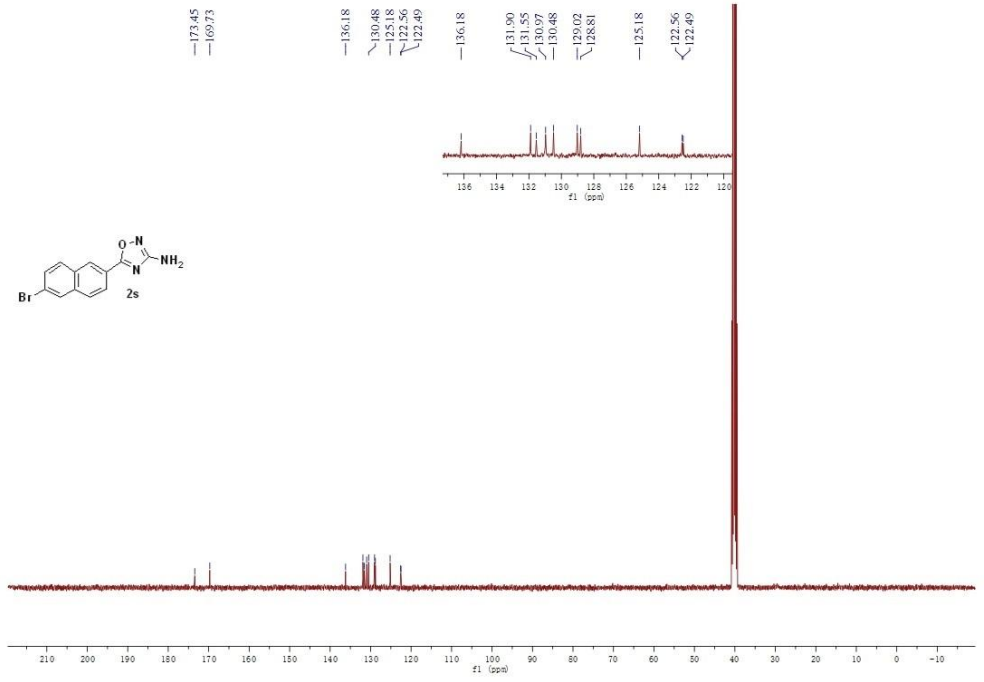

8.11
8.08
8.07
8.04
7.93
7.91
7.89
7.86
6.56
F
F
F 2q
1.00
1.03
1.94
f1 (ppm)

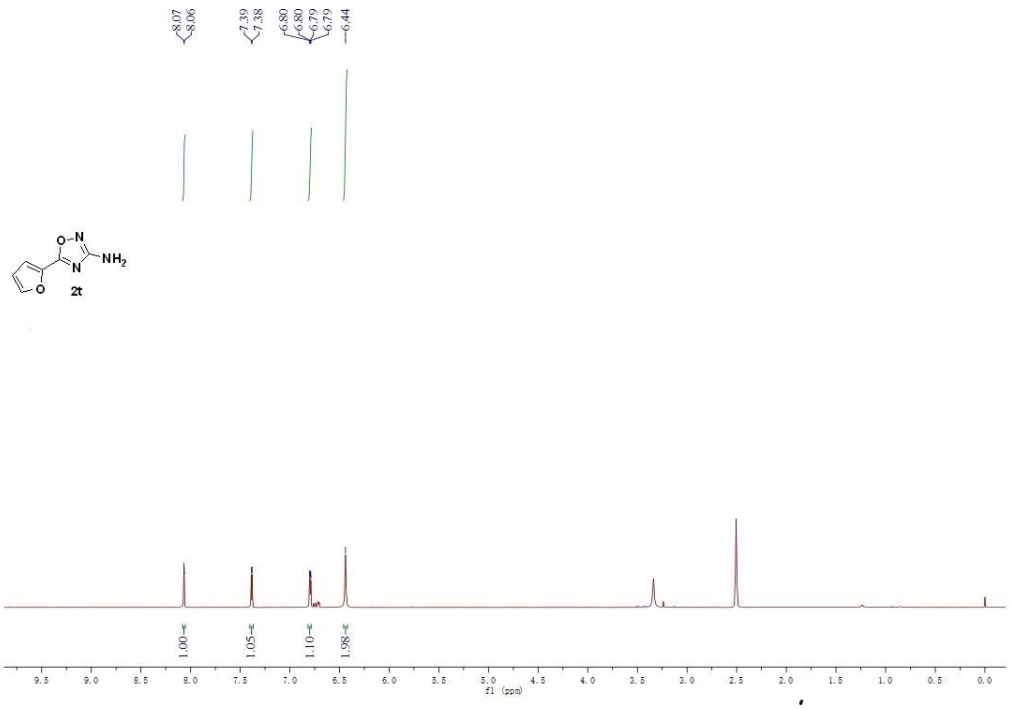

169.32
168.78
118.57
118.47
108.85
108.63
108.57
108.35
F
F
F 2q
f1 (ppm)

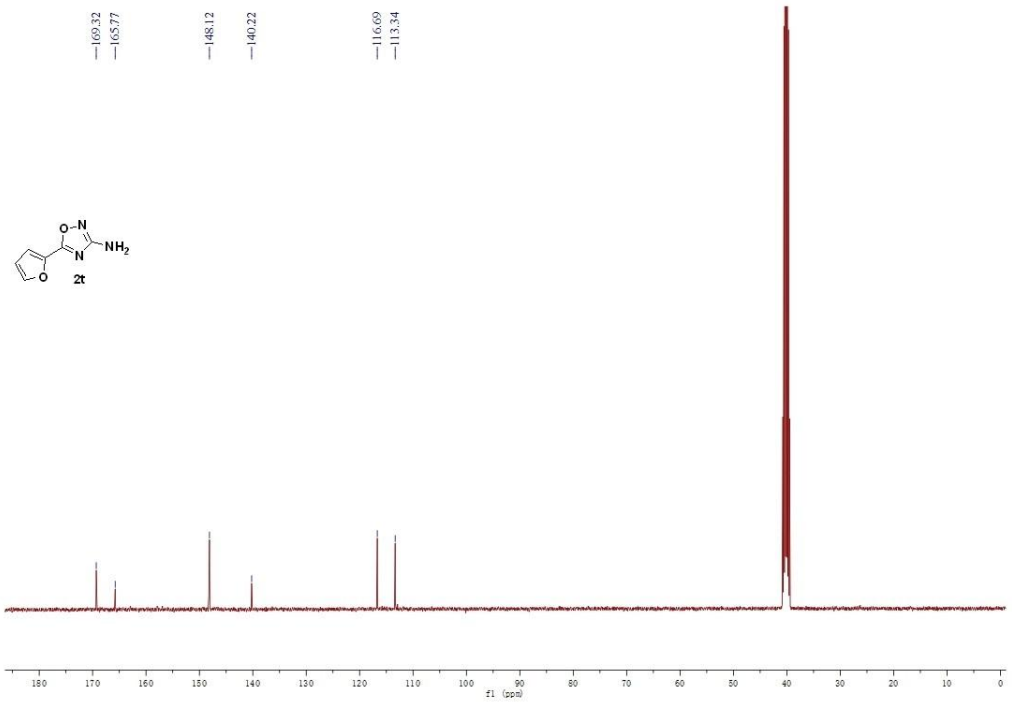

7.25
6.40
3.86
3.74
2r
2.00
2.00
6.08
3.00
f1 (ppm)

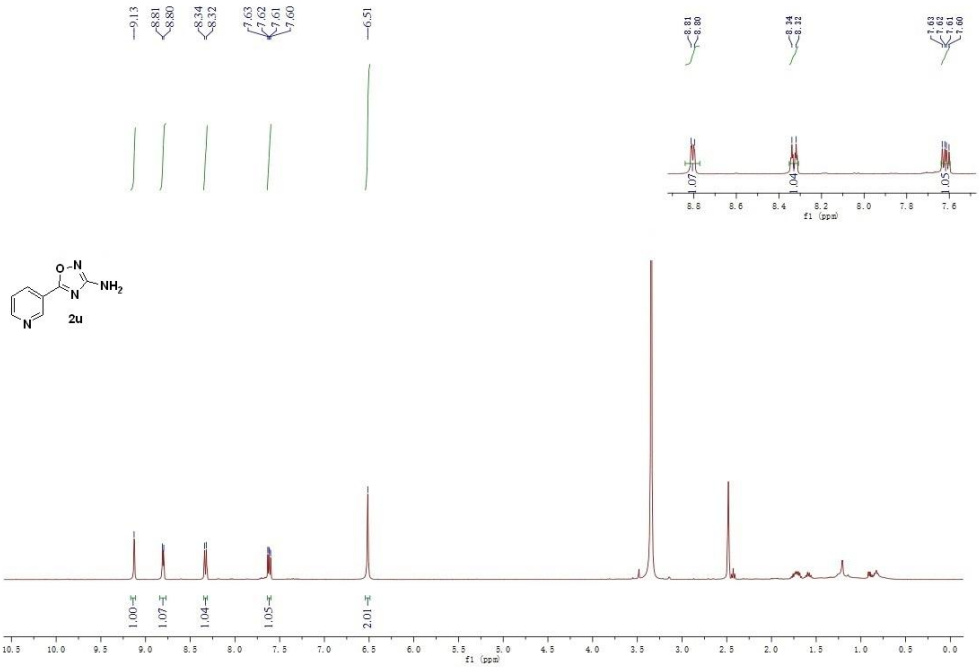

173.29
169.43
153.76
141.67
119.66
105.09
60.68
56.53
2r
f1 (ppm)

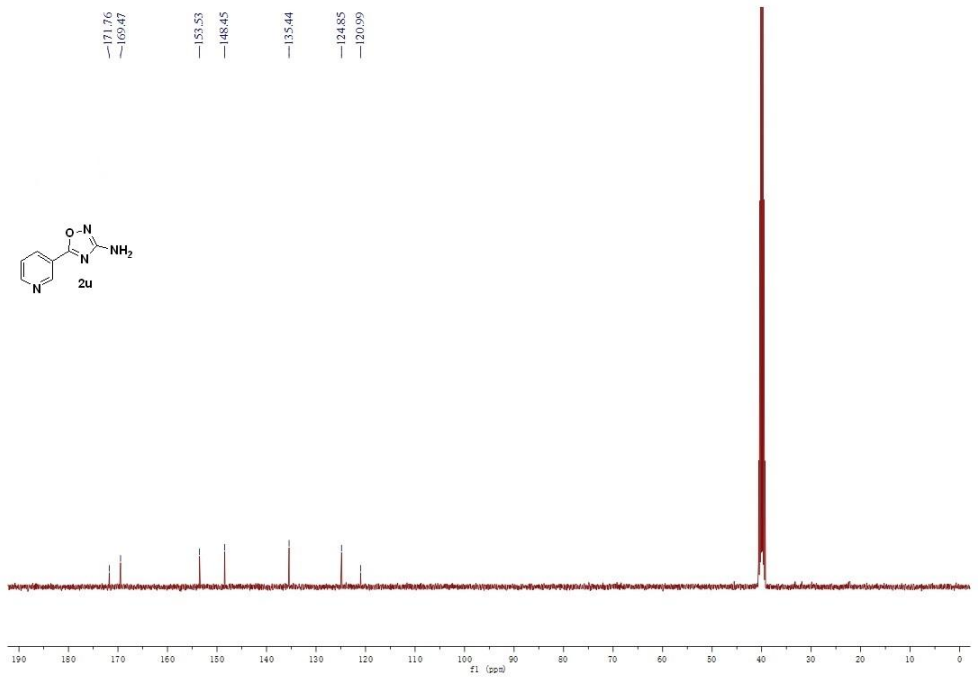

8.69
8.36
8.08
7.80
7.79
7.78
7.77
6.48
8.16
8.13
8.12
8.10
8.08
8.08
8.06
7.80
7.79
7.78
7.77
1.05
2.08
1.06
f1 (ppm)
Br
NH2
2s
1.00
1.06
2.08
1.06
1.94
f1 (ppm)

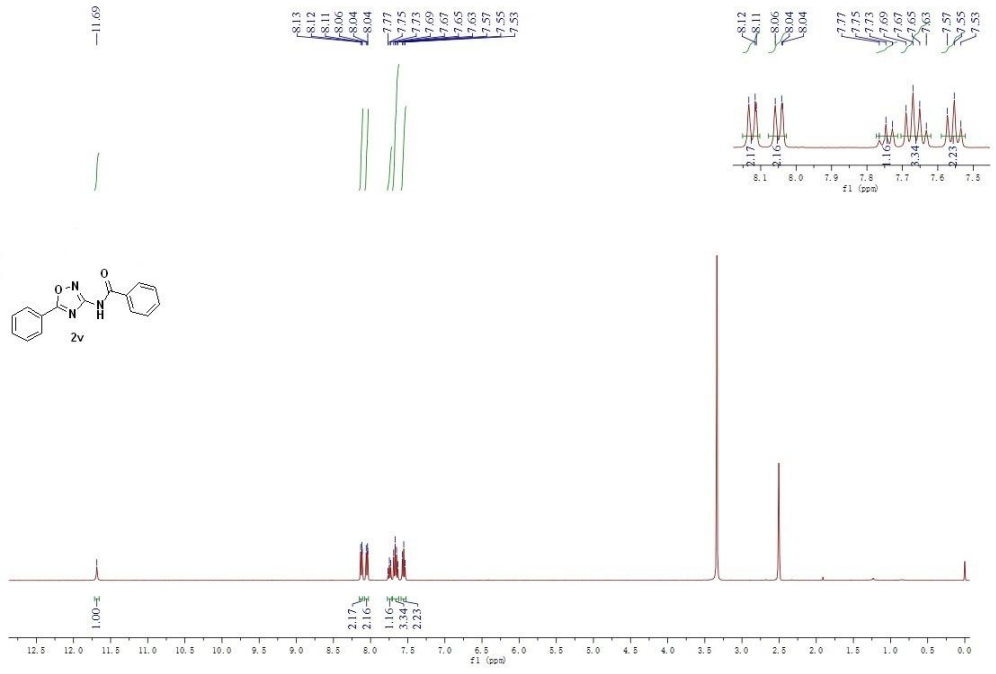

173.45
169.73
136.18
130.48
125.18
122.56
122.49
136.18
131.90
131.55
130.97
130.48
129.02
128.81
125.18
122.56
122.49
f1 (ppm)
Br
NH2
2s
f1 (ppm)

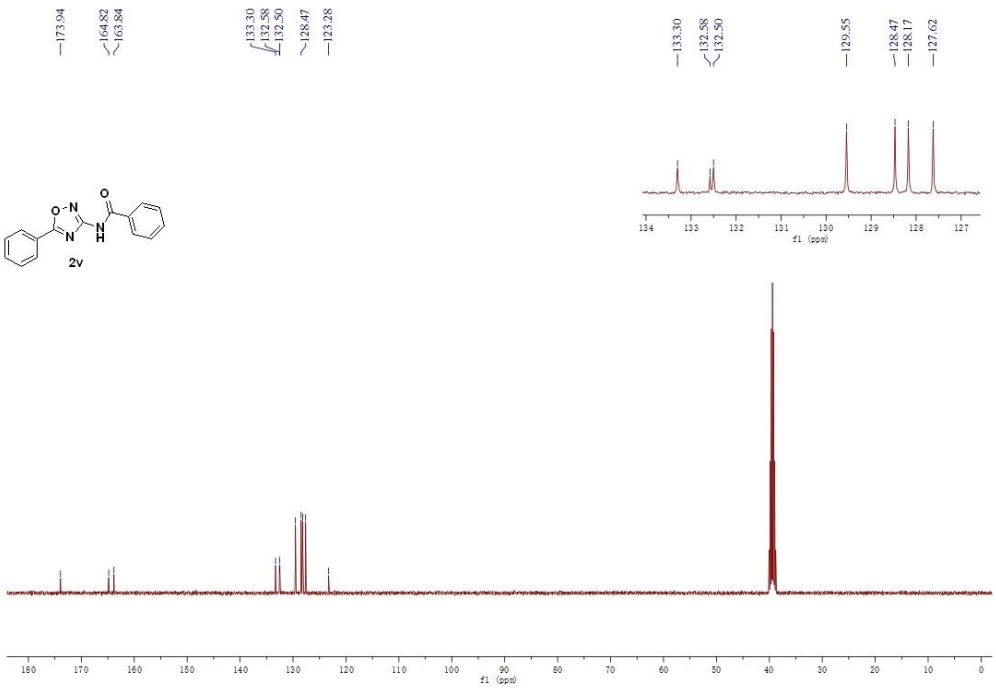

8.07
8.06
7.39
7.38
6.80
6.80
6.79
6.79
6.44
O
N
N
NH2
O
2t
1.00
1.05
1.10
1.98
f1 (ppm)

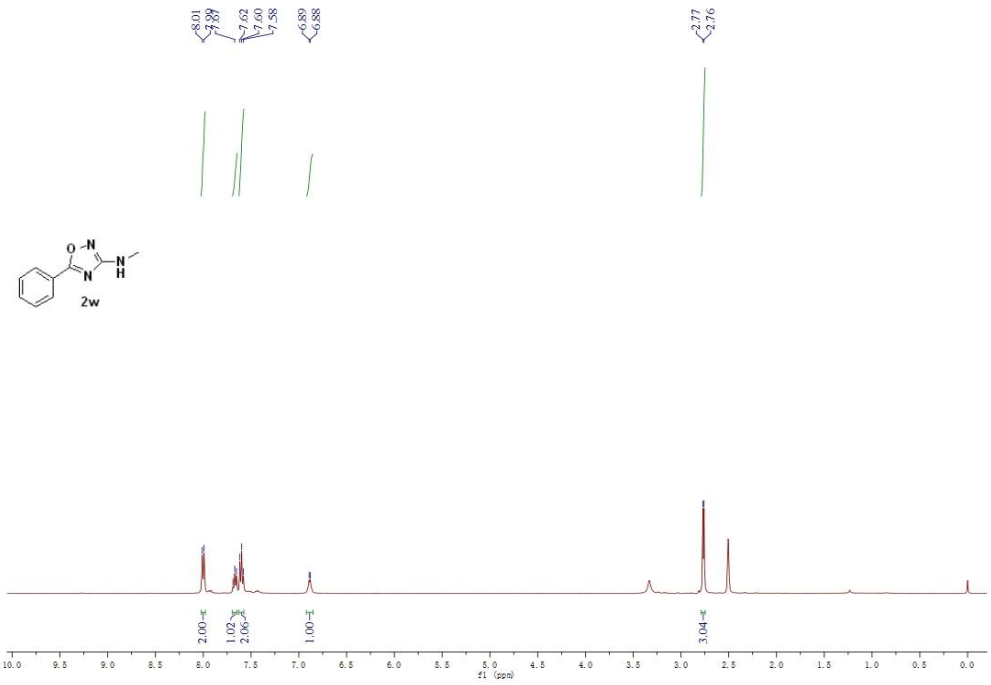

169.32
165.77
148.12
140.22
116.69
113.34
O
N
N
NH2
O
2t
f1 (ppm)

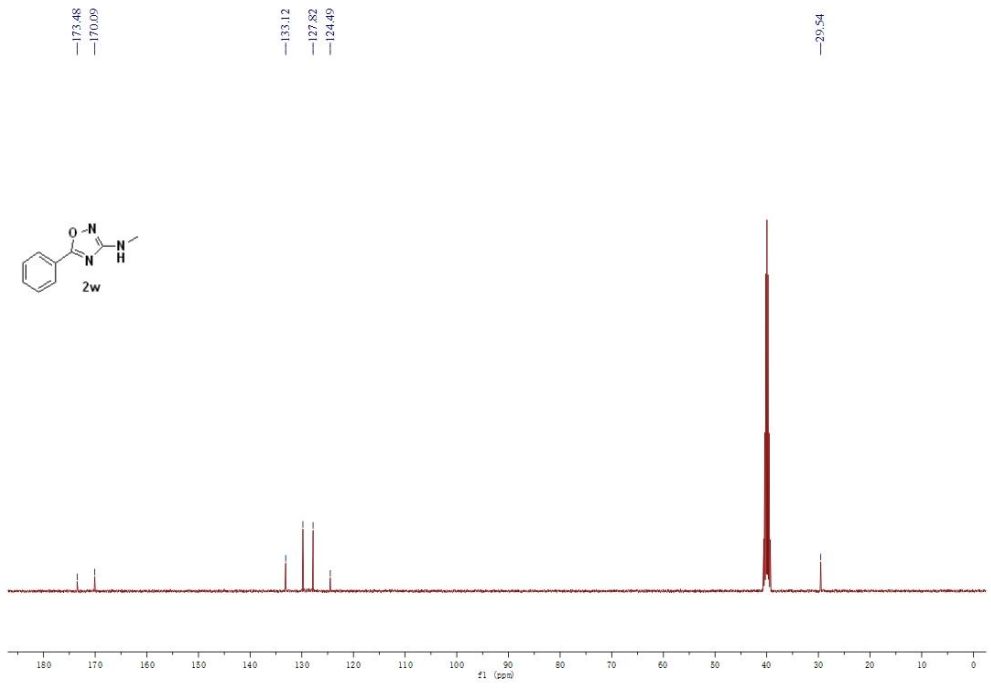

9.13
8.81
8.80
8.34
8.32
7.63
7.62
7.61
7.60
6.51
NH2
2u
1.00
1.07
1.04
1.05
2.01
f1 (ppm)

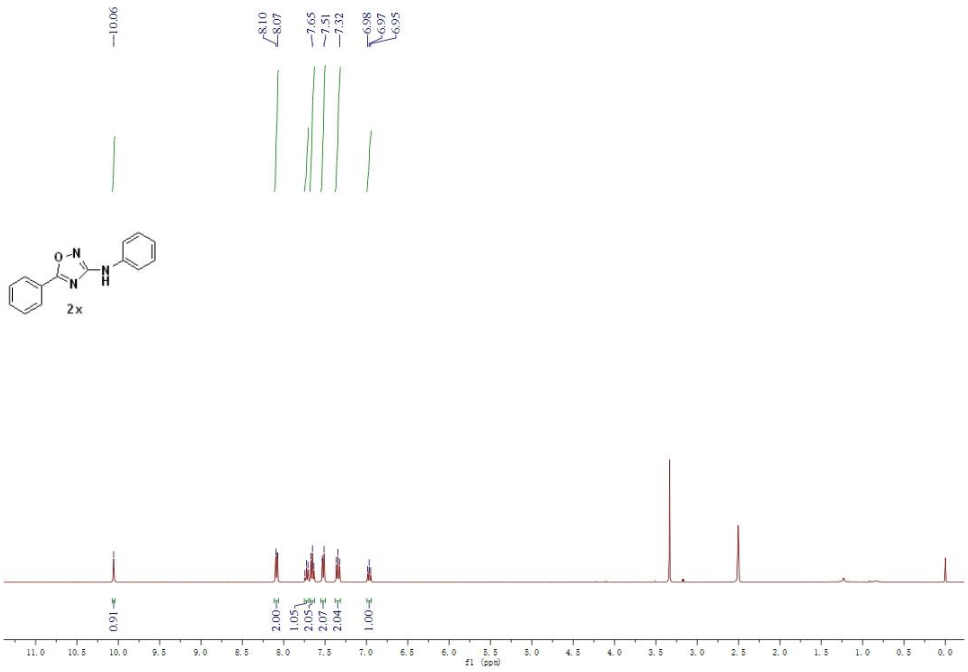

171.76
169.47
153.53
148.45
135.44
124.85
120.99
NH2
2u
f1 (ppm)

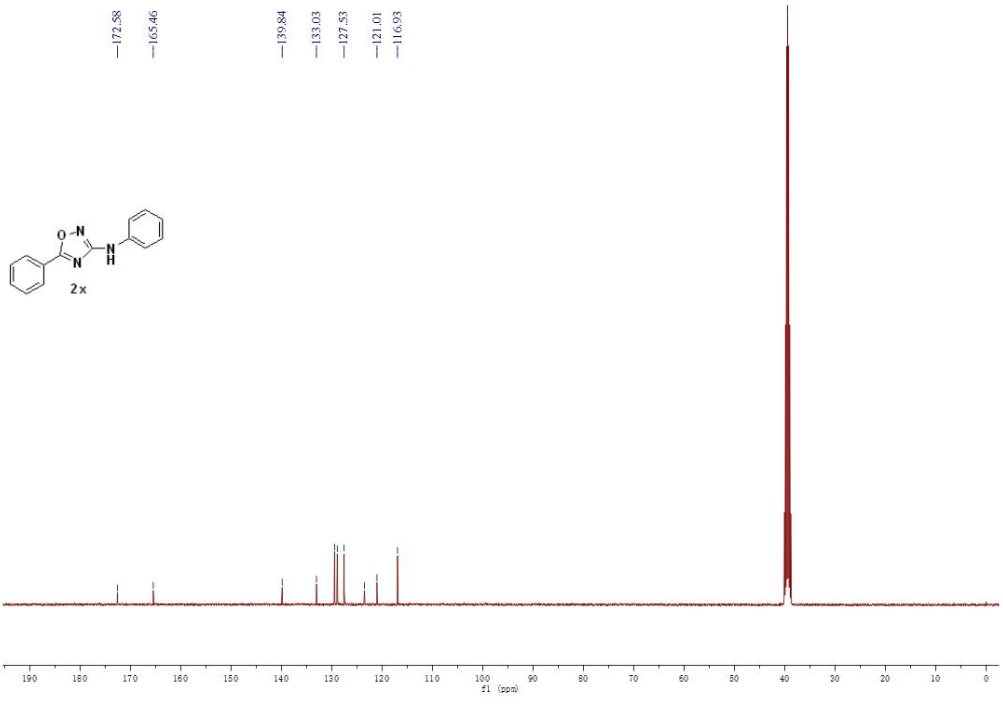

11.69
8.13
8.12
8.11
8.06
8.04
8.04
7.77
7.75
7.73
7.69
7.67
7.65
7.63
7.57
7.55
7.53
2v
1.00
2.17
2.16
1.16
3.34
2.23
f1 (ppm)

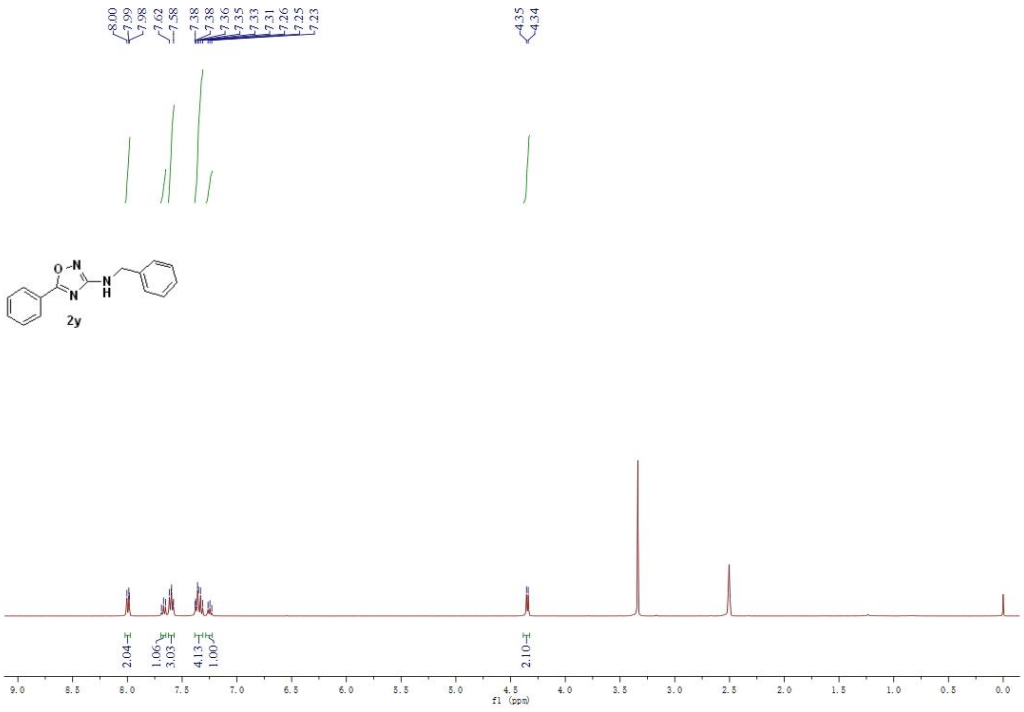

173.94
164.82
163.84
133.30
132.58
132.50
128.47
123.28
129.55
128.47
128.17
127.62
2v
f1 (ppm)

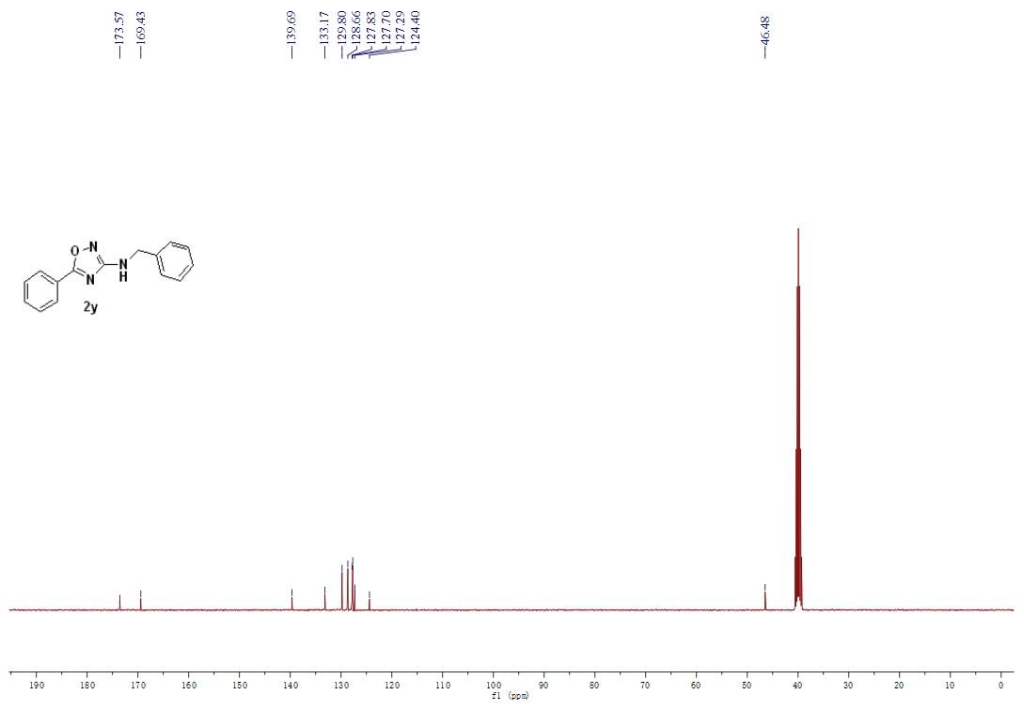

8.01
7.99
7.89
7.62
7.60
7.58
6.89
6.88
2.77
2.76
2w
2.00
1.02
2.06
1.00
3.04
f1 (ppm)


173.48
170.09
133.12
127.82
124.49
29.54
2w
f1 (ppm)


10.06
8.10
8.07
7.65
7.51
7.32
6.98
6.97
6.95
2x
0.91
2.00
1.05
2.05
2.07
2.04
1.00
f1 (ppm)


172.58
165.46
139.84
133.03
127.53
121.01
116.93
2x
f1 (ppm)


8.00
7.99
7.98
7.62
7.58
7.38
7.38
7.36
7.35
7.33
7.31
7.26
7.25
7.23
4.35
4.34
2y
2.04
1.06
3.03
4.13
1.00
2.10
f1 (ppm)


173.57
169.43
139.69
133.17
129.80
128.66
127.83
127.70
127.29
124.40
46.48
2y
f1 (ppm)