Electronic Supplementary Information

C−N Cleavage of Secondary Amide to Access Primary Amide by a Co(II)/Oxone Oxidation System

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1. General information

^{1}H-NMR and ^{13}C-NMR were recorded on a BRUKER AVANCE at 500 and 126 MHz, respectively. Chemical shifts (δ) were reported referenced to an internal tetramethylsilane (TMS) standard, the $CDCl_3$ residual peak (δ 7.26), or DMSO-*d6* (2.54) for ^{1}H-NMR. Chemical shifts of ^{13}C-NMR were reported relative to $CDCl_3$ (δ 77.0) or DMSO-*d6* (40.0). Data were reported in the following order: chemical shift (δ) in ppm; multiplicities were indicated s (singlet), bs (broad singlet), d (doublet), t (triplet), m (multiplet); coupling constants (*J*) were in Hz. MS were measured by Agilent 7890/7000D GC-MS (EI, 70 eV). The EPR spectra was recorded on an electron paramagnetic resonance spectrometer (Bruker EMXplus-9.5/12). The HR-MS was determined by a Waters ZQ4000 mass detector. The photoreactor (Model: PR-6) including the light source was purchased from Shanghai Taitan Technology (PR China). Analytical thin-layer chromatography (TLC) was performed on silica gel and visualized with UV light. The purification of organic compounds was carried out by flash chromatography on silica gel (200−300 mesh). The secondary amide substrates were prepared by the well-known condensation of the carboxylic acids and amines in the presence of stoichiometric EDCI and DMAP according to literature methods. All the secondary amides and primary amides were all known compounds and the characterization data were consistent with previous reports. Unless otherwise noted, other commercially available reagents and solvents with analytical grade were purchased from Adamas-beta (P. R. China) and used without further purification.

2. Experimental section

2.1 General procedure of catalytic reactions

In a clean test tube (2.5 cm × 20 cm), secondary amides (0.25 mmol), $Co(OAc)_2$ (2 mol%), and $NaHCO_3$ (3 equiv.) were added to the mixed solvent of $MeCN/H_2O$ (v/v = 1/1, 4 mL). After the addition of the oxidant (Oxone, 4 equiv.) in one batch, the tube was equipped with a balloon of air (atmospheric pressure) and the mixture was continuously stirred at 60°C. Monitoring the reaction by TLC. After the reaction was completed, the mixture was extracted by ethyl acetate (EtOAc) for 4 times and the combined organic phase was evaporated and purified by silicon column with EtOAc/petroleum ether (PE) as the eluents.

2.2 Procedure of the reaction under UV-light (Scheme 2d)

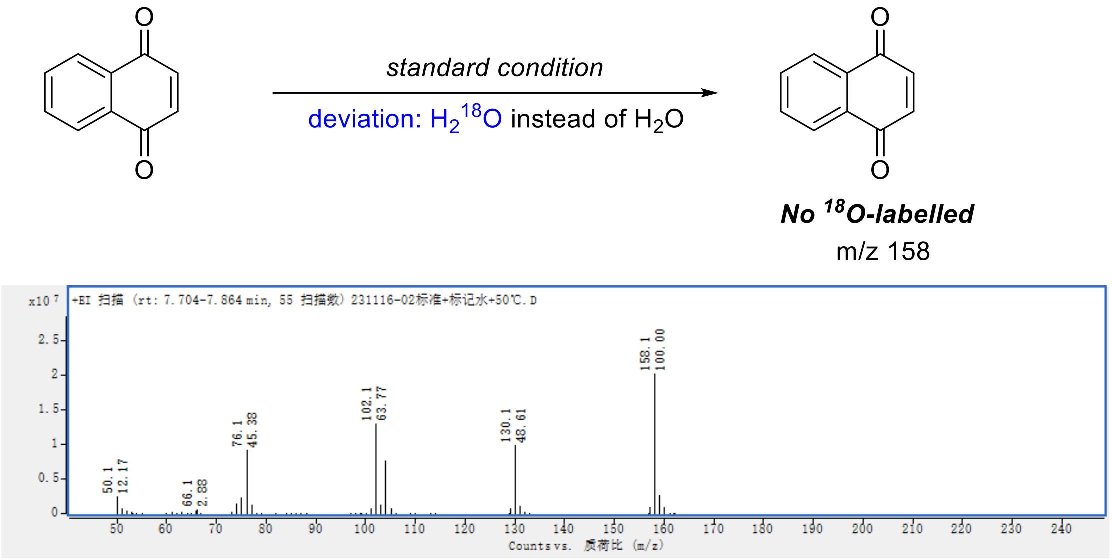
In a clean test tube (2.5 cm × 20 cm), **a1** (0.25 mmol), and $NaHCO_3$ (with or without, 3 equiv.) were added to the mixed solvent of $MeCN/H_2O$ (v/v = 1/1, 4 mL). After the addition of H_2O_2 (30% aq., 4 equiv.) in one batch, the tube was equipped with a balloon of air (atmospheric pressure) and the mixture was continuously stirred under purple light irradiation (365 nm) at 50°C. Monitoring the reaction by TLC. Almost no desirable products were found after 6 h.

2.3 Procedure of ^{18}O-Isotopical Labeling Experiments (Scheme 2e and 2f)

In a clean and dry test tube (2.5 cm × 20 cm), substrate (**a24** or **c24**, 0.12 mmol), $Co(OAc)_2$ (2 mol%), and $NaHCO_3$ (3 equiv.) were added to the mixed solvent of anhydrous $MeCN/H_2{}^{18}O$ (v/v = 1/1, 2 mL). After the addition of the oxidant (Oxone, 4 equiv.) in one batch, the tube was equipped with a balloon of air (atmospheric pressure) and the mixture was continuously stirred at 60°C for 6 h. After the reaction was completed, the mixture was extracted by anhydrous ethyl acetate for 4 times and the combined organic phase was dried with anhydrous Na_2CO_3. The solvent was then filtered and the filtrate was injected into GC-MS for mass analysis.

3. GC-MS spectra

(a) blank experiment



(b) isotope labelling reaction

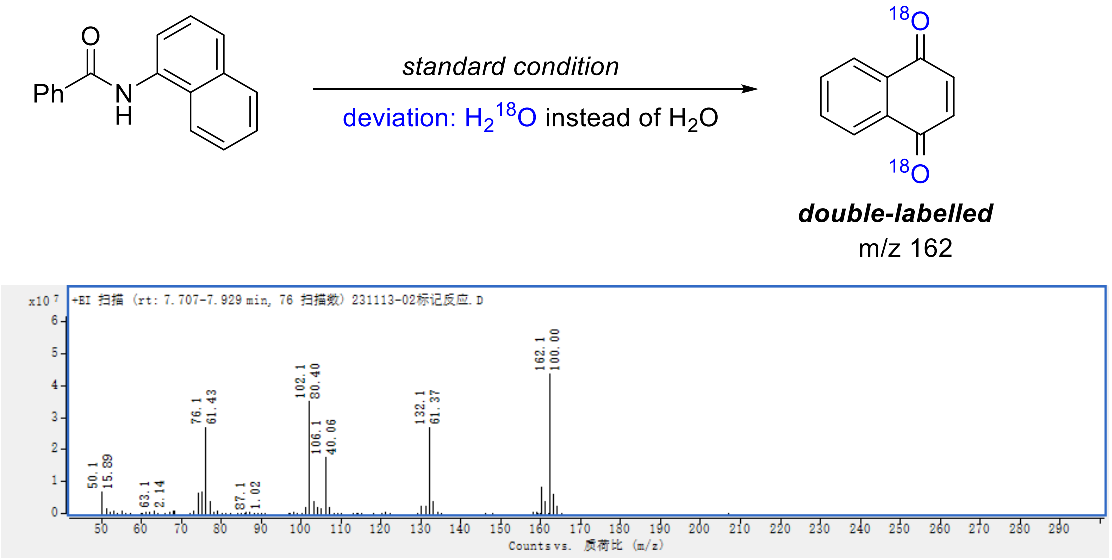


Figure S1. GC-MS spectra of the (a) blank experiment and (b) 18-O labelling experiment.

4. EPR and HR-MS spectra

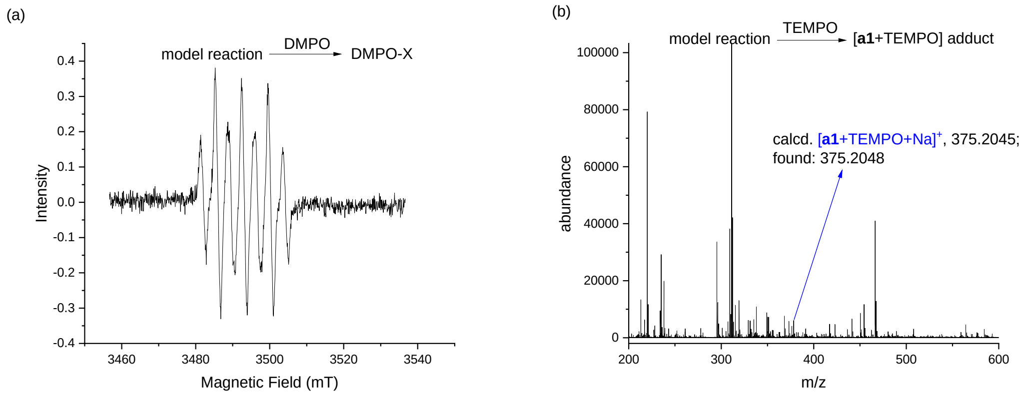


Figure S2. (a) EPR spectra of the model reaction in the presence of spin trapping reagent (test condition: **a1** (10 mM), $NaHCO_3$ (30 mM), $Co(OAc)_2$ (1 mM), Oxone (40 mM), DMPO (50 mM), MeCN-H_2O (v:v = 1:1), 77 K). (b) HR-MS spectra of the model reaction in the presence of radical trapping reagent (reaction condition: **a1** (0.25 mmol), $NaHCO_3$ (0.75 mmol), $Co(OAc)_2$ (0.01 mmol), Oxone (1 mmol), TEMPO (1.5 mmol), MeCN-H_2O (v:v = 1:1), RT).

5. DFT calculation

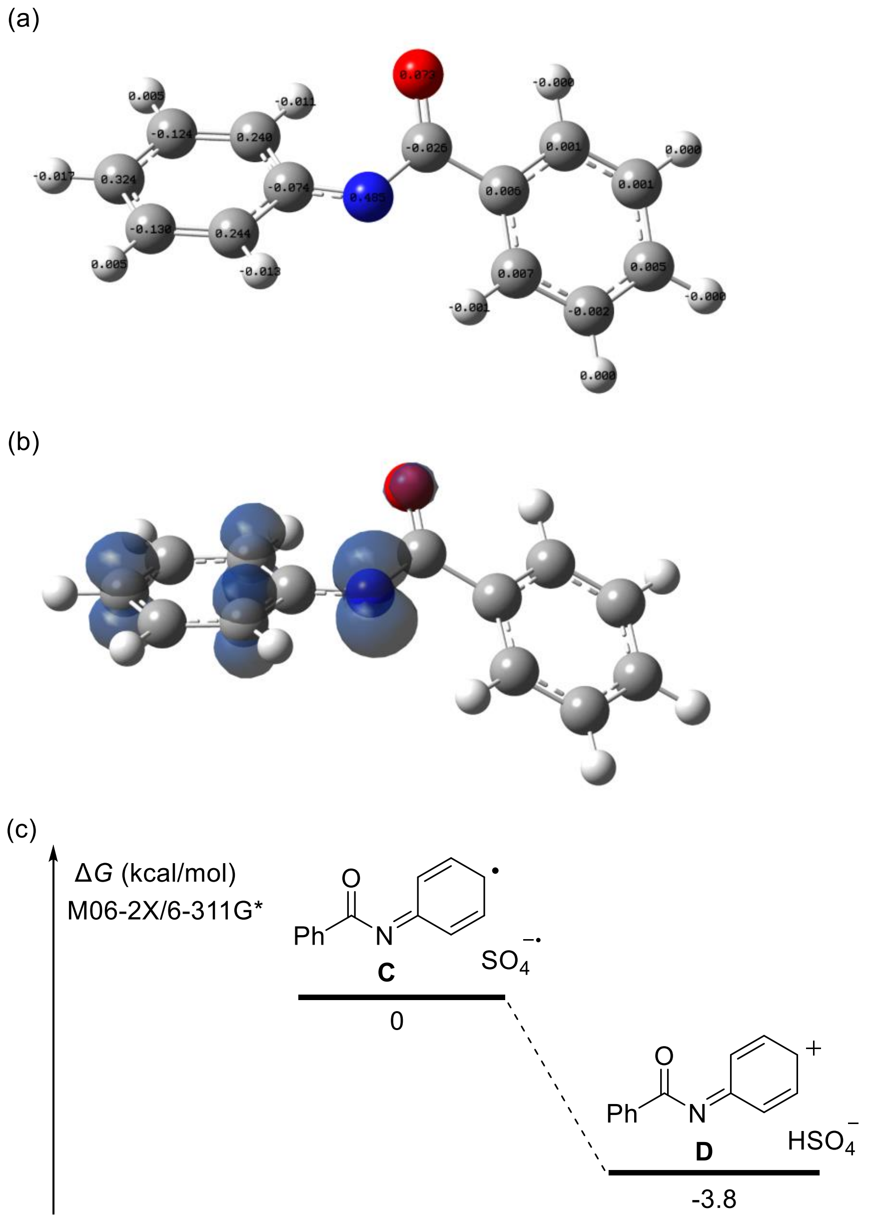
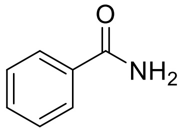


Figure S3. The (a) mulliken spin population and (b) spin density of the proposed intermediate **B** (or **C**), and the relative energy changes of the transformation from the intermediate **C** to **D** after structural optimization.

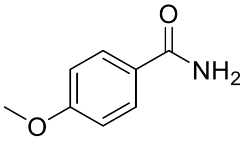
6. Characterization data of products



benzamide (**b1**)[1]

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 7.1 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 6.23 (s, 2H).

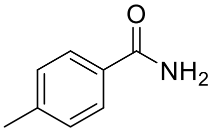
^{13}C NMR (126 MHz, DMSO-d_6) δ 168.39, 134.74, 131.67, 128.66, 127.93.



4-methoxybenzamide **(b2)**[1]

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 5.98 (s, 2H), 3.86 (s, 3H).

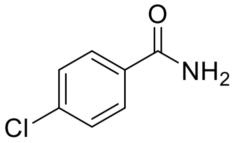
^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.07, 162.69, 129.34, 125.31, 113.83, 55.43.



4-methylbenzamide **(b3)**[1]

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 6.10 (s, 2H), 2.40 (s, 3H).

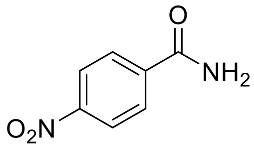
^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.57, 130.38, 129.26, 127.39, 21.45.



4-chlorobenzamide **(b4)**[1]

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.03 (s, 1H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.44 (s, 1H).

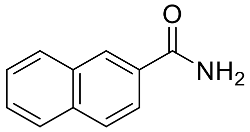
^{13}C NMR (126 MHz, DMSO-d_6) δ 167.27, 136.54, 133.52, 129.87, 128.75.



4-nitrobenzamide **(b5)**[1]

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.29 (t, J = 8.9 Hz, 3H), 8.09 (d, J = 8.6 Hz, 2H), 7.71 (s, 1H).

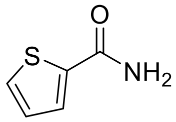
^{13}C NMR (126 MHz, DMSO-d_6) δ 166.19, 149.06, 139.99, 128.90, 123.43.



2-naphthamide **(b6)**[1]

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.53 (d, J = 1.3 Hz, 1H), 8.16 (s, 1H), 8.06 – 7.94 (m, 4H), 7.66 – 7.56 (m, 2H), 7.49 (s, 1H).

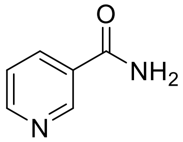
^{13}C NMR (126 MHz, DMSO-d_6) δ 168.46, 134.64, 132.63, 132.14, 129.31, 128.27, 128.21, 128.04, 128.00, 127.08, 124.87.



thiophene-2-carboxamide **(b7)**[2]

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.95 (s, 1H), 7.73 (d, J = 3.5 Hz, 2H), 7.37 (s, 1H), 7.18 – 7.08 (m, 1H).

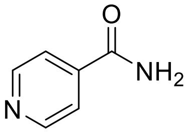
^{13}C NMR (126 MHz, DMSO-d_6) δ 162.85,140.31, 130.94, 128.63, 127.85.



nicotinamide (**b8**)[1]

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.04 (d, *J* = 2.2 Hz, 1H), 8.70 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.21 (dt, *J* = 7.9, 2.0 Hz, 1H), 8.15 (s, 1H), 7.58 (s, 1H), 7.50 (dd, *J* = 8.0, 4.8 Hz, 1H).

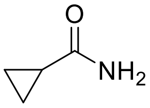
^{13}C NMR (126 MHz, DMSO-d_6) δ 166.91, 152.33, 149.13, 135.59, 130.15, 123.84.



isonicotinamide (**b9**)[3]

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.76 – 8.68 (m, 2H), 8.23 (s, 1H), 7.80 – 7.75 (m, 2H), 7.70 (s, 1H).

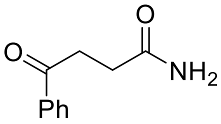
^{13}C NMR (126 MHz, DMSO-d_6) δ 166.77, 150.66, 141.76, 121.85.



cyclopropanecarboxamide **(b10)**[1]

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.49 (s, 1H), 6.73 (s, 1H), 1.50 (tt, *J* = 7.4, 4.9 Hz, 1H), 0.89 – 0.41 (m, 4H).

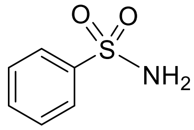
^{13}C NMR (126 MHz, DMSO-d_6) δ 174.67, 13.21, 6.18.



4-oxo-4-phenylbutanamide **(b11)**[4]

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.97 (d, *J* = 7.2 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.37 (s, 1H), 6.79 (s, 1H), 3.21 (t, *J* = 6.6 Hz, 2H), 2.46 (t, *J* = 6.6 Hz, 2H).

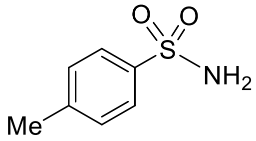
^{13}C NMR (126 MHz, DMSO) δ 198.93, 173.26, 136.65, 133.04, 128.66, 127.80, 33.22, 28.87.



benzenesulfonamide **(b12)**[5]

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.87 – 7.80 (m, 2H), 7.63 – 7.53 (m, 3H), 7.34 (s, 2H).

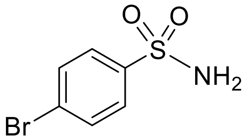
^{13}C NMR (126 MHz, DMSO-d_6) δ 144.62, 132.24, 129.38, 126.04.



4-methylbenzenesulfonamide (**b13**)[5]

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.74 – 7.68 (m, 2H), 7.36 (d, J = 8.0 Hz, 2H), 2.37 (s, 3H).

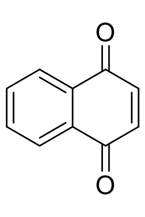
^{13}C NMR (126 MHz, DMSO-d_6) δ 142.30, 141.92, 129.74, 126.08, 21.37.



4-bromobenzenesulfonamide (**b14**)[5]

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.84 – 7.73 (m, 4H), 7.46 (s, 2H).

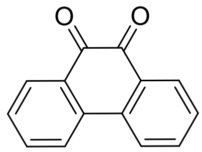
^{13}C NMR (126 MHz, DMSO-d_6) δ 143.87, 132.45, 128.20, 125.89.



naphthalene-1,4-dione **(c24)**[6]

^{1}H NMR (500 MHz, Chloroform-d) δ 8.15 – 8.05 (m, 2H), 7.77 (dd, J = 5.7, 3.3 Hz, 2H), 6.99 (s, 2H).

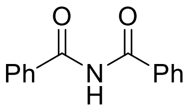
^{13}C NMR (126 MHz, Chloroform-d) δ 184.98, 138.65, 133.90, 131.92, 126.39.



phenanthrene-9,10-dione **(c31)**[7]

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.13 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.73 – 7.65 (m, 2H), 7.44 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 180.24, 136.04, 135.80, 130.97, 130.44, 129.57, 123.98.

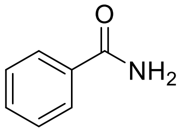


N-benzoylbenzamide **(c32)**[8]

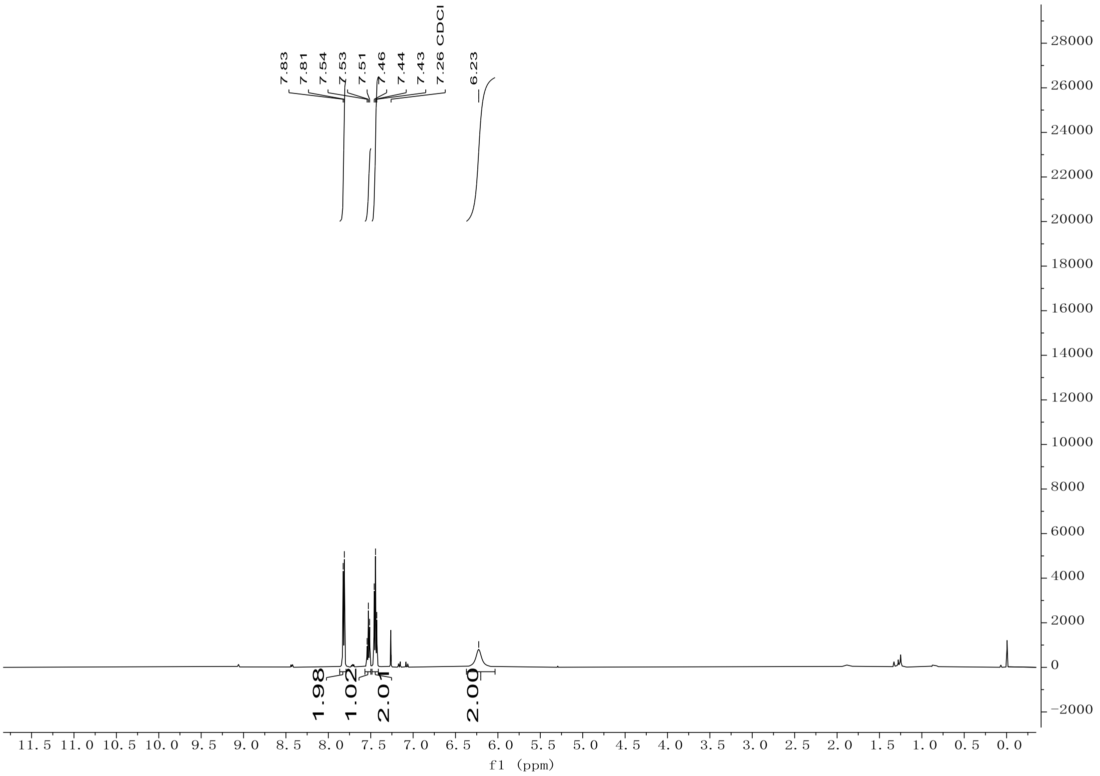
^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.07 (s, 1H), 7.86 (d, *J* = 7.6 Hz, 4H), 7.59 (t, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 4H).

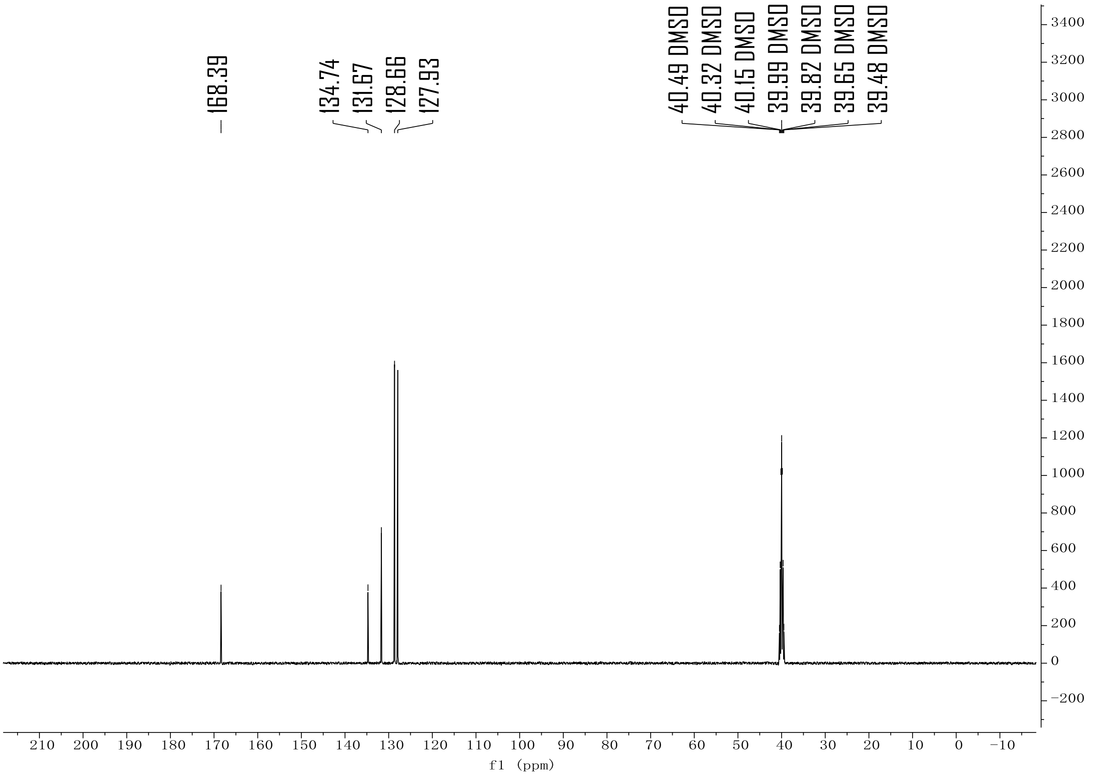
^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.56, 133.25, 132.98, 128.73, 127.94.

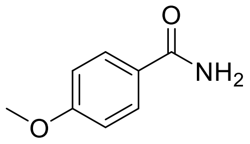
7. NMR spectra



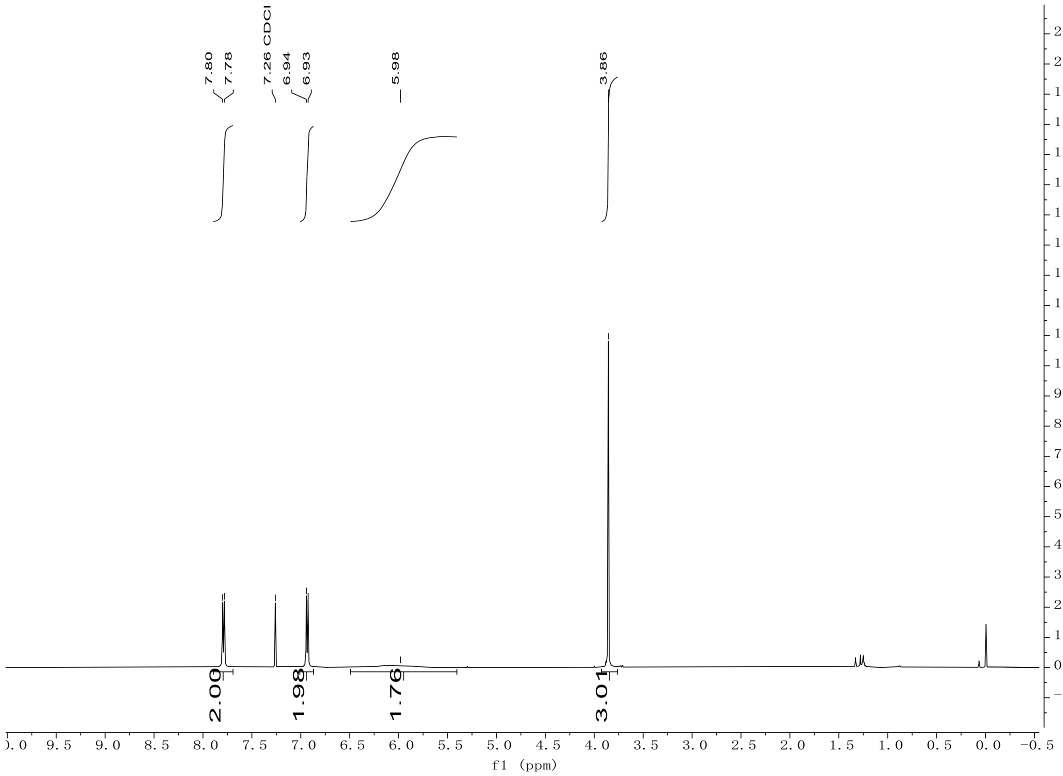
benzamide **(b1)**

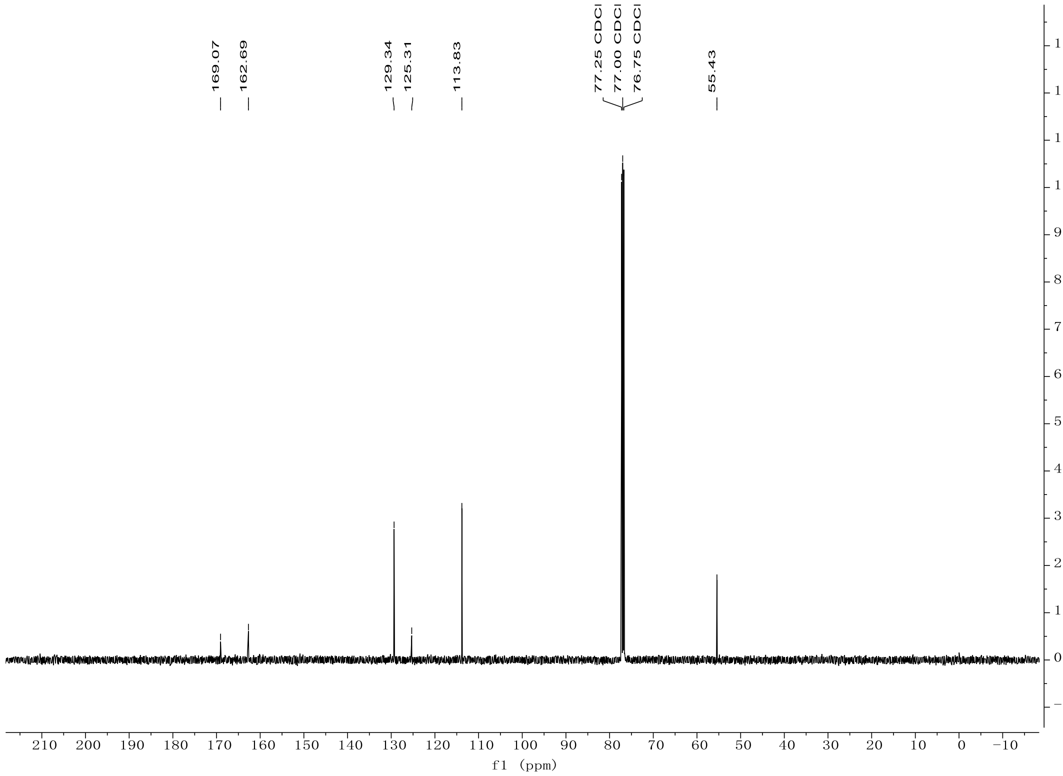


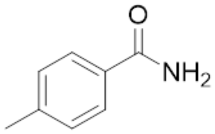




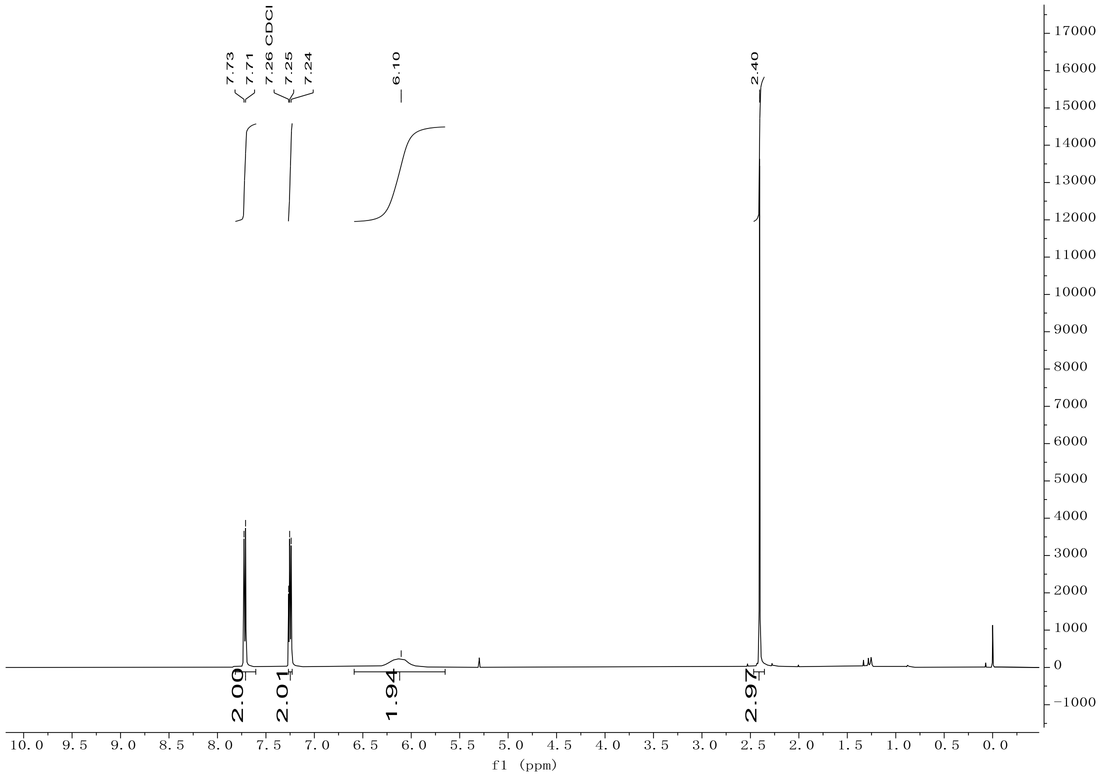
4-methoxybenzamide **(b2)**

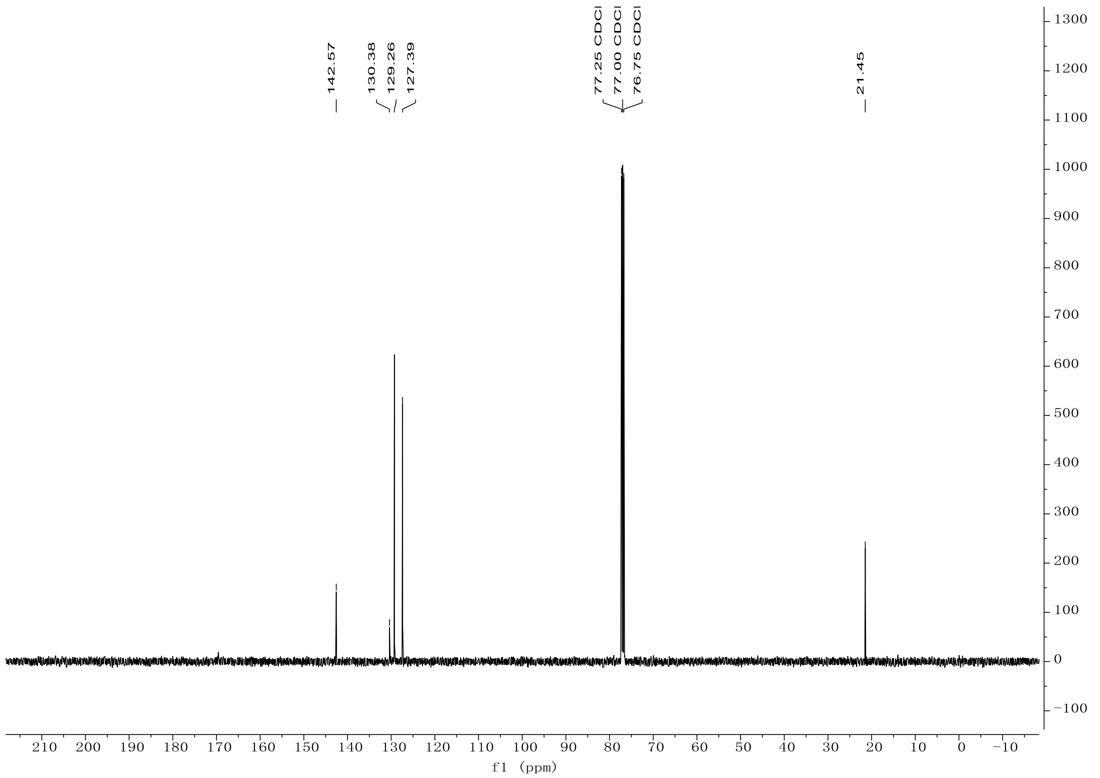


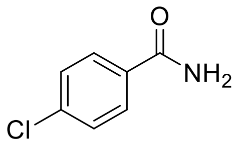




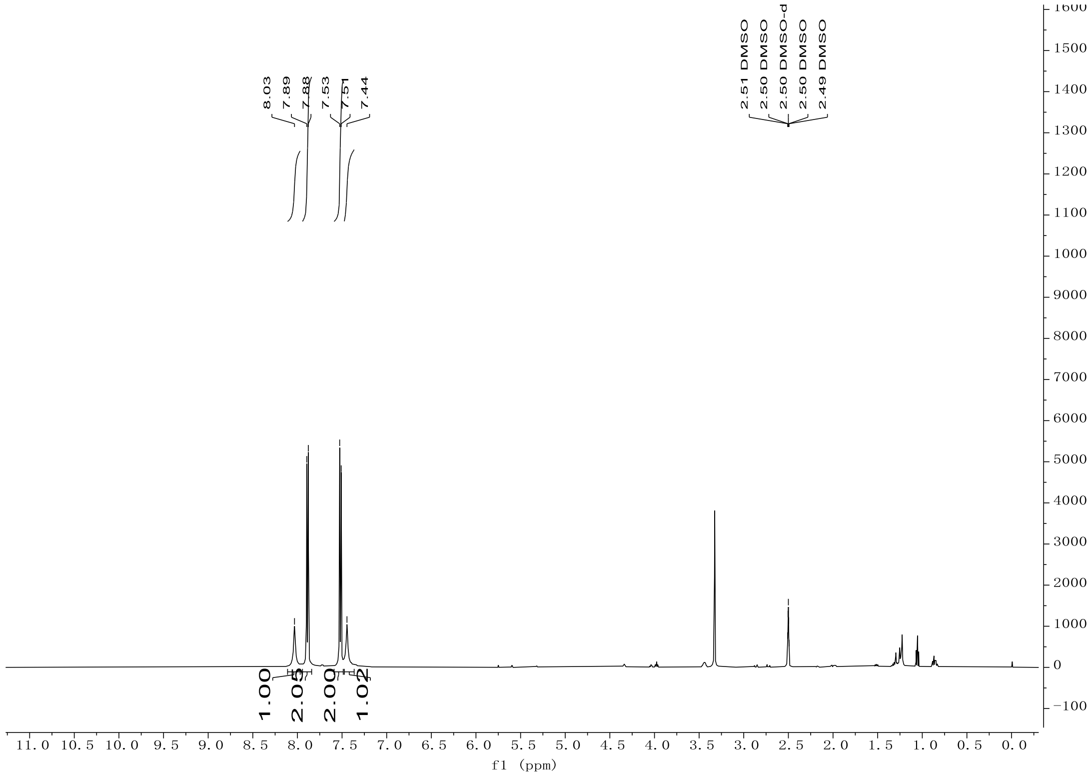
4-methylbenzamide **(b3)**

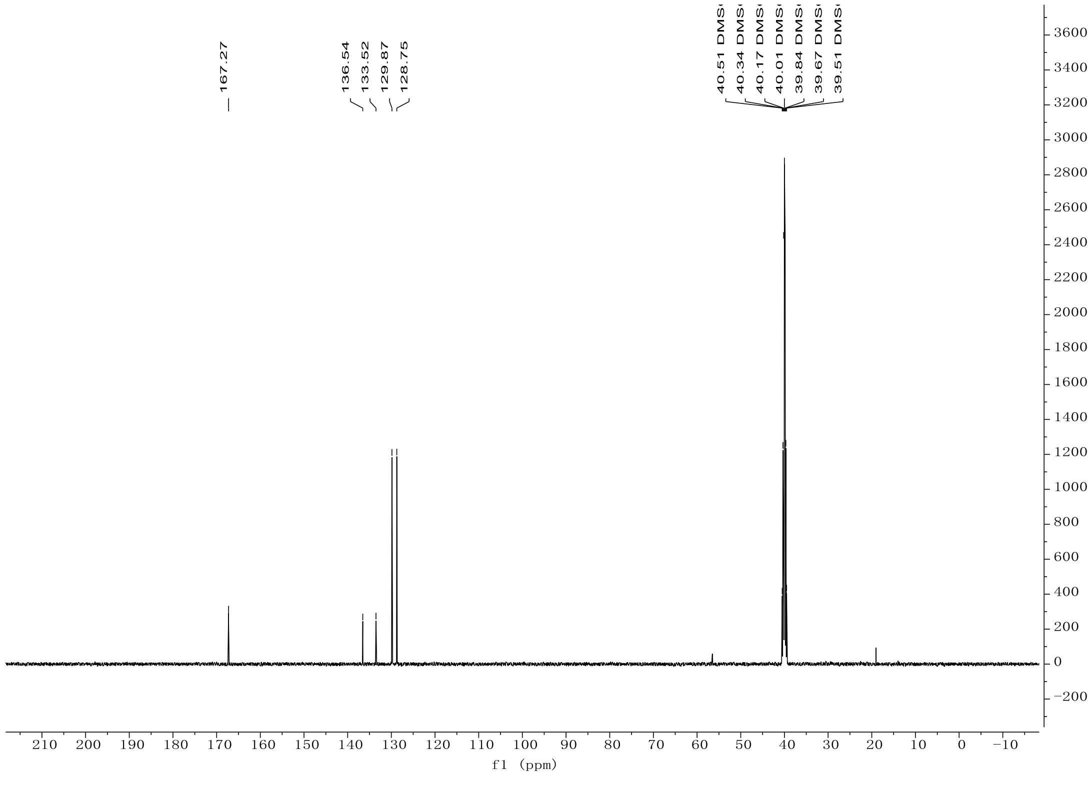


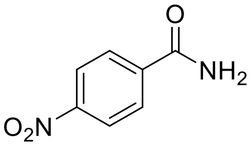




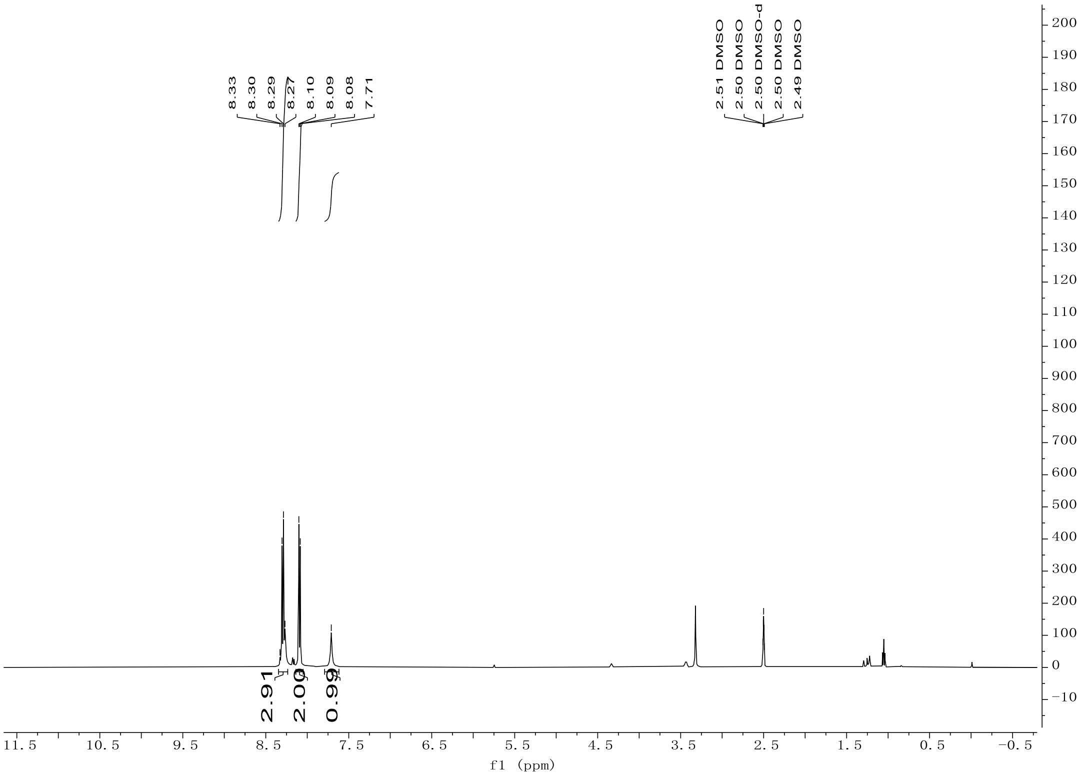
4-chlorobenzamide **(b4)**

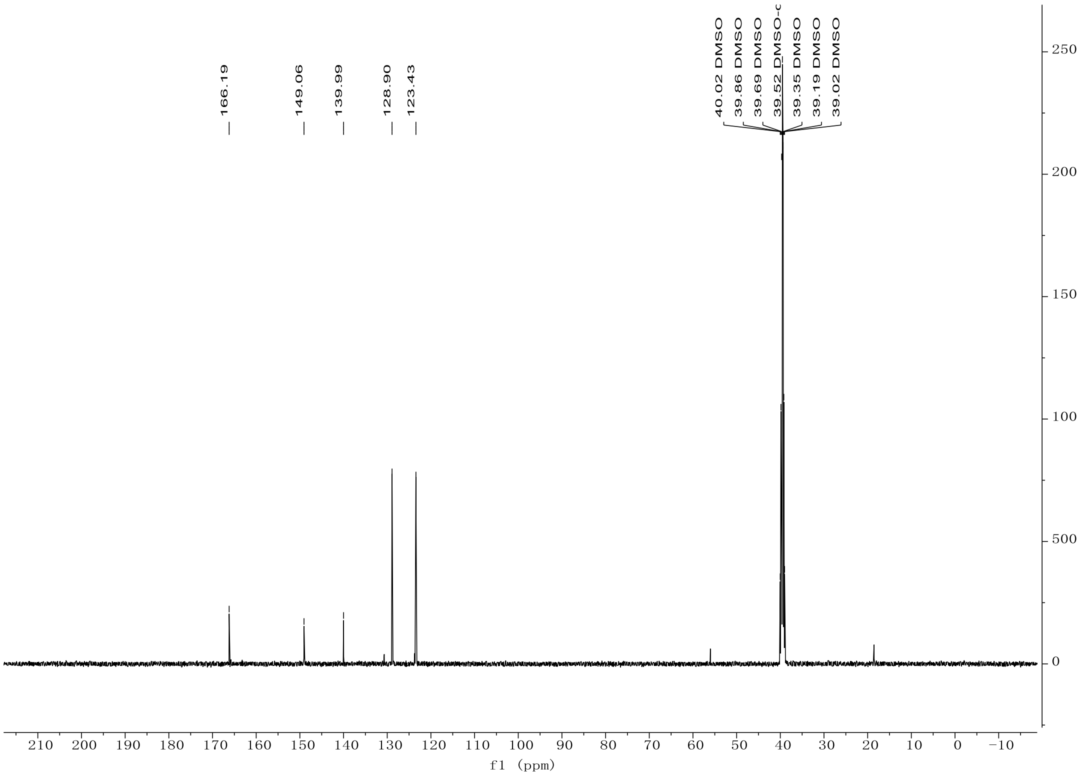


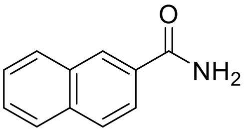




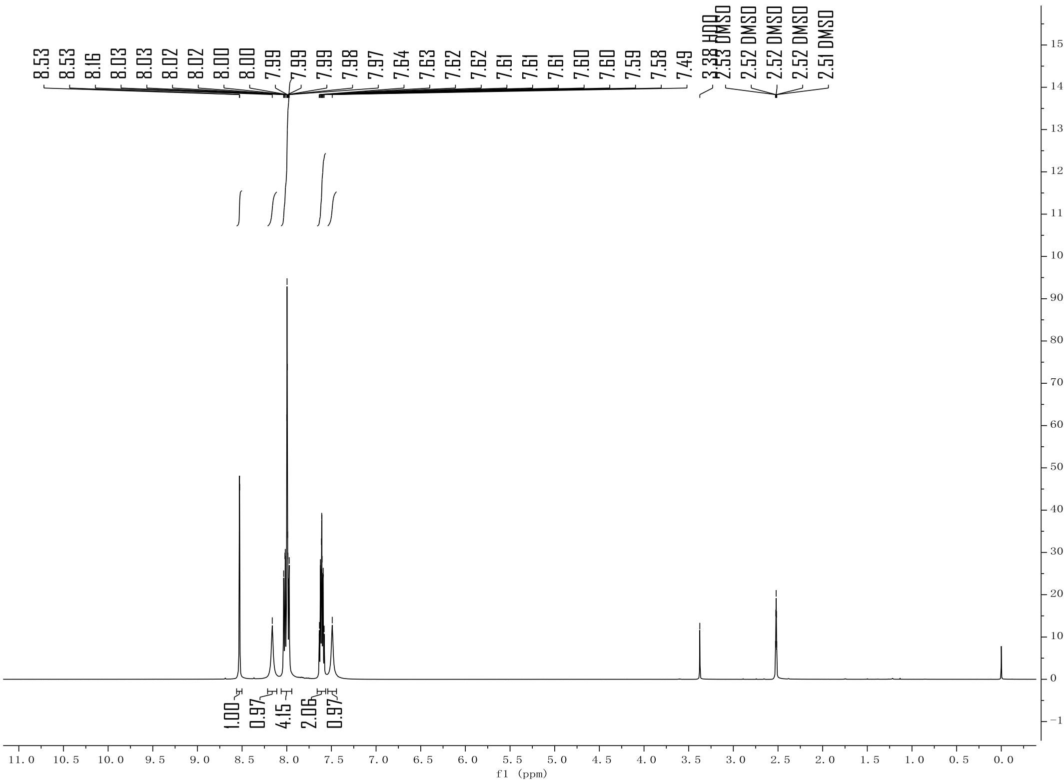
4-nitrobenzamide **(b5)**

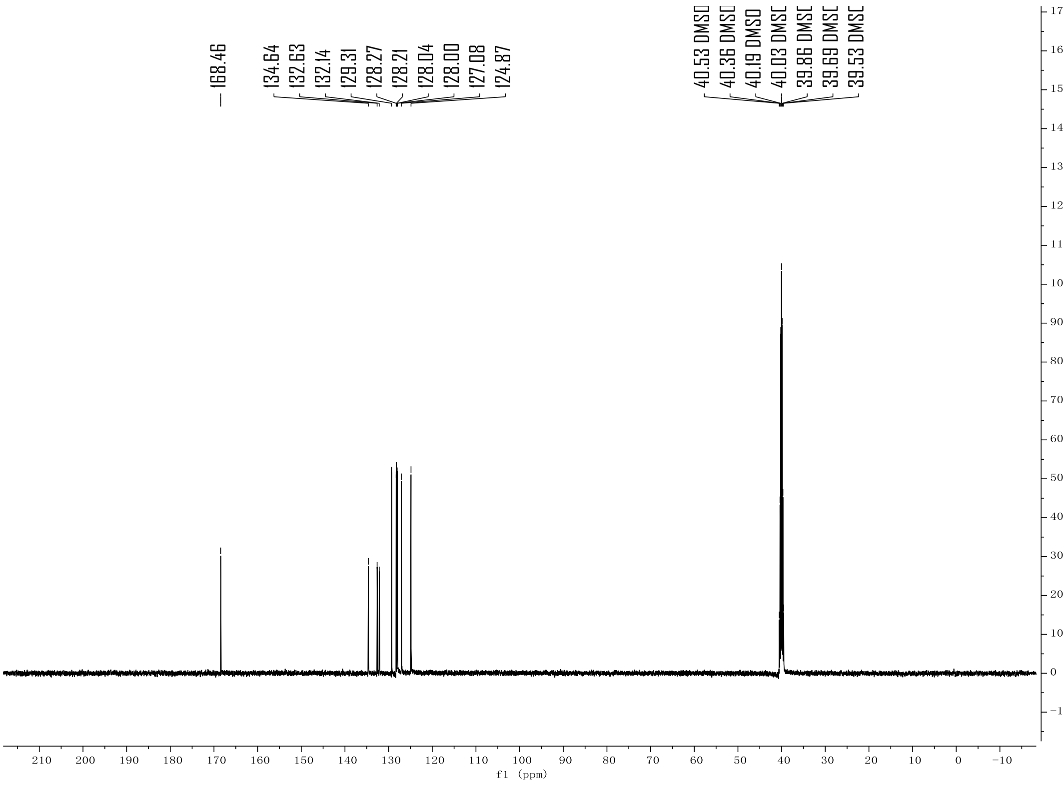


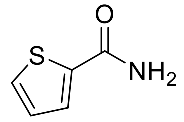




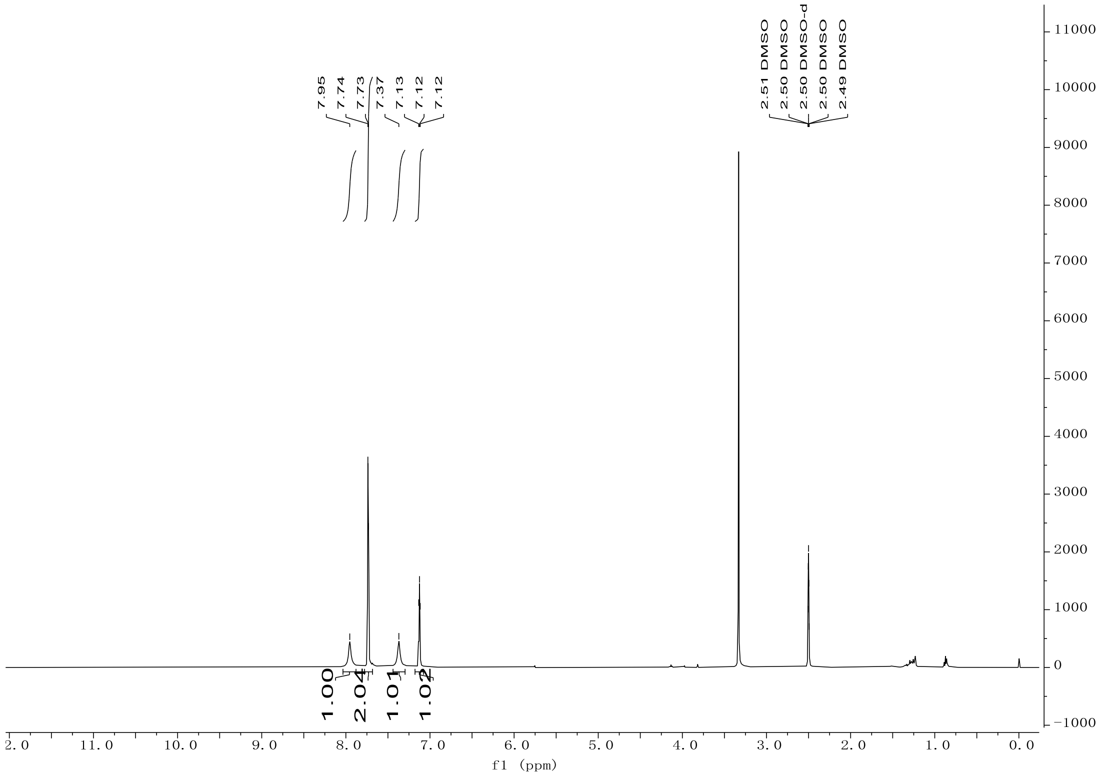
2-naphthamide **(b6)**

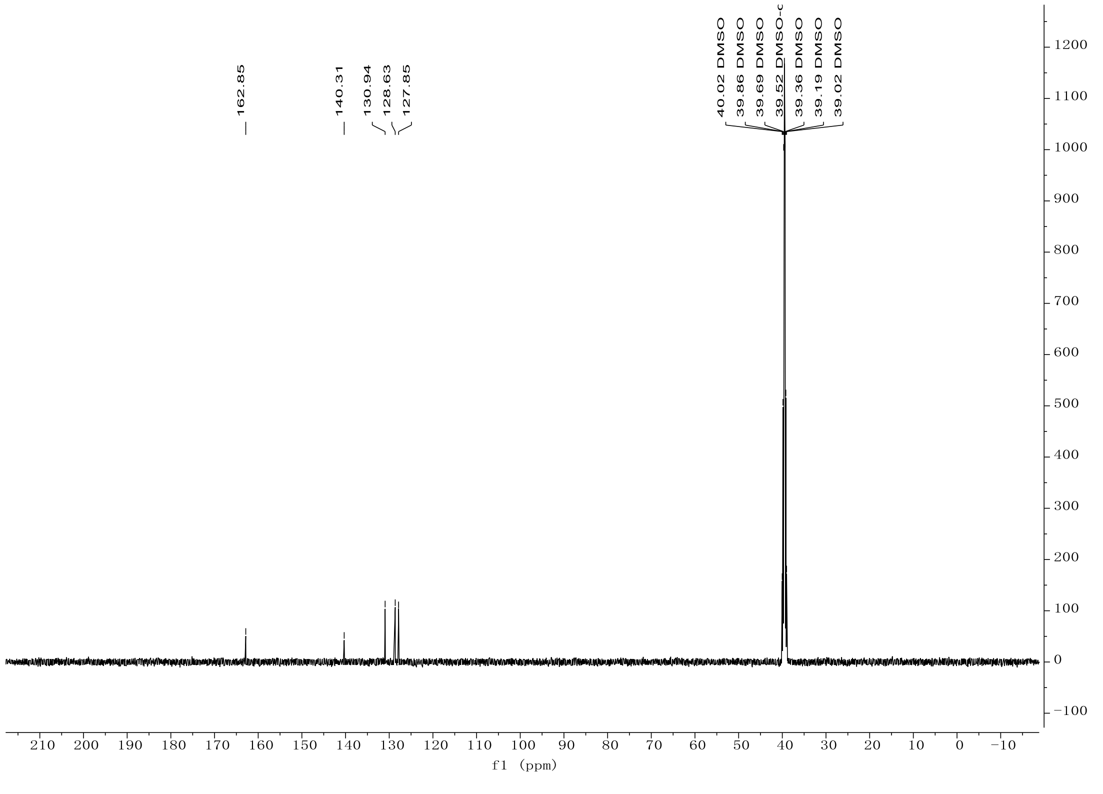


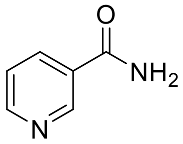




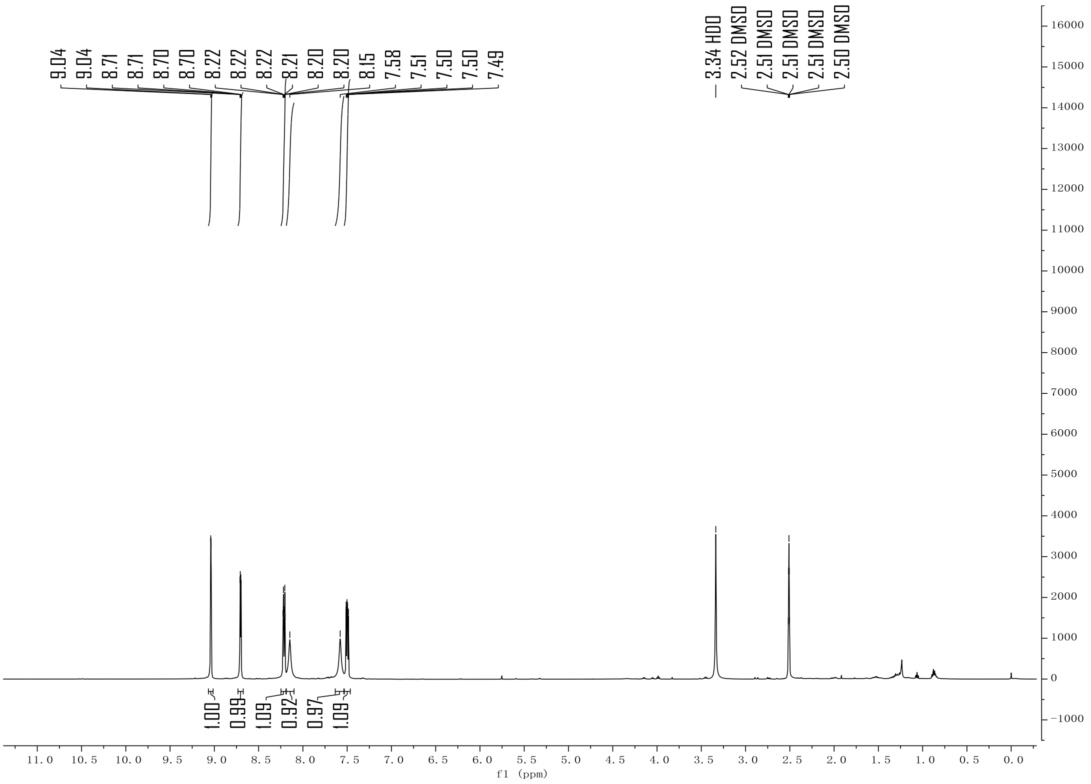
thiophene-2-carboxamide **(b7)**

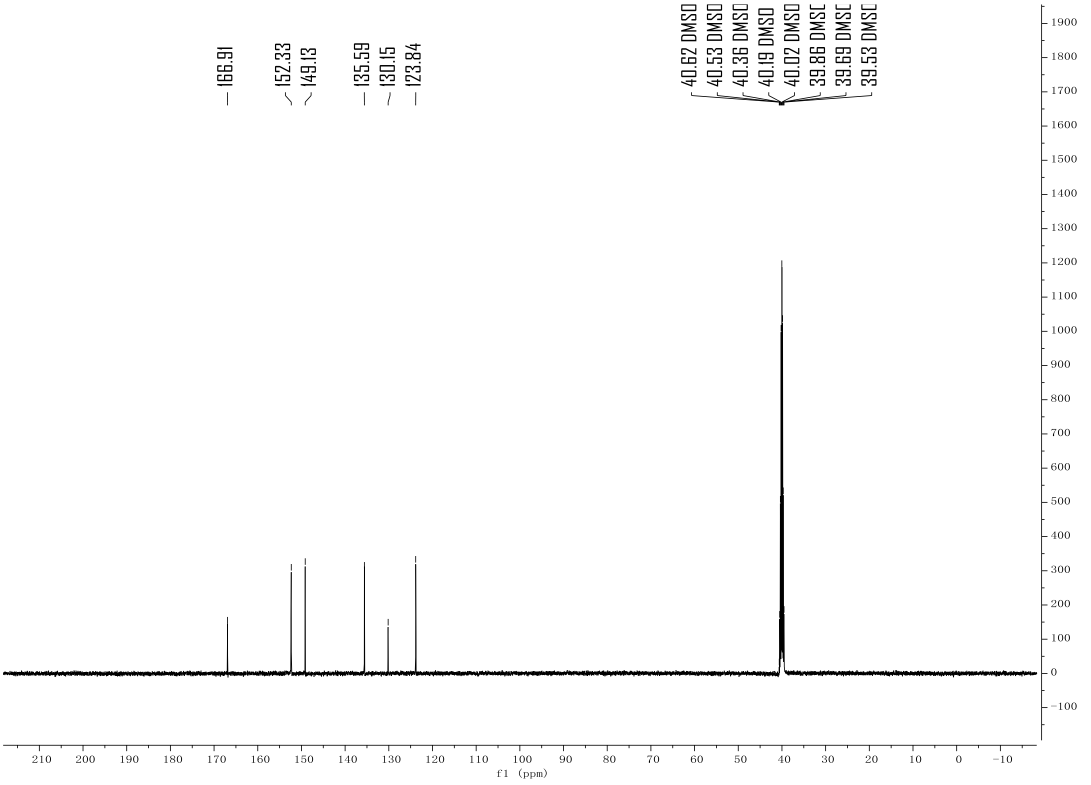


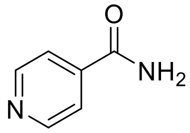




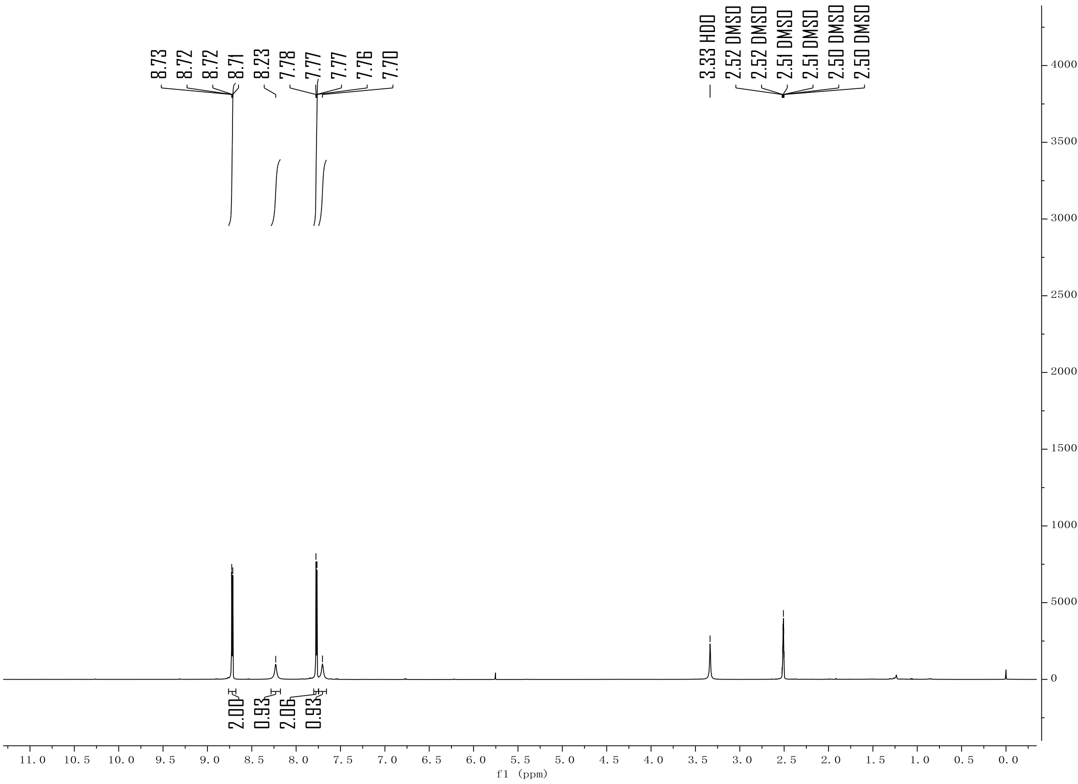
nicotinamide (**b8**)

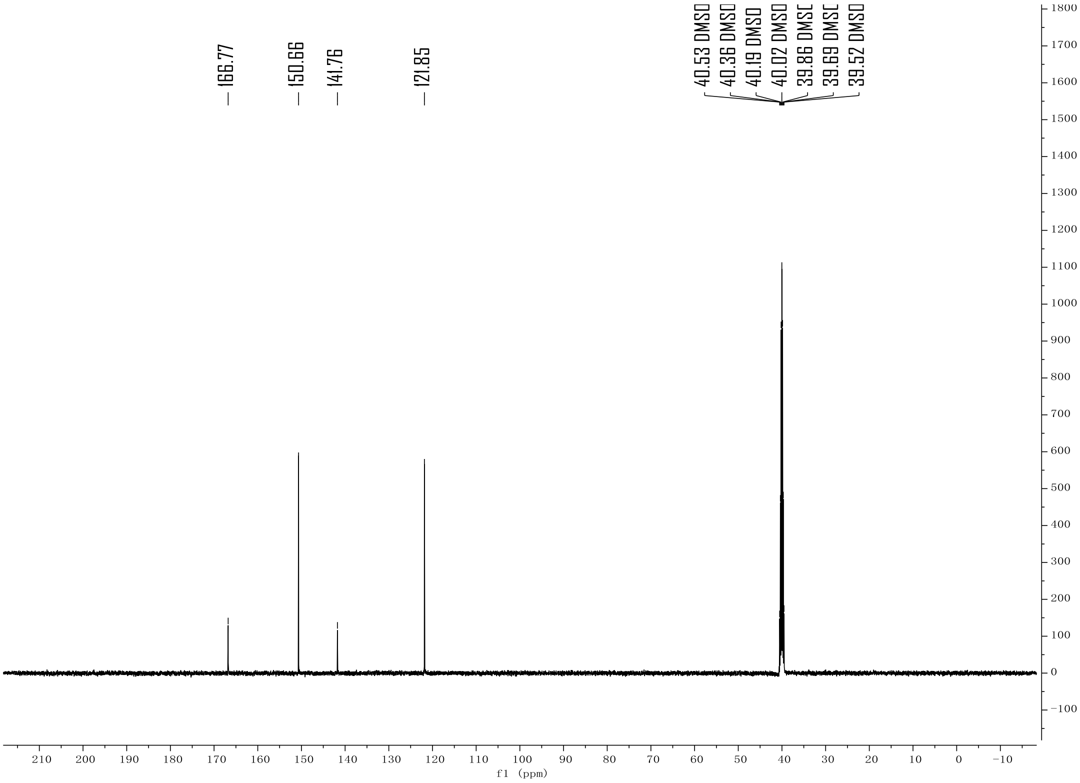


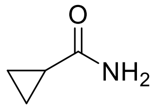




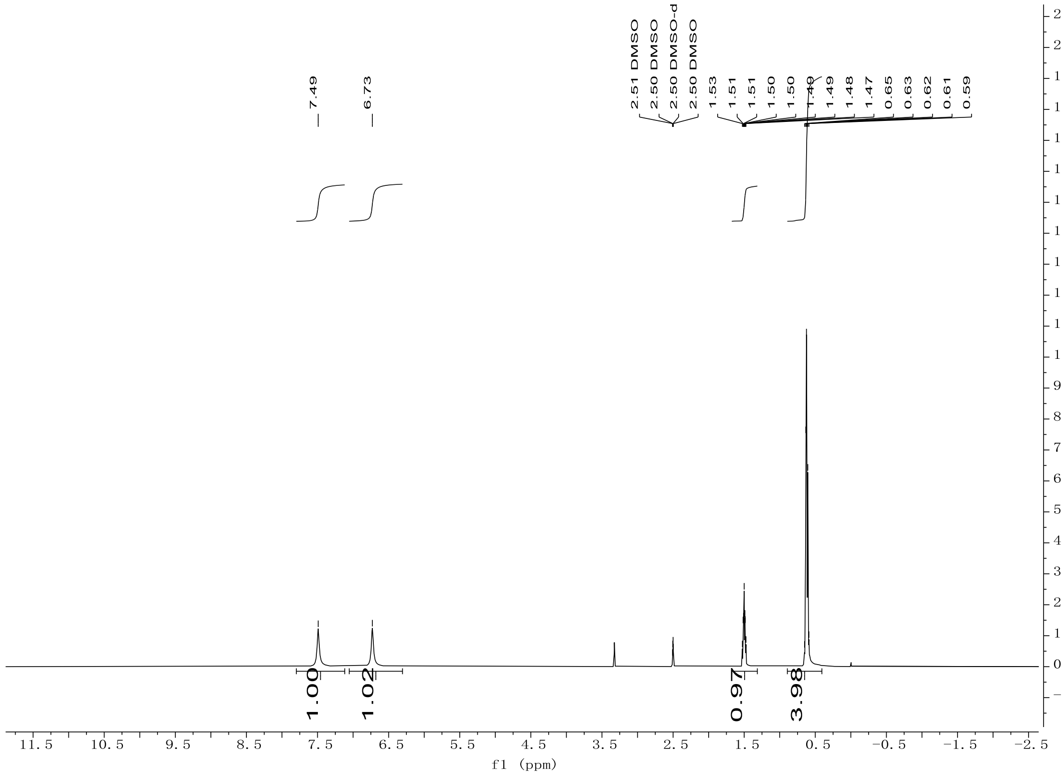
isonicotinamide (**b9**)

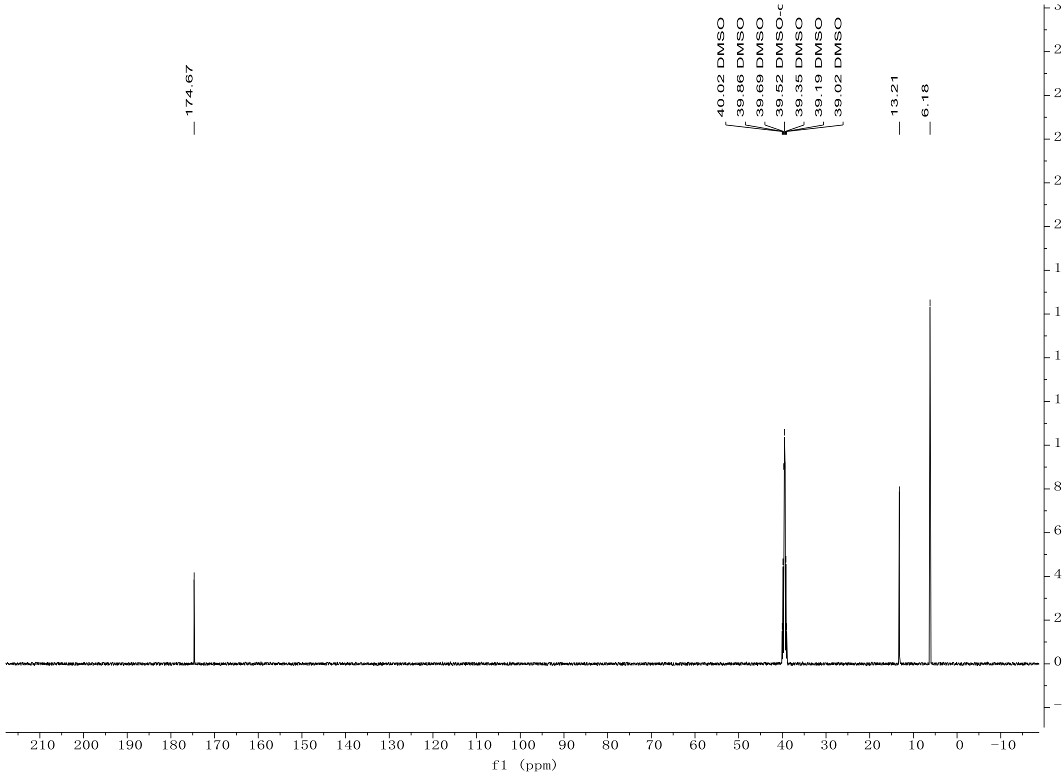


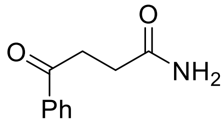




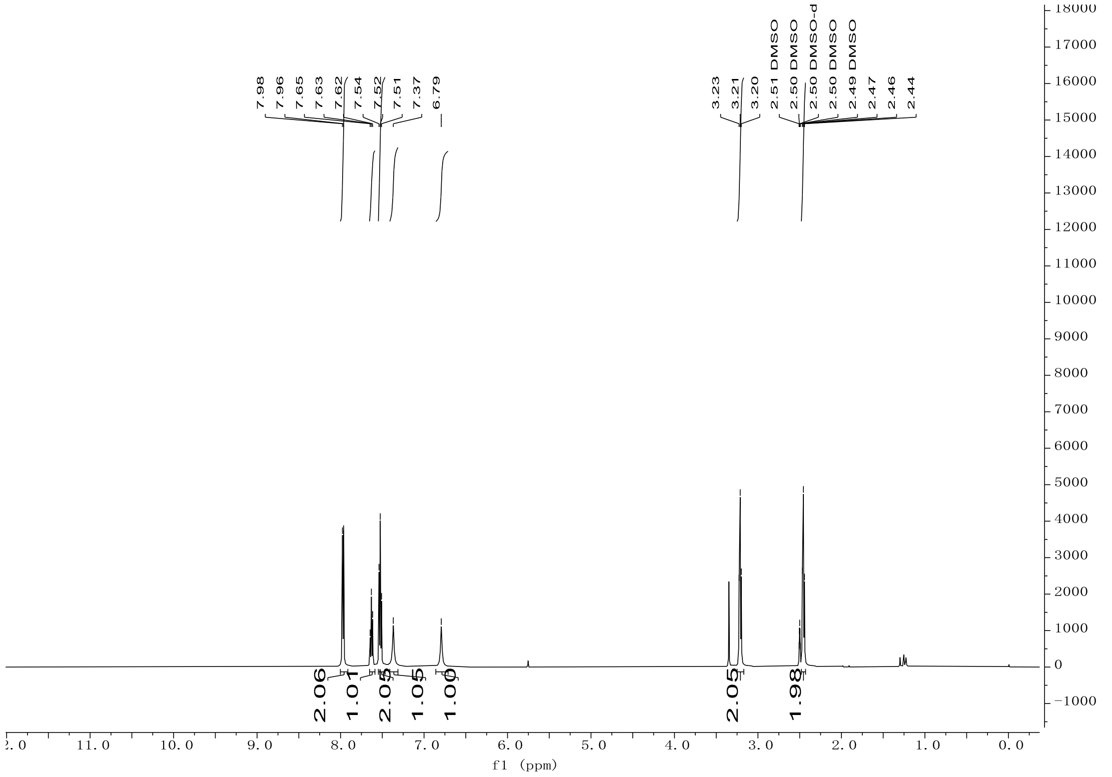
cyclopropanecarboxamide **(b10)**

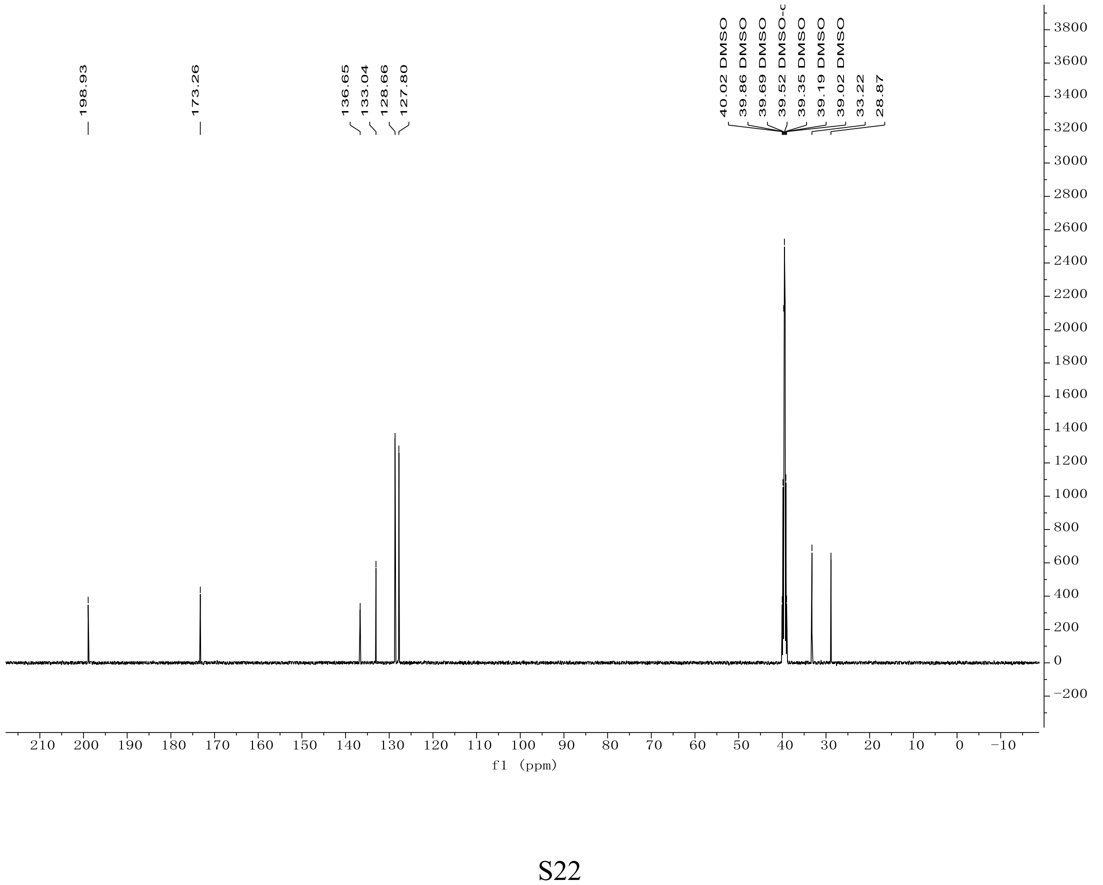


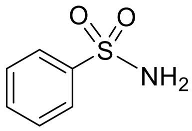




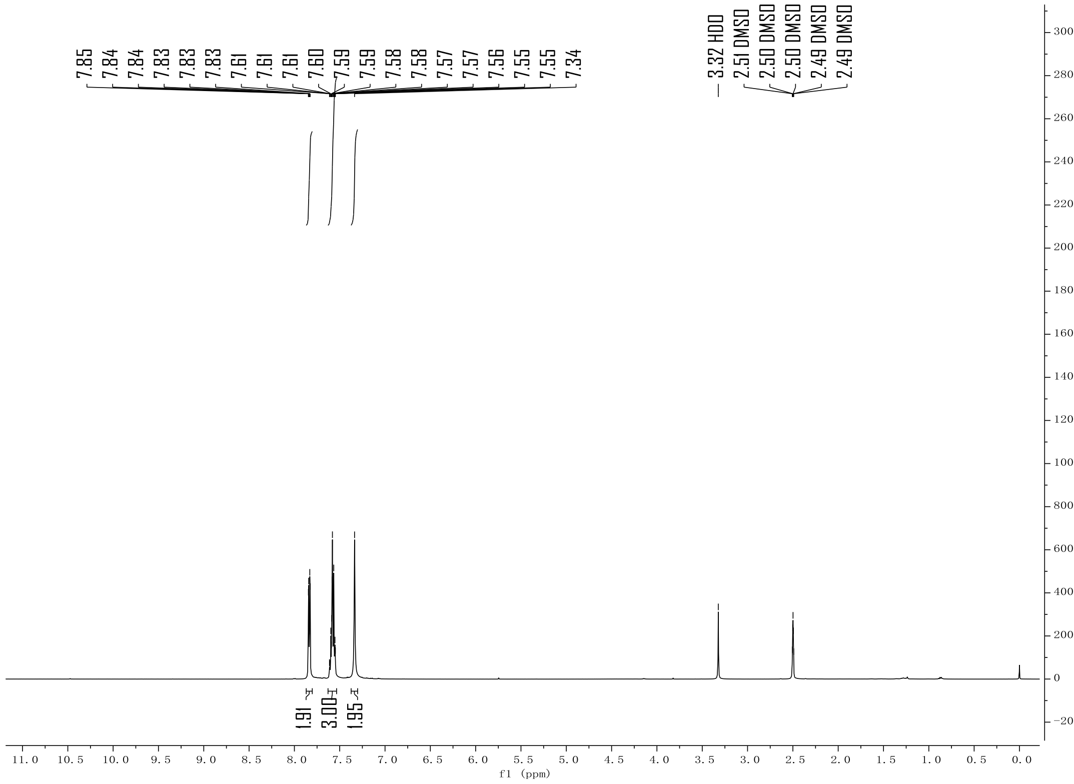
4-oxo-4-phenylbutanamide **(b11)**

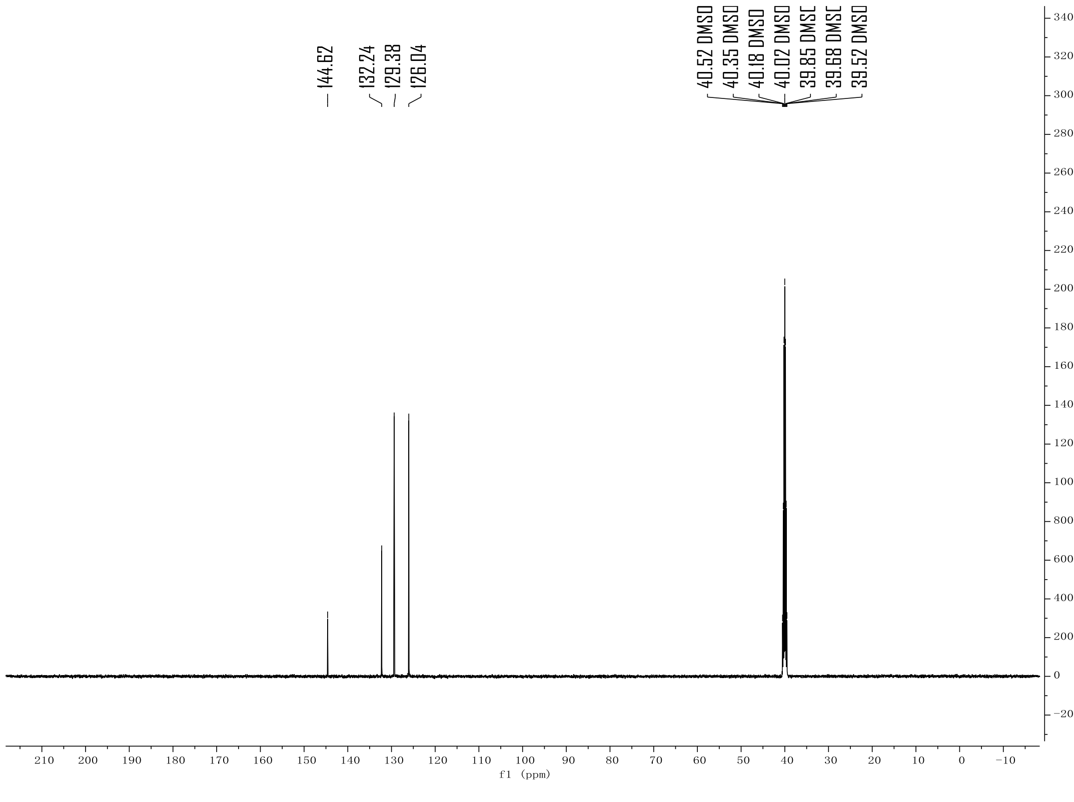


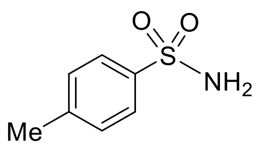




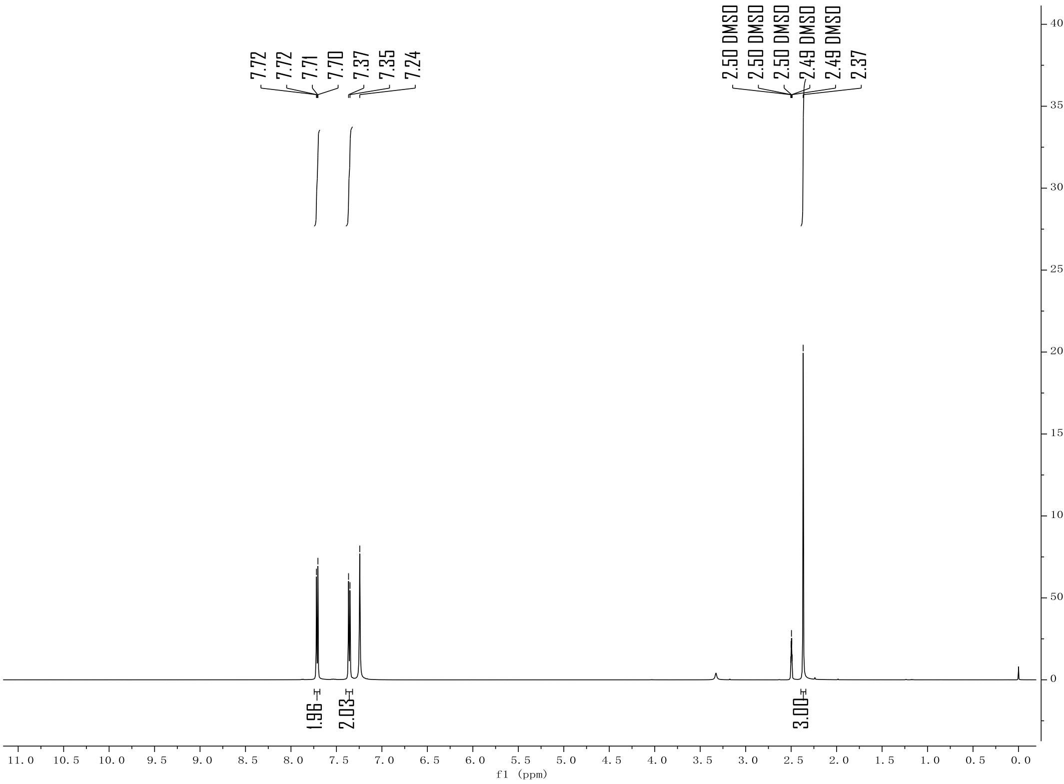
benzenesulfonamide **(b12)**

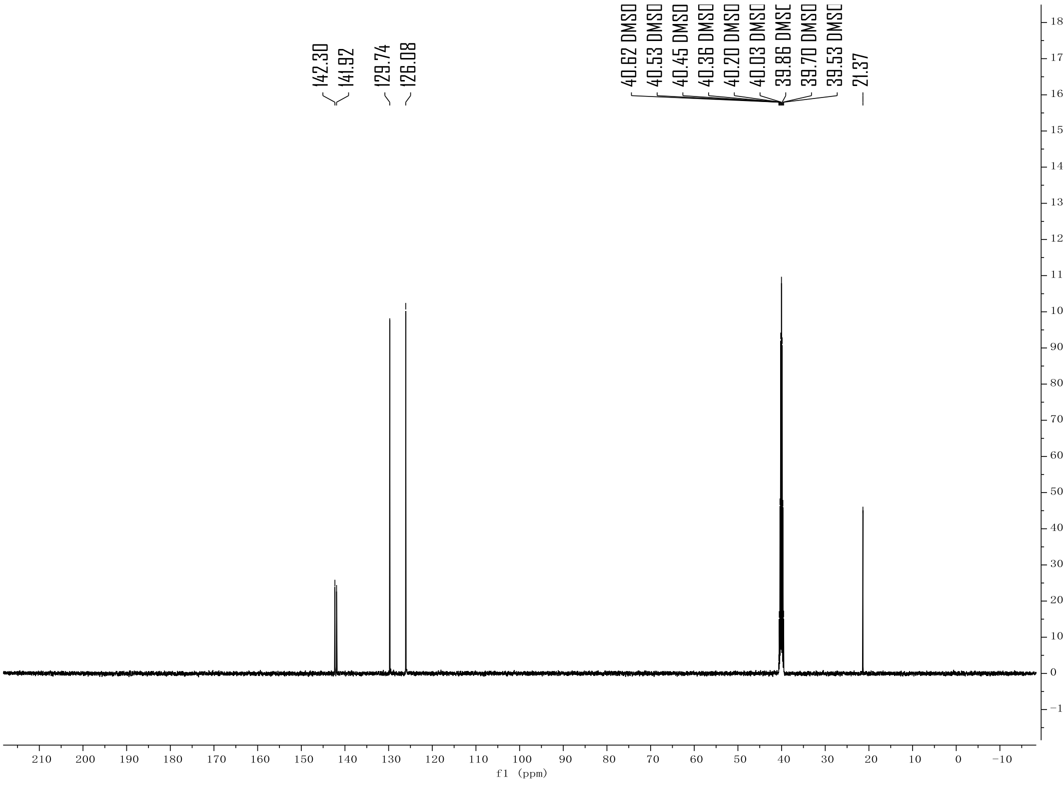


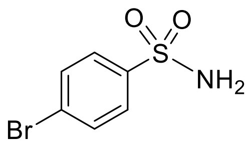




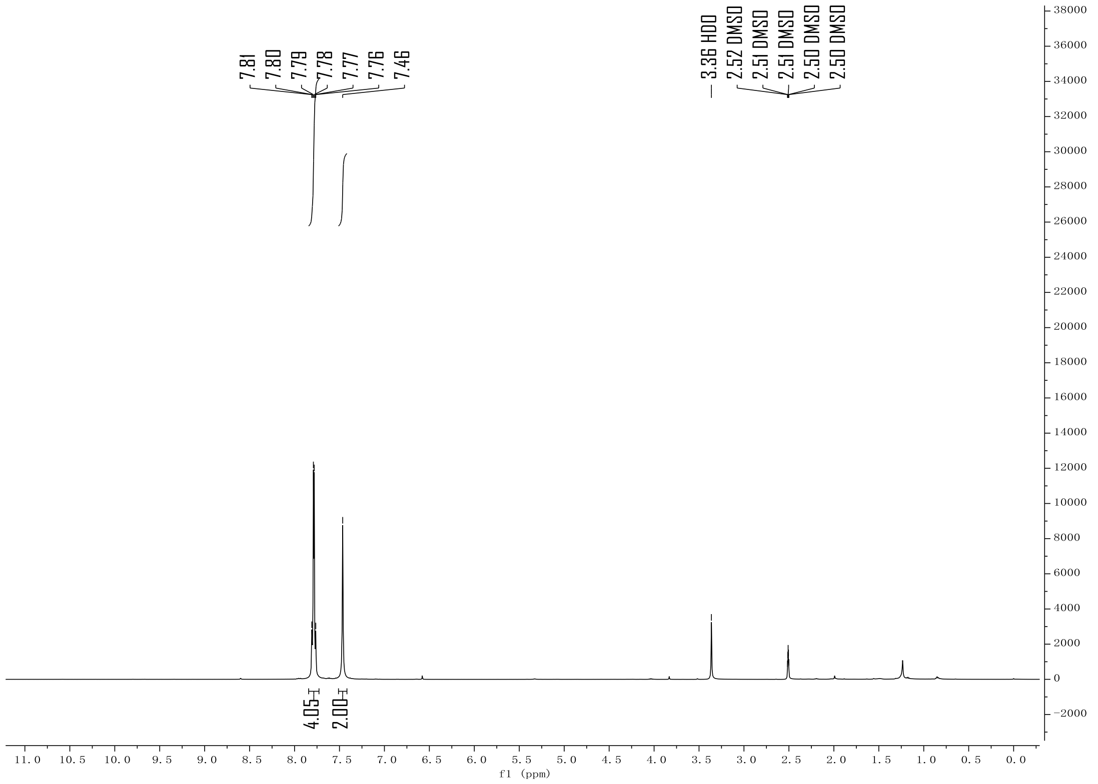
4-methylbenzenesulfonamide (**b13**)

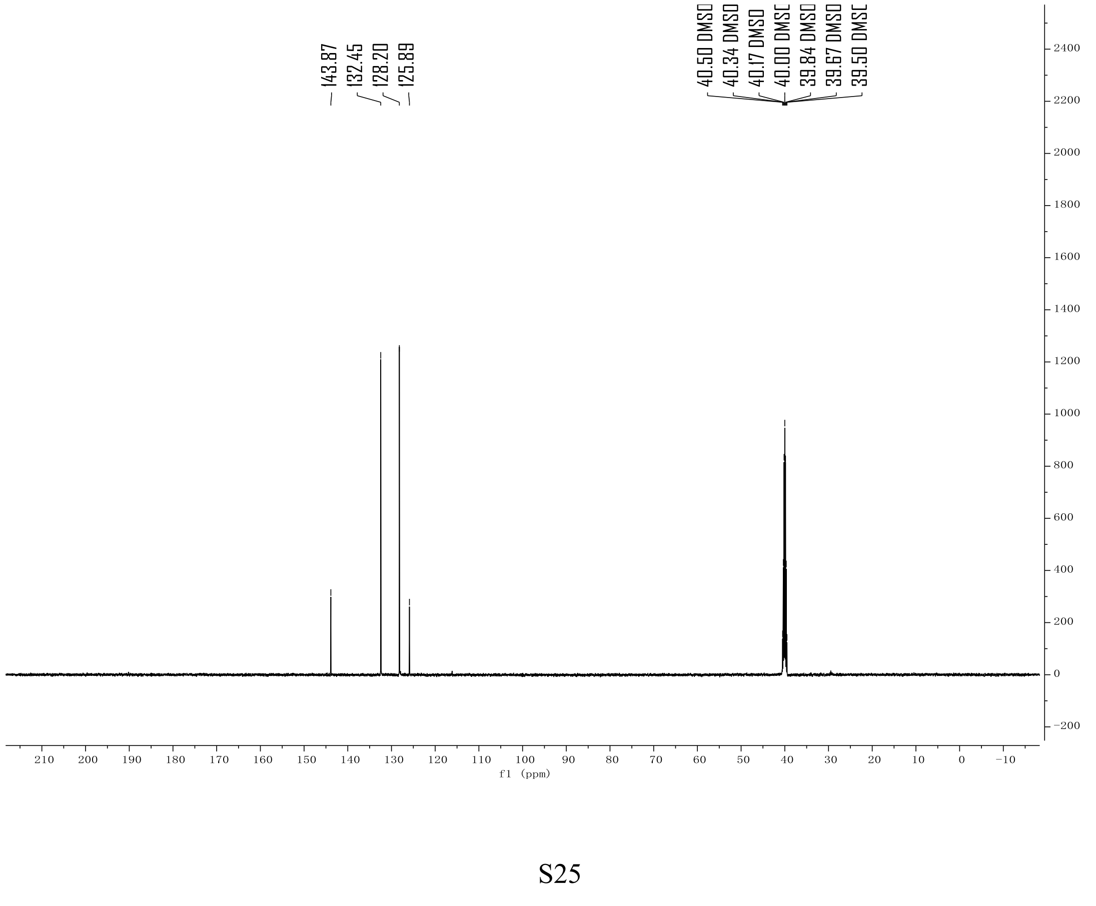


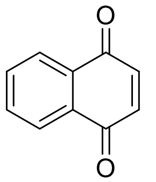




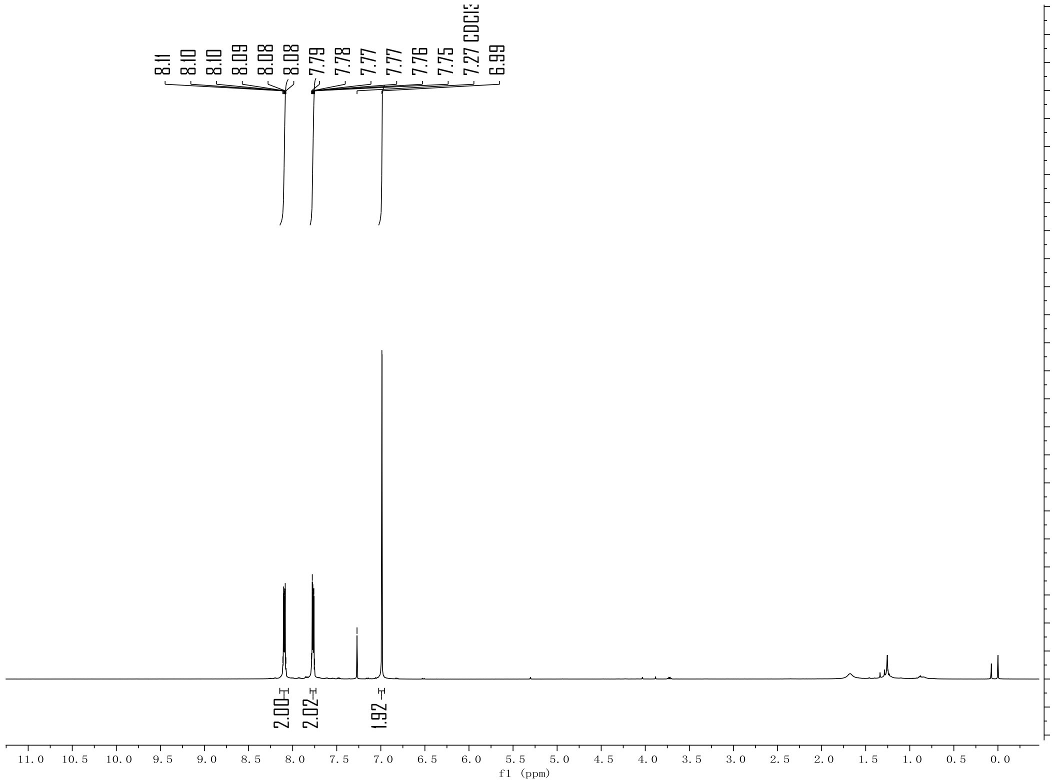
4-bromobenzenesulfonamide (**b14**)

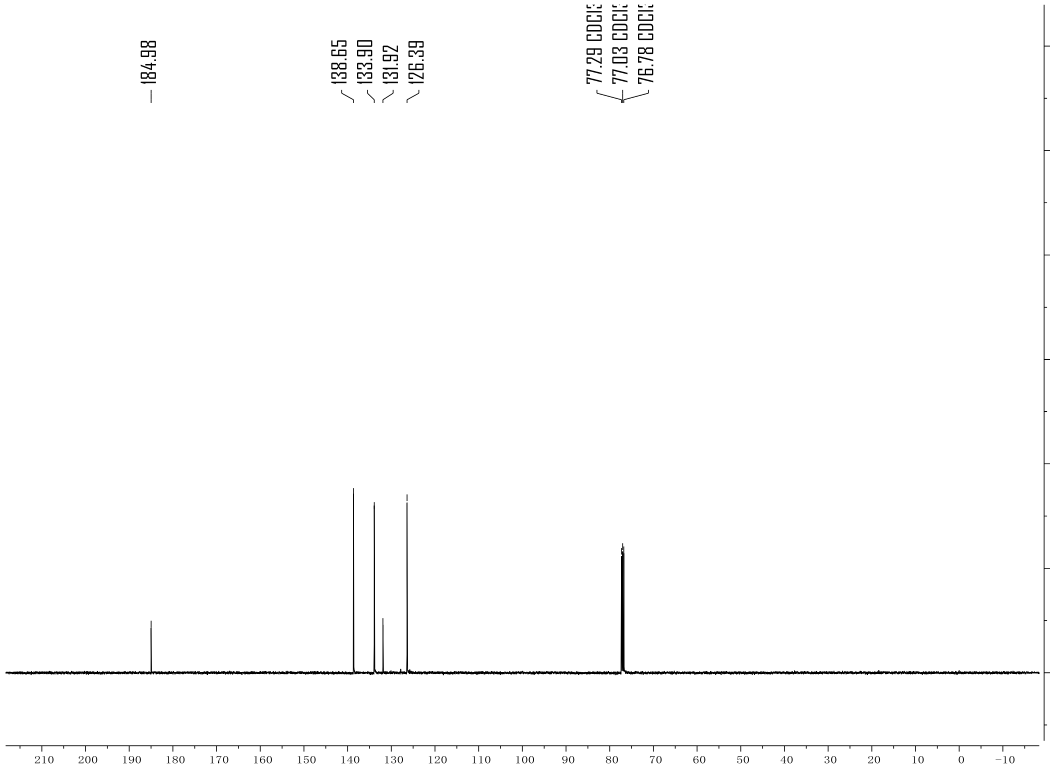


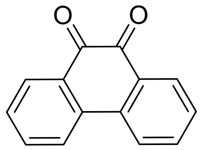




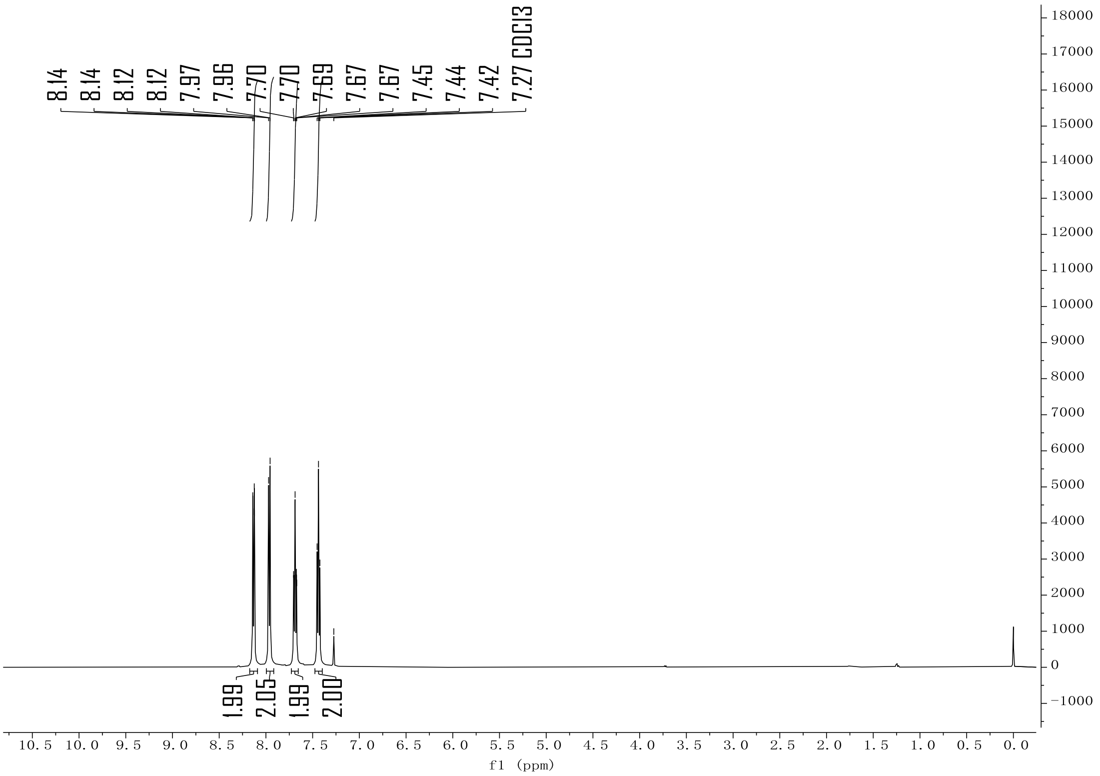
naphthalene-1,4-dione **(c24)**

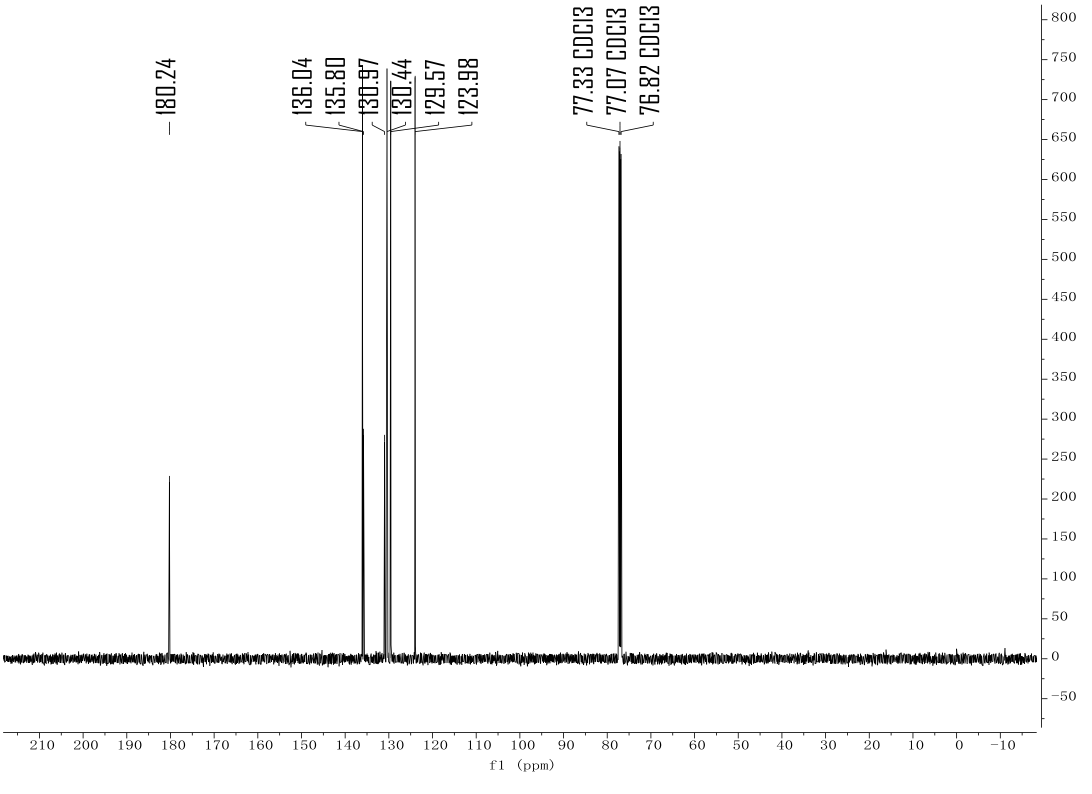


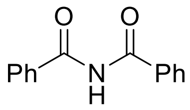




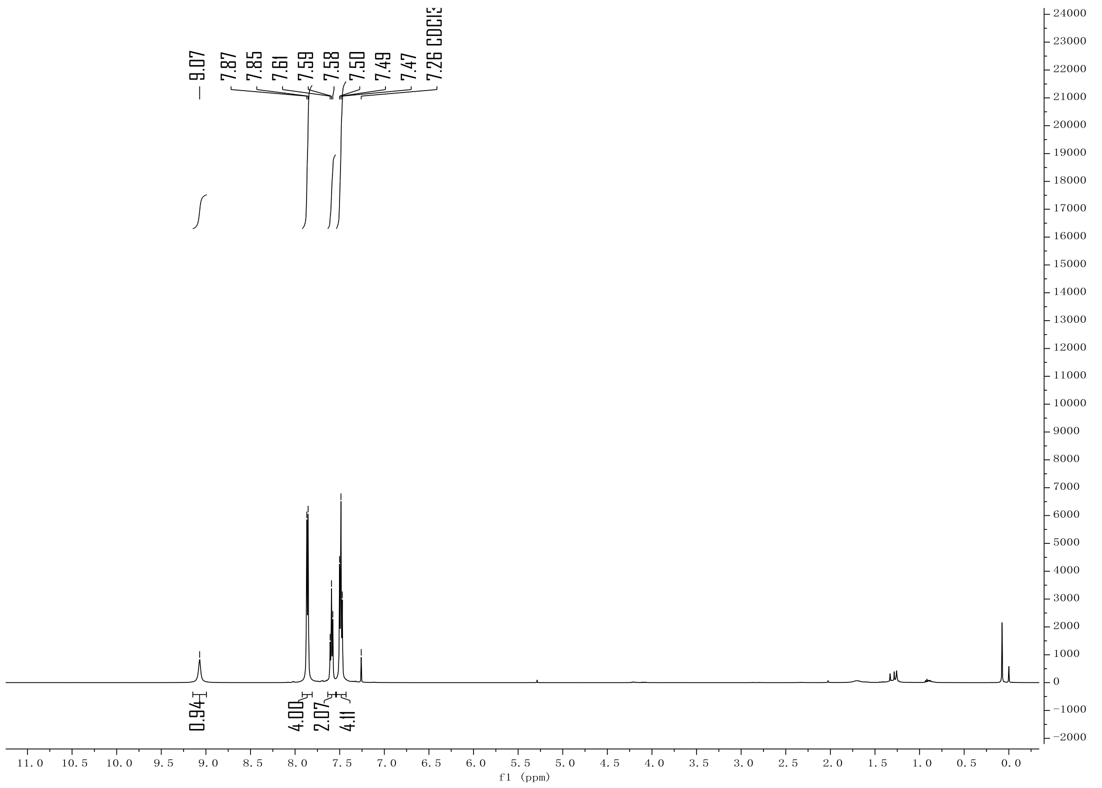
phenanthrene-9,10-dione **(c31)**

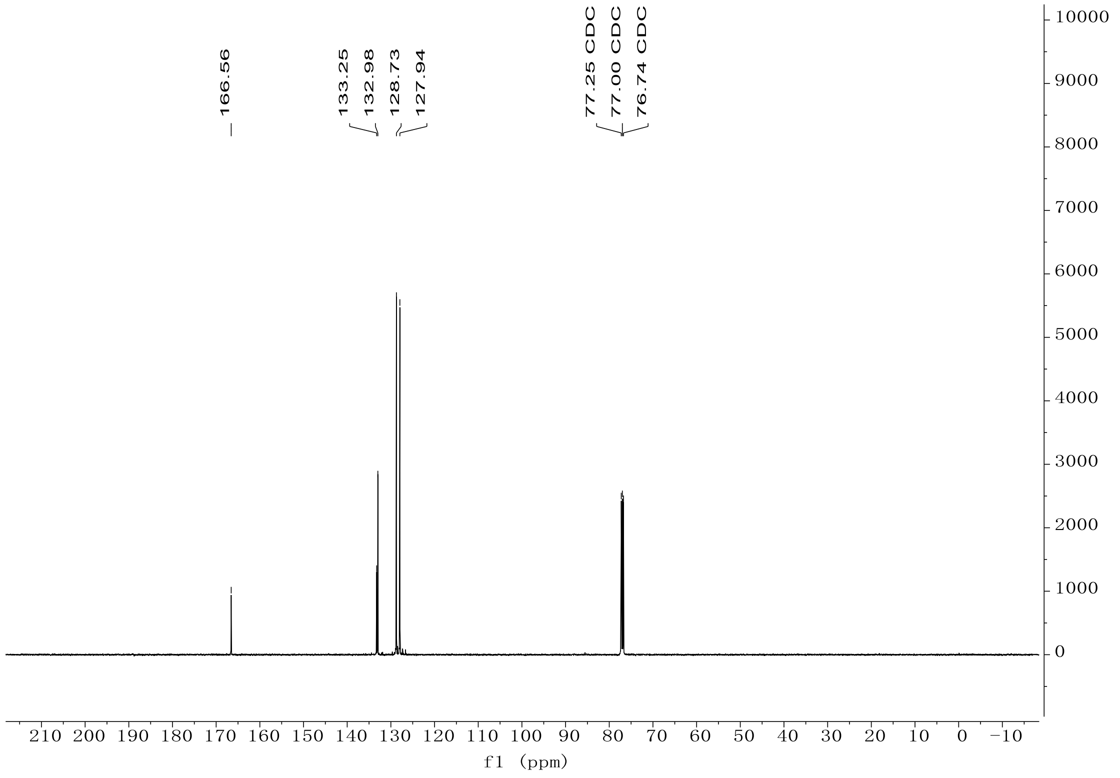






N-benzoylbenzamide **(c32)**





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