Supplementary Material (ESI) for Organic & Biomolecular Chemistry
This journal is (c) The Royal Society of Chemistry 2018

Synthesis of benzimidaziles by CuI-catalyzed three-componet reaction of 2-haloaniline, ammonia and aldehyde in water

Fang Ke,*[a] Peng Zhang,[a] Chen Lin,[a] Xiaoyan Lin,[a] Jianhua Xu,[a] and Xiangge Zhou *[b]

[a] College of Pharmacy, Fujian Medical University, Fuzhou 350004, China.

[b] Institute of Homogeneous Catalysis, College of Chemistry, Sichuan University, Chengdu 610041, China

E-mail: zhouxiangge@scu.edu.cn

Fax: +86-28-85412026

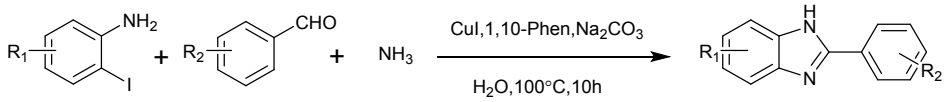
Supplementary Information

Table of Contents

1. General information

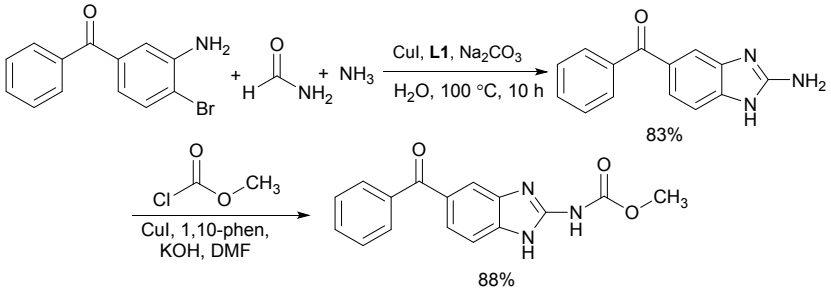
All reagents were purchased from commercial suppliers and used without further purification. All experiments were carried out in hydrothermal reactor (100 mL). Column chromatography was carried out with silica gel (200-300 mesh). Thin layer chromatography was carried out using Merck silica gel GF254 plates. All products were characterized by NMR. ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra were recorded at 100 MHz (Bruker DPX) with Acetonitrile-d_3, Acetone-d_6 and DMSO-d_6 as solvent. Chemical shifts are reported in ppm using TMS as internal standard. Gas chromatography-mass spectra (GC/MS) were recorded on an Agilent Technologies 6890 N instrument with an Agilent 5973N mass detector (EI) and a HP5-MS 30 m x 0.25 mm capillary apolar column (Stationary phase: 5% diphenyldimethylpolysiloxane film, 0.25 µm). GC/MS method: Initial temperature: 150 °C; Initial time: 1 min; Ramp: about 15°C/min until 250 °C then 20 min.

2. General procedure for the catalytic reactions



In a 100 mL hydrothermal reactor 2-iodoanilines (0.5 mmol), aldehyde(0.6 mmol)，CuI (0.05 mmol), L1 (0.05 mmol), ammonia(1.0 mL)and Na_2CO_3 (2.0 equiv) and 2.0 mL water were was stirred at 100 °C for 10 h. The reaction mixture was cooled to room temperature, quenched with water (3 mL), and diluted with ethyl acetate (5 mL). The layers were separated and the aqueous layer was extracted with (3×10mL) ethyl acetate. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by silica-gel (eluent: petroleum ether/EtOAc) column chromatography to afford the corresponding product. All the products were fully characterized by the usual spectroscopic techniques.

3. Synthesis of mebendazole



(1) synthesis of Intermediate (2-amino-1H-benzo[d]imidazol-6-yl)(phenyl)methanone.

In a 100 mL hydrothermal reactor 3-amino-4-bromo-benzophenone (1 mmol), formamide (1.2 mmol)，CuI (0.1mmol), L1 (0.1 mmol), ammonia(2.0mL)and Na_2CO_3 (2.0 equiv) and 4.0 mL water were was stirred at 100 °C for 10 h. The reaction mixture was cooled to room temperature, quenched with water (6 mL), and diluted with ethyl acetate (10mL). The layers were separated and the aqueous layer was extracted with (3×10mL) ethyl acetate. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by silica-gel (eluent: petroleum ether/EtOAc=2:1) column chromatography to afford the Intermediate (2-amino-1H-benzo[d]imidazol-6-yl)(phenyl)methanone, yield 83%.

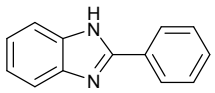
(2) synthesis of mebendazole

In a 100 mL Flask (2-amino-1H-benzo[d]imidazol-6-yl)(phenyl)methanone (0.5mmol), methyl carbonochloridate (0.5 mmol)，CuI (0.05mmol), 1,10-Phenanthroline (0.05 mmol), KOH(2.0 equiv) and 10.0 mL DMF were was stirred at 120 °C for 24 h. The reaction mixture was cooled to room temperature, quenched with water (10mL),

and diluted with ethyl acetate (20mL). The layers were separated and the aqueous layer was extracted with (3×10mL) ethyl acetate. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by silica-gel (eluent: petroleum ether/EtOAc=1:2) column chromatography to afford mebendazole, yield 88%.

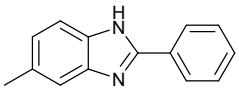
4. Experimental procedures and characterization data

2-phenyl-1H-benzo[d]imidazole[1]（Table 2, entry 1）：



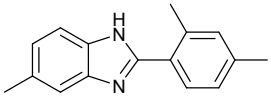
white solid; mp = 294–295 °C； ^{1}H NMR (400 MHz, Acetonitrile-d_3)： δ 7.25 – 7.29 (m, 2H), 7.53 – 7.66 (m, 5H), 8.13 (d, J = 4.0 Hz, 2H), 10.95 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 151.70, 144.29, 135.48, 130.65, 130.30, 129.42, 126.91, 123.00, 122.14, 119.35, 111.79; IR (KBr): 3047, 2966, 2846, 1537, 1462, 1441 cm^{-1}; ESI-MS (m/z): 195.1 $[M+H]^+$.

5-methyl-2-phenyl-1H-benzo[d]imidazole[2]（Table 2, entry 2）：



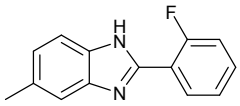
white solid; mp = 251–252 °C； ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 2.49 (s, 3H), 7.11 (d, J = 8.0 Hz, 1H), 7.40 – 7.62 (m, 5H), 8.11 (d, J = 8.0 Hz, 2H), 12.03 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 151.18, 135.73, 132.30, 130.77, 130.07, 129.34, 126.75, 124.42, 123.69, 118.90, 111.48, 21.83; IR (KBr): 3045, 2965, 2960, 2863, 1541, 1449, 1402, 1309 cm^{-1}; ESI-MS (m/z): 209.1 $[M+H]^+$.

2-(2,4-dimethylphenyl)-5-methyl-1H-benzo[d]imidazole（Table 2, entry 3）：



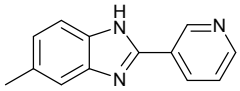
yellow solid; mp = 291–292 °C； ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 2.40 (s, 3H), 2.49 (s, 3H), 2.61 (s, 3H), 7.10 (d, J = 8.0 Hz, 1H), 7.16 – 7.24 (m, 2H), 7.41 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.62 (d, J =8.0 Hz, 1H), 10.52 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 151.94, 144.56, 142.37, 139.07, 137.21, 132.37, 129.69, 127.81, 126.97, 123.97, 123.23, 118.86, 111.28, 21.77, 21.49, 21.22; IR(KBr): 3020, 2967, 2915, 2658, 1738, 1619, 1452, 1399, 1265, 980, 803 cm^{-1}; ESI-MS (m/z): 237.1 $[M+H]^+$.

2-(2-fluorophenyl)-5-methyl-1H-benzo[d]imidazole（Table 2, entry 4）:



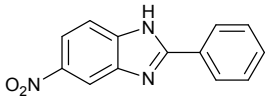
white solid; mp = 251–252 °C; ^{1}H NMR (400 MHz, Acetone-d_6): δ 2.47 (s, 3H), 7.10 (d, J = 8.0 Hz, 1H), 7.32 – 7.42 (m, 2H), 7.47 (s, 1H), 7.54 (ddd, J = 4.0, 8.0, 3.5 Hz, 2H), 8.45 (t, J = 8.0 Hz, 1H), 11.57 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6):δ 161.10, 158.61, 146.42, 141.72, 135.76, 133.59, 131.99 (d, $J_{C,F}$ = 8.0 Hz), 130.58 (d, $J_{C,F}$ = 3.0Hz), 125.43 (d, $J_{C,F}$ = 3.0 Hz), 123.93, 118.79 (d, $J_{C,F}$ = 12.0 Hz), 117.00 (d, $J_{C,F}$ = 21.0 Hz), 112.00, 21.80; IR(KBr): 3055, 2960, 2962, 2855, 1631, 1586, 1439, 1387, 1317, 1212 cm^{-1}; ESI-MS (m/z): 227.2 $[M+H]^+$.

5-methyl-2-(pyridin-3-yl)-1H-benzo[d]imidazole[1]（Table 2, entry 5）:



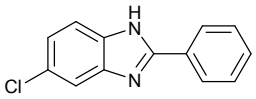
white solid; mp = 256–257 °C; ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 2.50 (s, 3H), 7.14 (d, J = 8.0 Hz, 1H), 7.46 (s, 1H), 7.50 – 7.57 (m, 2H), 8.40 (d, J = 8.0 Hz, 1H), 8.68 (d, J = 8.0 Hz, 1H), 9.28 (d, J = 1.8 Hz, 1H), 11.10 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 150.73, 148.87, 147.87, 139.43, 138.44, 134.05, 132.25, 126.70, 124.44, 124.38, 115.78, 114.90, 21.76; IR (KBr): 3045, 2960, 2888, 2878, 2795, 1636, 1579, 1455, 1465, 1317 cm^{-1}; ESI-MS (m/z): 210.1 $[M+H]^+$.

5-nitro-2-phenyl-1H-benzo[d]imidazole[3]（Table 2, entry 6）:



yellow solid; mp = 201–203 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.60 (d, J = 8.0 Hz, 4H), 8.18 (dd, J = 40.0, 8.0 Hz, 3H), 8.50 (s, 1H), 13.61 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.99, 142.99, 133.12, 131.17, 129.67, 129.35, 128.85, 127.35, 118.19, 115.01, 112.00; IR (KBr): 3042, 2990, 2920, 2853, 1621, 1596, 1481, 1339, 1591, 1262; ESI-MS (m/z): 240.1 $[M+ H]^+$.

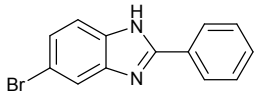
5-chloro-2-phenyl-1H-benzo[d]imidazole[1]（Table 2, entry 7）:



white solid; mp = 294–295 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.25 (t, J = 8.0 Hz, 1H), 7.52 – 7.76 (m, 5H), 8.20 (d, J = 4.0 Hz, 2H), 13.14 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.29, 143.95, 135.07, 130.98, 129.76, 129.50, 127.20, 125.20,

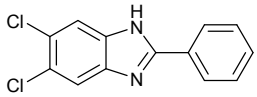
124.71, 120.40, 113.15; IR (KBr):3580, 2918, 1583, 1430, 1272,1108, 805, 691 cm^{-1}; ESI-MS (m/z): 229.1 $[M+H]^+$.

5-bromo-2-phenyl-1H-benzo[d]imidazole[1]（Table 2, entry 8）：



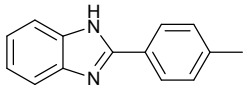
white solid; mp = 206–208 °C； ^1H NMR (400 MHz, Acetonitrile-d_3): δ 7.39 (d, J = 12.0 Hz, 1H), 7.54 – 7.83 (m, 5H), 8.12 (d, J = 8.0 Hz, 2H), 11.03 (s, 1H);^{13}C NMR (100 MHz, DMSO-d_6): δ 167.82, 152.95, 133.22, 130.62, 130.16, 129.74, 129.41, 128.95, 127.09, 125.41, 114.74; IR (KBr):3067, 2960, 2905, 2855, 1683, 1584, 1469, 1399, 701 cm^{-1} ; ESI-MS (m/z): 273.1 $[M+H]^+$.

5,6-dichloro-2-phenyl-1H-benzo[d]imidazole[4]（Table 2, entry 9）：



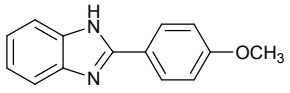
white solid; mp = 223–225 °C； ^1H NMR (400 MHz, Acetonitrile-d_3): δ 7.56 – 7.62 (m, 3H), 7.82 (d, J = 56.0 Hz, 2H), 8.11 (d, J = 8.0 Hz, 2H), 11.10 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.29, 143.94, 135.03, 130.98, 129.76, 129.50, 127.20, 125.19, 124.70, 120.40, 113.14; IR (KBr)：3057, 2997, 2952, 2910, 2860, 1646, 1576, 1544, 1464, 1297, 858, 783, 694 cm^{-1}; ESI-MS (m/z): 264.1 $[M+H]^+$.

2-(p-tolyl)-1H-benzo[d]imidazole[1]（Table 2, entry 10）：



white solid; mp = 279–280 °C； ^1H NMR (400 MHz, Acetonitrile-d_3): δ 2.45 (s, 3H), 7.26 (dd, J = 8.0, 4.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.62 (s, 2H), 8.02 (d, J = 8.0 Hz, 2H), 11.11 (s, 1H);^{13}C NMR (100 MHz, DMSO-d_6): δ 145.21, 143.07, 136.22, 134.30, 130.65, 130.16, 129.45, 127.04, 123.03, 120.56, 118.71, 113.08; IR (KBr): 3057, 2957, 2970, 2860, 1539, 1506, 1449, 1399 cm^{-1}; ESI-MS (m/z): 209.1 $[M+H]^+$.

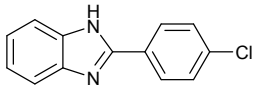
2-(4-methoxyphenyl)-1H-benzo[d]imidazole[1]（Table 2, entry 11）：



white solid; mp = 231–233 °C； ^1H NMR (400 MHz, Acetonitrile-d_3)：δ 3.90 (s, 3H), 7.11 (d, J = 8.0 Hz, 2H), 7.25 (dd, J = 4.0, 3.0 Hz, 2H), 7.56 – 7.65 (m, 2H), 8.07 (d, J

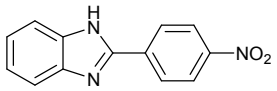
= 8.0 Hz, 2H), 10.98 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.06, 151.81, 144.38, 135.44, 128.46, 123.19, 122.50, 121.88, 118.95, 114.82, 111.47, 55.79; IR (KBr): 3052, 2957, 2952, 2860, 1611, 1499, 1391, 1292 cm^{-1}; ESI-MS (m/z): 225.1 $[M+H]^+$.

2-(4-chlorophenyl)-1H-benzo[d]imidazole[1]（Table 2, entry 12）:



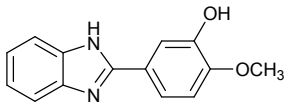
white solid; mp = 304–305 °C; ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 7.30 (s, 2H), 7.51 – 7.72 (m, 4H), 8.12 (d, J = 4.0 Hz, 2H), 10.96 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 150.62, 134.94, 129.49, 128.59, 122.72, 118.95, 112.16, 99.99, 34.93, 31.59, 30.30; IR (KBr): 3055, 2992, 2987,1541, 1447, 1404, 1317, 741 cm^{-1}; ESI-MS (m/z): 229.1 $[M+H]^+$.

2-(4-nitrophenyl)-1H-benzo[d]imidazole[5]（Table 2, entry 13）:



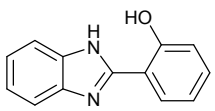
yellow solid; mp = 264–268 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.30 (s, 2H), 7.69 (d, J = 36.0 Hz, 2H), 8.44 (s, 4H), 13.32 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 149.46, 148.28, 136.50, 135.71, 130.81, 127.86, 124.74, 123.91, 122.85, 119.87, 112.29; IR (KBr): 3430, 2658, 2115, 1658, 1610, 1520, 1435, 1343 cm^{-1}; ESI-MS (m/z): 240.1 $[M+H]^+$.

5-(1H-benzo[d]imidazol-2-yl)-2-methoxyphenol[12]（Table 2, entry14）:



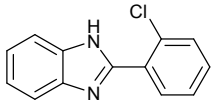
white solid; mp = 249–251 °C; ^{1}H NMR (400 MHz, Acetone-d_6): δ 3.94 (s, 3H), 7.11 (d, J = 8.0 Hz, 1H), 7.19 (dd, J = 8.0, 4.0 Hz, 2H), 7.57 (dd, J = 8.0, 4.0 Hz, 2H), 7.70 – 7.77 (m, 2H), 9.72 (s, 1H), 12.09 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 151.88, 149.85, 147.05, 139.59, 123.17, 122.27, 118.51, 115.13, 114.18, 112.63, 56.14; IR (KBr): 3309, 3060, 2965, 2930, 2838, 1596, 1429, 1314 cm^{-1}; ESI-MS (m/z): 241.1 $[M+H]^+$.

2-(1H-benzo[d]imidazol-2-yl)phenol[6]（Table 2, entry 15）:



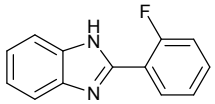
white solid; mp = 241–243 °C; ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 7.04 – 7.10 (m, 2H), 7.39 (d, J = 32.0 Hz, 3H), 7.69 (d, J = 28.0 Hz, 2H), 7.84 (d, J = 8.0 Hz, 1H), 11.11 (s, 1H), 13.20 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.47, 152.15, 141.33, 133.63, 132.18, 126.66, 123.73, 122.85, 119.57, 118.41, 117.64, 113.06, 111.98; IR (KBr): 3326, 3055, 1591, 1530, 1488 cm^{-1}; ESI-MS (m/z): 221.1 $[M+H]^+$.

2-(2-chlorophenyl)-1H-benzo[d]imidazole[5]（Table 2, entry 16）:



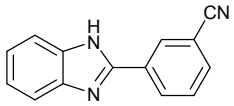
white solid; mp = 231–233 °C; ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 7.29 – 7.35 (m, 2H), 7.50 – 7.76 (m, 5H), 8.14 – 8.18 (m, 1H), 10.93 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 149.55, 143.67, 135.10, 132.53, 132.10, 131.64, 130.79, 130.44, 127.87, 123.19, 122.14, 119.54, 112.15; IR(KBr): 3065, 2957, 2908, 1541, 1447, 1404, 1317, 741 cm^{-1}; ESI-MS (m/z): 229.1 $[M+H]^+$.

2-(2-fluorophenyl)-1H-benzo[d]imidazole[7]（Table 2, entry 17）:



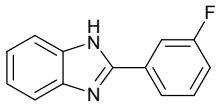
white solid; mp = 181–183 °C; ^{1}H NMR (400 MHz, Acetone-d_6): δ 7.23 – 7.29 (m, 2H), 7.34 – 7.44 (m, 2H), 7.54 – 7.60 (m, 1H), 7.68 (d, J = 2.7 Hz, 2H), 8.47 (d, J = 4.0 Hz, 1H), 11.67 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.16, 158.68, 146.87, 146.85 (d, $J_{C,F}$ = 2.0 Hz), 132.33, 132.25 (d, $J_{C,F}$ = 8.0 Hz), 130.70, 130.67 (d, $J_{C,F}$ = 3.0 Hz), 125.54, 125.50 (d, $J_{C,F}$ = 4.0 Hz), 122.76, 118.62, 118.50 (d, $J_{C,F}$ = 12.0 Hz), 117.06, 116.85 (d, $J_{C,F}$ = 21.0 Hz); IR(KBr): 3061, 2967, 2932, 1624, 1600, 1494, 1460, 1412, 1350 cm^{-1}; ESI-MS (m/z): 213.1 $[M+H]^+$.

3-(1H-benzo[d]imidazol-2-yl)benzonitrile[11]（Table 2, entry 18）:



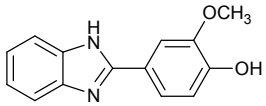
white solid; mp = 255–256 °C; ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 7.32 (dd, J = 8.0, 4.0 Hz, 2H), 7.67 (dd, J = 8.0, 4.0 Hz, 2H), 7.72 (t, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 8.45 (s, 1H), 10.99 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 149.65, 143.81, 135.35, 133.47, 131.81, 131.32, 130.73, 130.18, 123.05, 118.84, 112.62, 60.19, 21.18, 14.51; IR(KBr): 3052, 2995, 2900, 2845, 2234, 1541, 1477, 1369 cm^{-1}; ESI-MS (m/z): 220.1 $[M+H]^+$.

2-(3-fluorophenyl)-1H-benzo[d]imidazole[11]（Table 2, entry 19）:



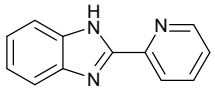
white solid; mp = 255–257 °C； ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 7.30 (dd, J = 8.0, 4.0 Hz, 3H), 7.55 – 7.68 (m, 3H), 7.86 – 7.96 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.13, 161.71, 150.39, 150.36 (d, $J_{C,F}$ = 3.0 Hz), 139.68, 132.95, 132.87 (d, $J_{C,F}$ = 8.0 Hz), 131.60, 131.51 (d, $J_{C,F}$ = 9.0 Hz), 122.99, 122.97, 122.89 (d, $J_{C,F}$ = 8.0 Hz), 117.14, 116.93 (d, $J_{C,F}$ = 21.0 Hz), 115.71, 113.62, 113.38 (d, $J_{C,F}$ = 24.0 Hz); IR(KBr): 3060, 2920, 2848, 1620, 1486, 1464, 1394, 1314, 1205 cm^{-1}; ESI-MS (m/z): 213.1 $[M+H]^+$.

4-(1H-benzo[d]imidazol-2-yl)-2-methoxyphenol[8]（Table 2, entry 20）：



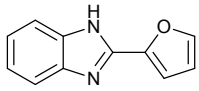
white solid; mp = 216–218 °C； ^{1}H NMR (400 MHz, Acetone-d_6): δ 3.97 (s, 3H), 6.98 (d, J = 8.0 Hz, 1H), 7.19 (dd, J = 8.0, 4.0 Hz, 2H), 7.57 (dd, J = 6.0, 3.2 Hz, 2H), 7.71 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 4.0 Hz, 1H), 8.12 (s, 1H), 11.07 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.20, 148.86, 148.29, 122.13, 121.86, 120.16, 116.12, 114.90, 110.89, 56.17, 30.30, 29.47, 22.51, 14.39; IR(KBr): 3506, 3336, 3057, 2960, 2922, 2853, 1601, 1506, 1460, 1325 cm^{-1}; ESI-MS (m/z): 241.1 $[M+H]^+$.

2-(pyridin-2-yl)-1H-benzo[d]imidazole[2]（Table 2, entry 21）：



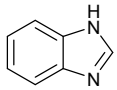
yellow solid; mp = 216–219 °C； ^{1}H NMR (400 MHz, Acetone-d_6): δ 7.25 – 7.28 (m, 2H), 7.48 (d, J = 1.6 Hz, 1H), 7.70 (dd, J = 8.0, 4.0 Hz, 2H), 7.97 – 8.01 (m, 1H), 8.43 (d, J = 8.0 Hz, 1H), 8.69 (d, J = 4.0 Hz, 1H), 12.10 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 151.19, 149.81, 148.91, 139.84, 137.97, 125.16, 123.01, 121.88, 116.11; IR (KBr): 3057, 2970, 1601, 1544, 1500, 1404, 1312 cm^{-1}; ESI-MS (m/z): 196.1 $[M+H]^+$.

2-(furan-2-yl)-1H-benzo[d]imidazole[12]（Table 2, entry 22）：



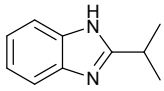
brown solid; mp = 287–289 °C； ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 7.57 (d, J = 1.6 Hz, 3H), 7.32 – 7.29 (m, 2H), 7.24 (d, J = 4.0 Hz, 1H), 6.61 (dd, J = 3.6, 2.0 Hz, 1H). ^{13}C NMR (100 MHz, CD_3OD-d_4) δ 176.49, 149.03, 148.32, 147.93, 126.63, 121.41, 115.75, 114.37, 91.81, 56.65；IR(KBr): 3057, 1631, 1525, 1411, 1360, 1275, 1234 cm^{-1}; ESI-MS (m/z): 185.1 $[M+H]^+$.

1H-benzo[d]imidazole[13]（Table 2, entry 23）：



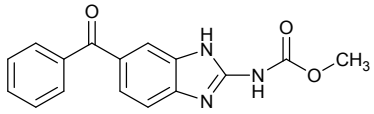
white solid; mp = 168–170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.13 (s, 1H), 7.71 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.33 (dt, *J* = 7.2, 3.6 Hz, 2H). ^{13}C NMR (100 MHz, CD_3OD-d_4) δ 141.07, 137.41, 122.69, 122.41, 122.11, 114.83, 99.99; IR(KBr):3113, 3052, 1770, 1580, 1458, 1406, 1243, 747 cm^{-1}; ESI-MS (m/z): 185.1 $[M+H]^+$.

2-isopropyl-1H-benzo[d]imidazole[9]（Table 2, entry 24）:



yellow solid; mp = 232–234 °C； ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 1.41 (d, *J* = 7.0 Hz, 6H), 3.21 (m, 1H), 7.18 (dd, *J* = 6.0, 4.0 Hz, 2H), 7.51 (dd, *J* = 8.0, 4.0 Hz, 2H); ^{13}C NMR (100 MHz, Acetone-d_6): δ 205.44, 205.05, 159.75, 121.21, 114.31, 30.79, 28.86, 28.79, 20.88; IR (KBr): 3051, 2971, 2883, 1534, 1455, 1415, 1273 cm^{-1}; ESI-MS (m/z): 161.1 $[M+H]^+$.

Mebendazole[10]



white solid; mp = 288–289 °C； ^{1}H NMR (400 MHz, Acetonitrile-d_3): δ 3.84 (s, 3H), 7.54 – 7.60 (m, 4H), 7.68 (dd, *J* = 16.0, 4.0 Hz, 3H), 7.80 (d, *J* = 4.0 Hz, 2H), 7.94 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 196.02, 154.88, 149.93, 138.89, 132.27, 130.28, 129.77, 128.80, 124.15, 53.11; IR(KBr):3400, 2750, 1718, 1648 cm^{-1}; ESI-MS (m/z): 119.1 $[M+H]^+$.

5.References

1 C. Chen, C. Chen, B. Li, J. Tao, and J. Peng, *Molecules.*, 2012, **17**, 12506-12520.

2 O. Ravi, A. Shaikh, A. Upare, K. K. Singarapu, and S. R. Bathula, *J. Org. Chem.*, 2017, **82**, 4422-4428.

3 Y. Qu, L. Pan, Z. Wu and X. Zhou, *Tetrahedron*, 2013, **69**, 1717–1719.

4 S. Park, J. Jung and E. J. Cho, *Eur. J. Org. Chem.*, 2014, **2014**, 4148-4154.

5 M. Saha, P. Mukherjee and A. R. Das, *Tetrahedron Lett.*, 2017, **58**, 1046–1049.

6 H. Sharghi, O. Asemani, and R. Khalifeh, *Synthetic Commun.*, 2008, **38**, 1128-1136.

7 M. L. P. R. Alapati, S. R. Abburi, S. B. Mukkamala, and Rao, M. Krishnaji, *Synthetic Commun.*, 2015, **45**, 2436-2443.

8 P. Ghosh and R. Subba, *Tetrahedron Lett.*, 2015, **56**, 2691–2694.

9 P. Sun and Z. Hu, *J. Heterocyclic. Chem.,* 2006, **43**, 773-775.

10 N. Viswanathan and A. R. Sidhaye, *Indian. J. Chem. B*, 1985, **24**, 948-951.

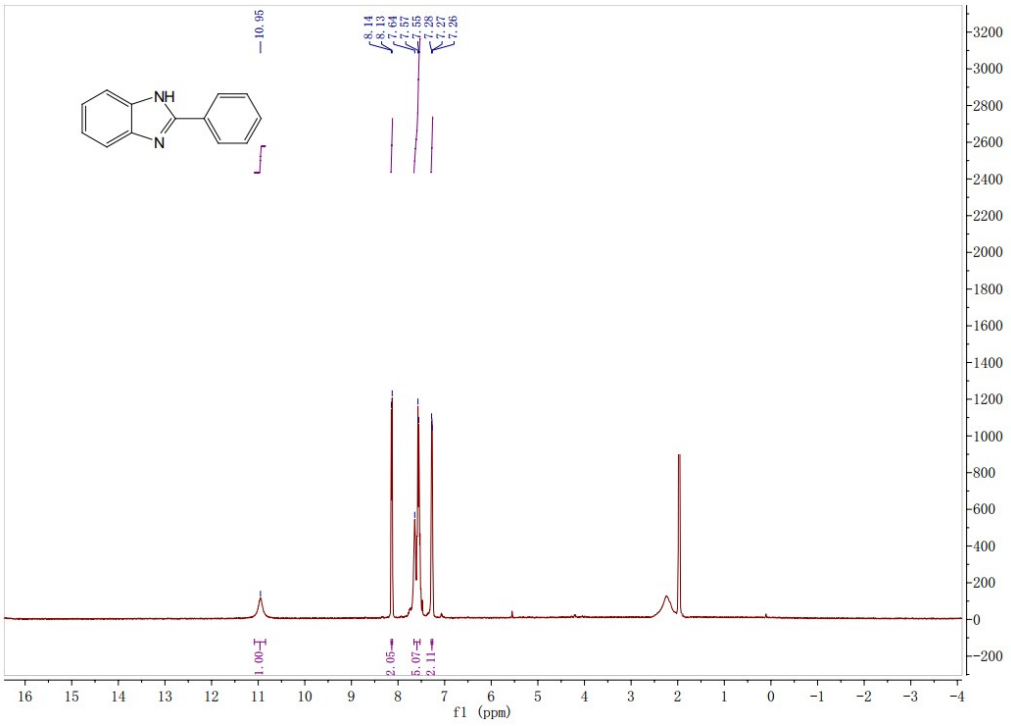
11 D. Qiu, H. Wei, L. Zhou and Q. Zeng, *Appl. Organometal. Chem.,* 2014, **28**, 109-112.

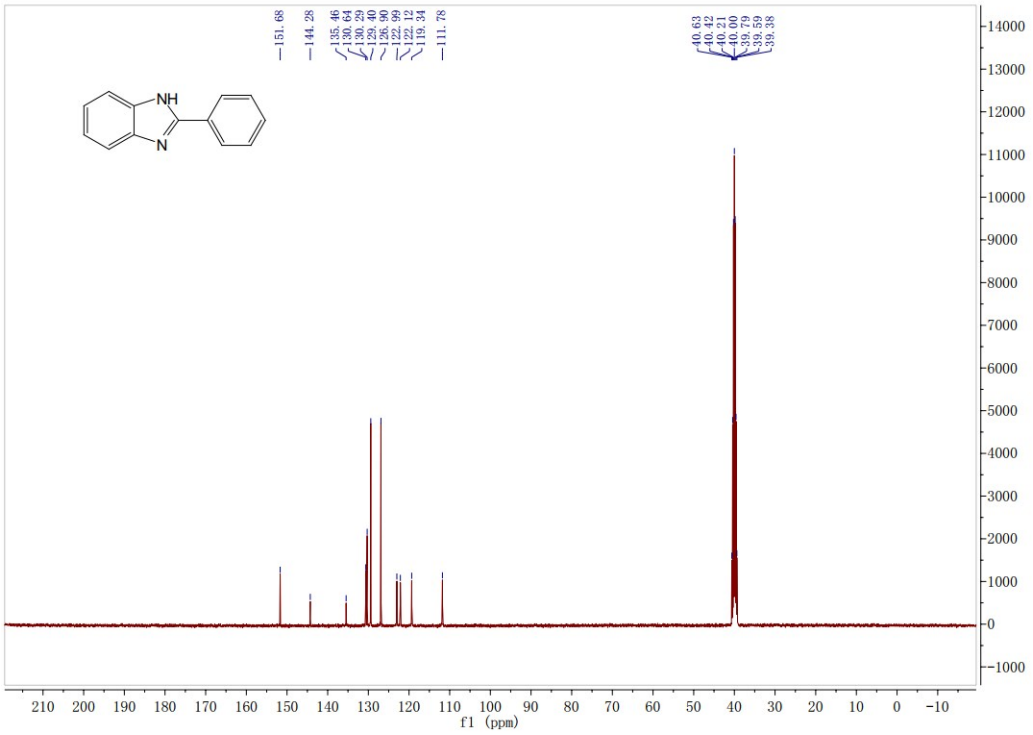
12 J. Qiu, Y. Zhang, C. Hua, X. Gou, B. Chen, and J. Zhao, *Heterocycles,* 2015, **91**, 2153-2162.

13 Y. Kim, M. R. Kumar, N. Park, Y. Heo and S. Lee, *J. Org. Chem*., 2011, **76**, 9577-9583.

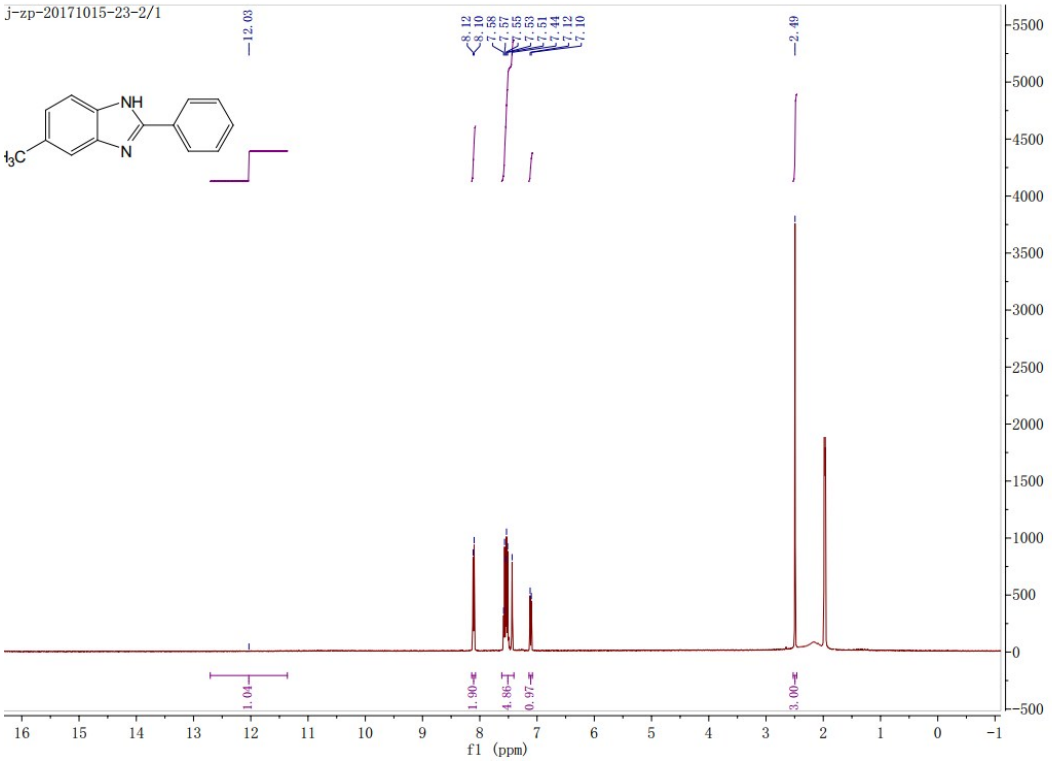
6.^{1}H NMR and ^{13}C NMR spectra for the products

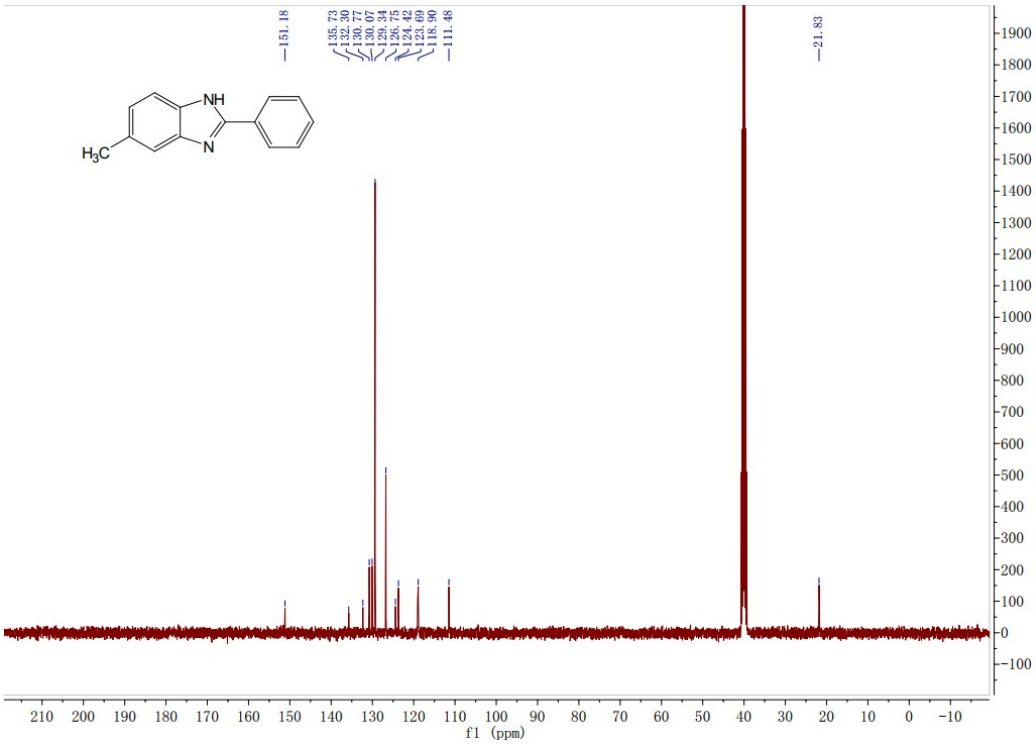
2-phenyl-1H-benzo[d]imidazole[1] (Table 2, entry 1)



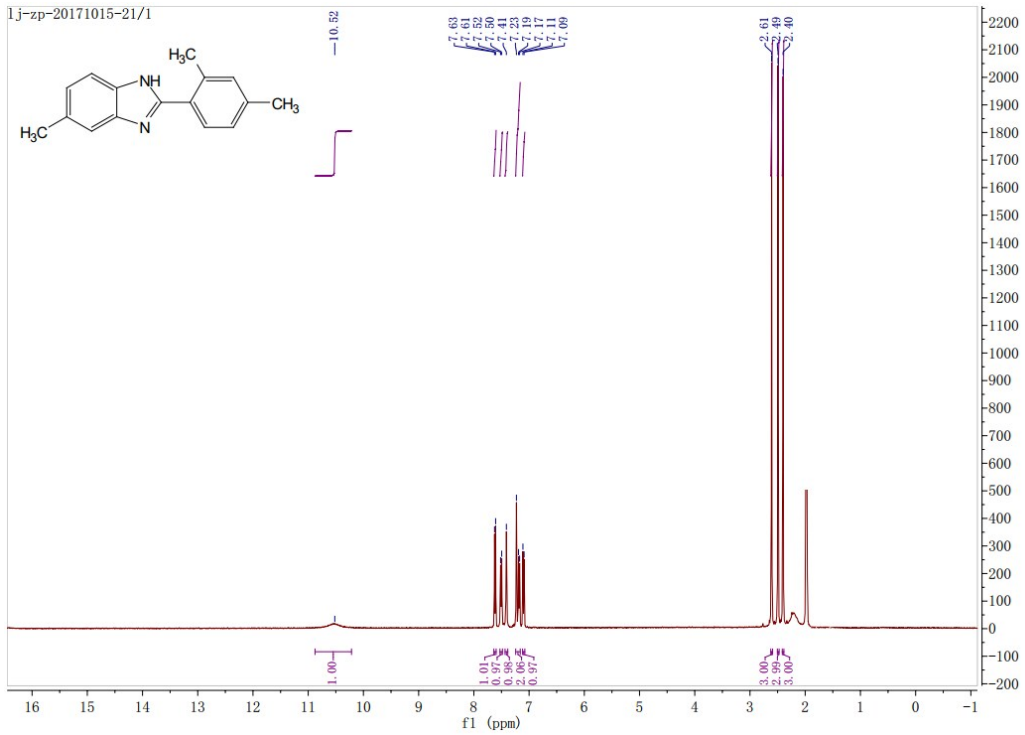


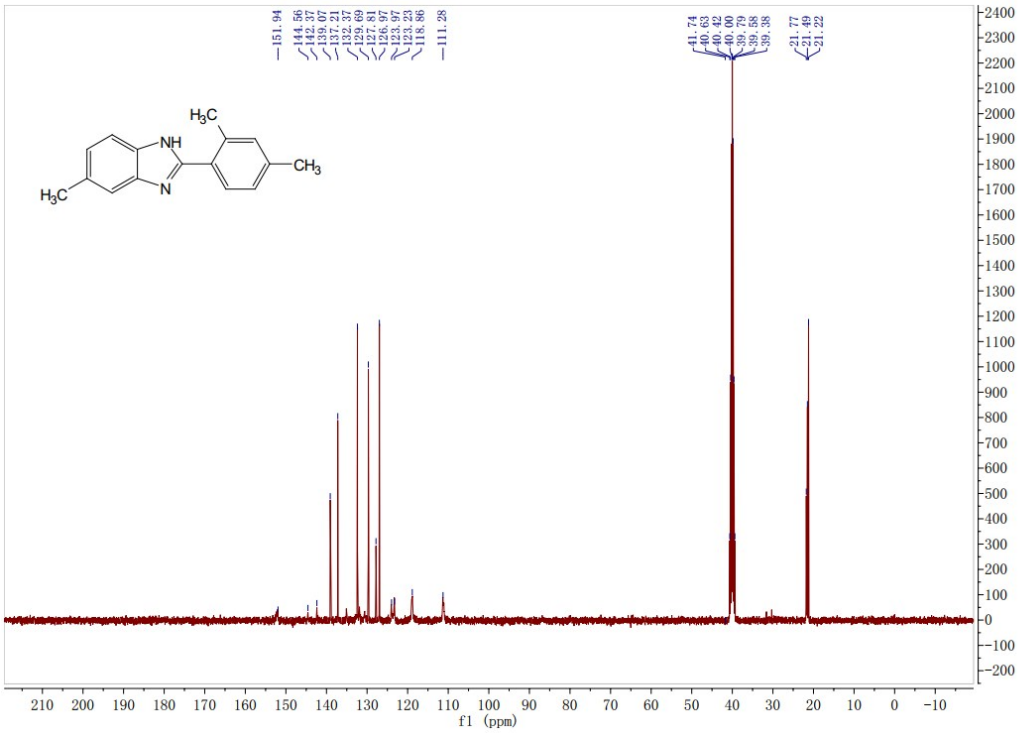
5-methyl-2-phenyl-1H-benzo[d]imidazole[3] (Table 2, entry 2)



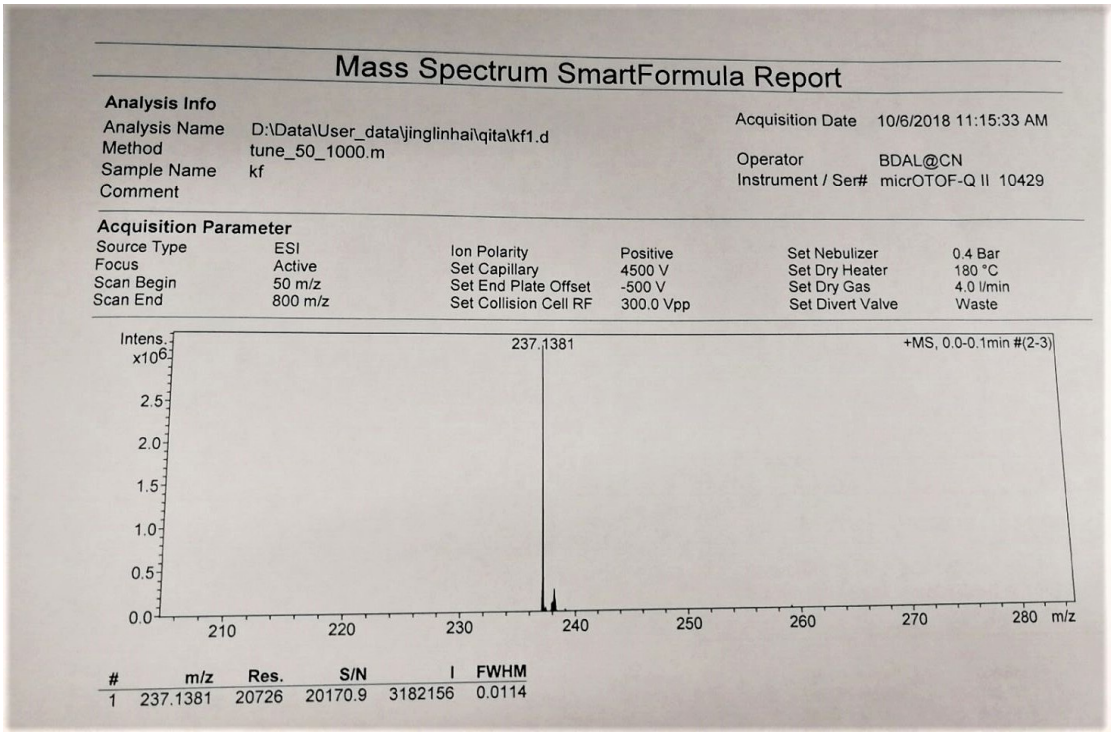


2-(2,4-dimethylphenyl)-5-methyl-1H-benzo[d]imidazole（Table 2, entry 3）

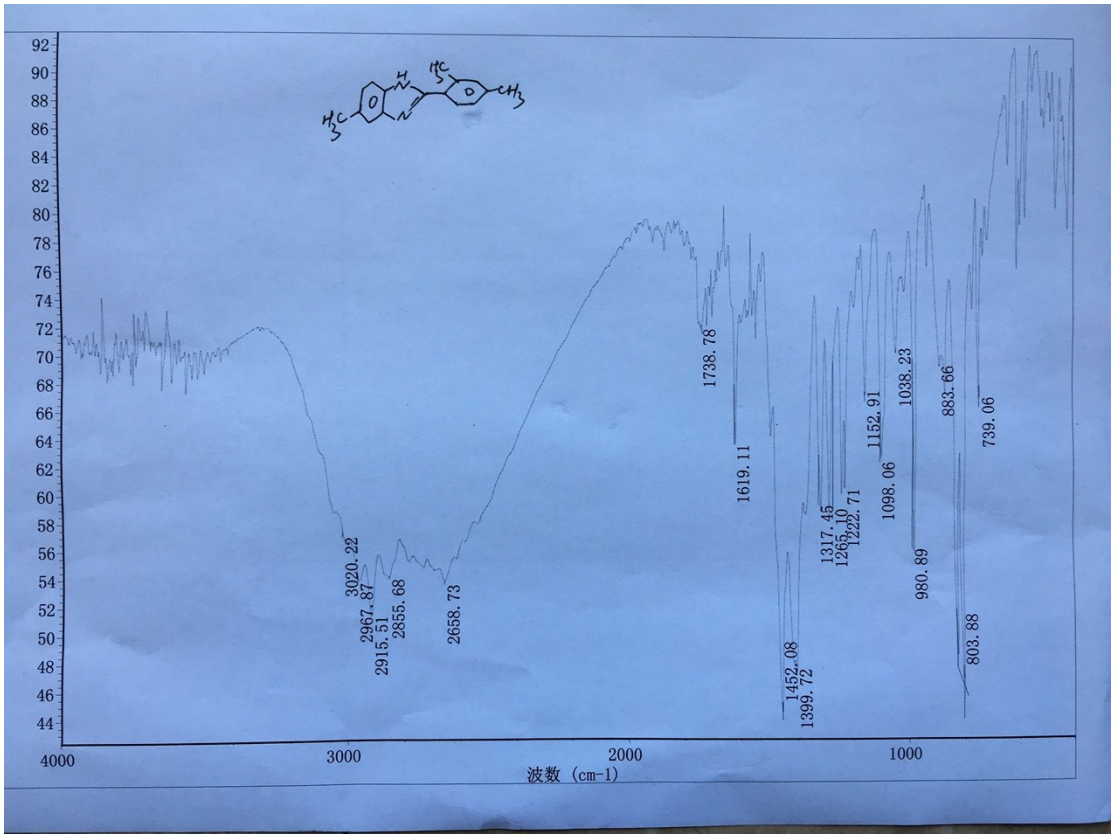



151.94
144.56
142.37
139.07
137.21
132.37
129.69
127.84
125.97
123.23
118.86
111.28
41.74
40.63
40.42
40.00
39.79
39.58
39.38
21.77
21.49
21.22
H3C
NH
N
CH3
H3C
f1 (ppm)

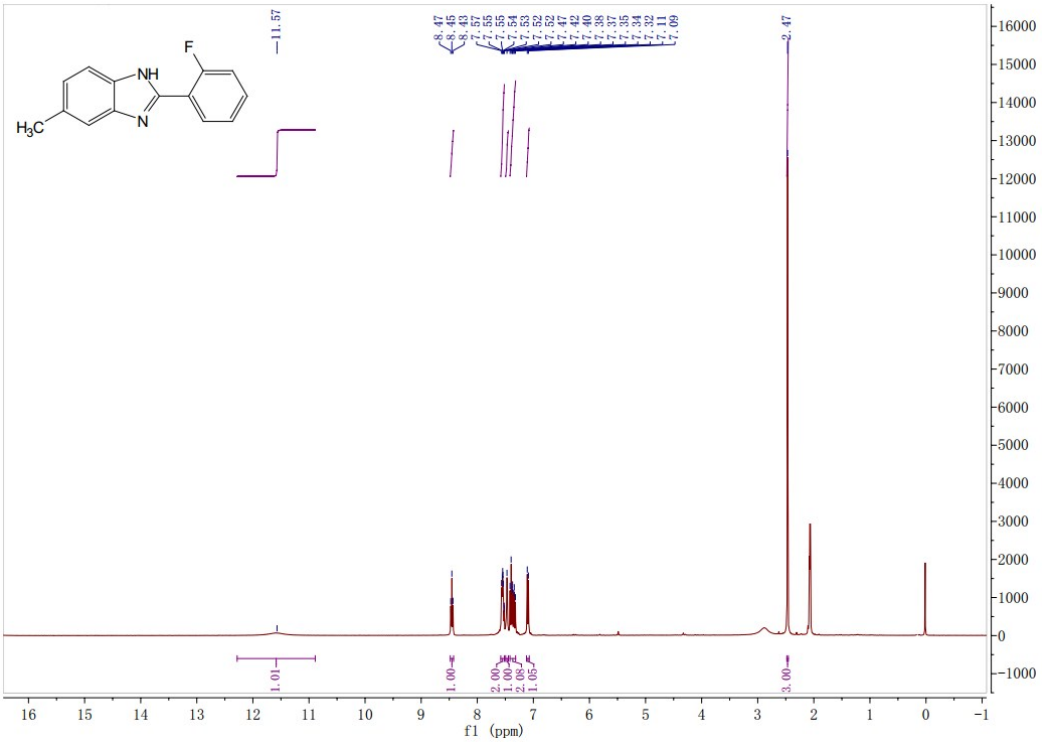
HRMS:

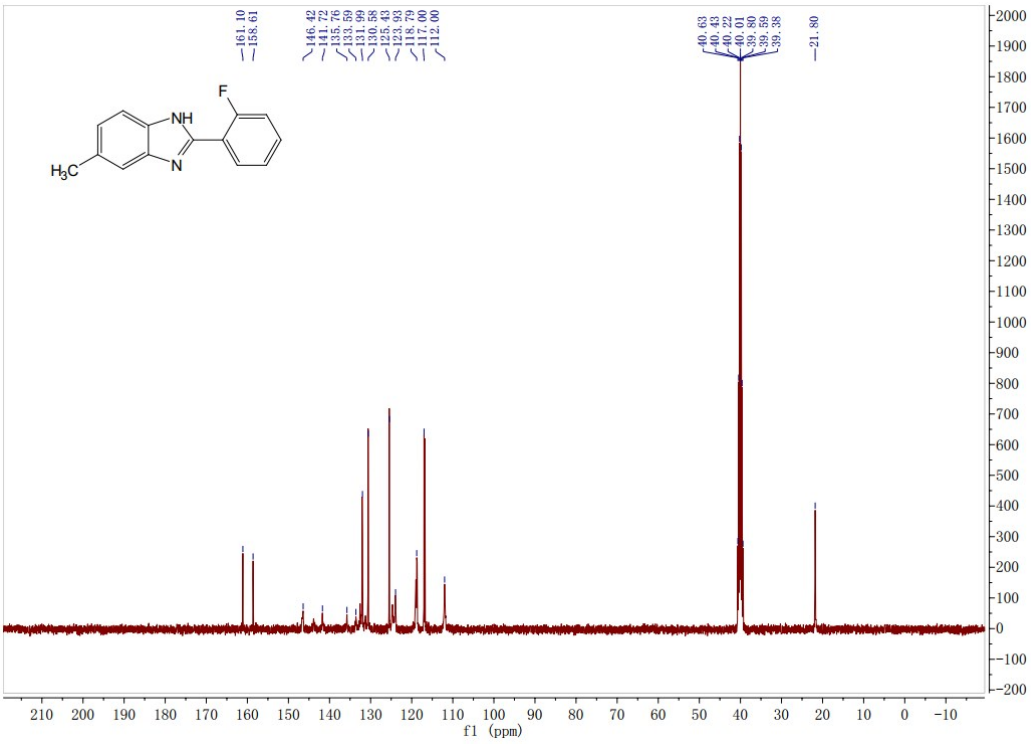

Mass Spectrum SmartFormula Report
Analysis Info
Analysis Name D:\Data\User_data\jinglinhai\qita\kf1.d
Method tune_50_1000.m
Sample Name kf
Comment
Acquisition Date 10/6/2018 11:15:33 AM
Operator BDAL@CN
Instrument / Ser# micrOTOF-Q II 10429
Acquisition Parameter
Source Type ESI
Focus Active
Scan Begin 50 m/z
Scan End 800 m/z
Ion Polarity Positive
Set Capillary 4500 V
Set End Plate Offset -500 V
Set Collision Cell RF 300.0 Vpp
Set Nebulizer 0.4 Bar
Set Dry Heater 180 °C
Set Dry Gas 4.0 l/min
Set Divert Valve Waste
Intens.
x10^6
237.1381
+MS, 0.0-0.1min #(2-3)
m/z
m/z Res. S/N I FWHM
1 237.1381 20726 20170.9 3182156 0.0114

IR：

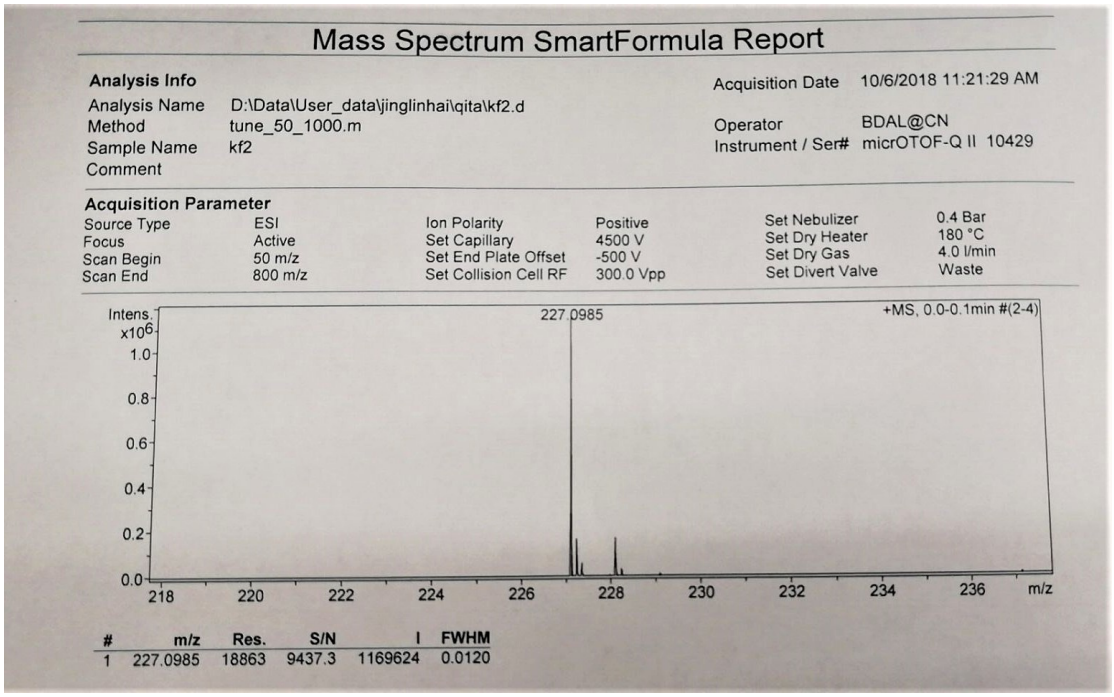


2-(2-fluorophenyl)-5-methyl-1H-benzo[d]imidazole（Table 2, entry 4）

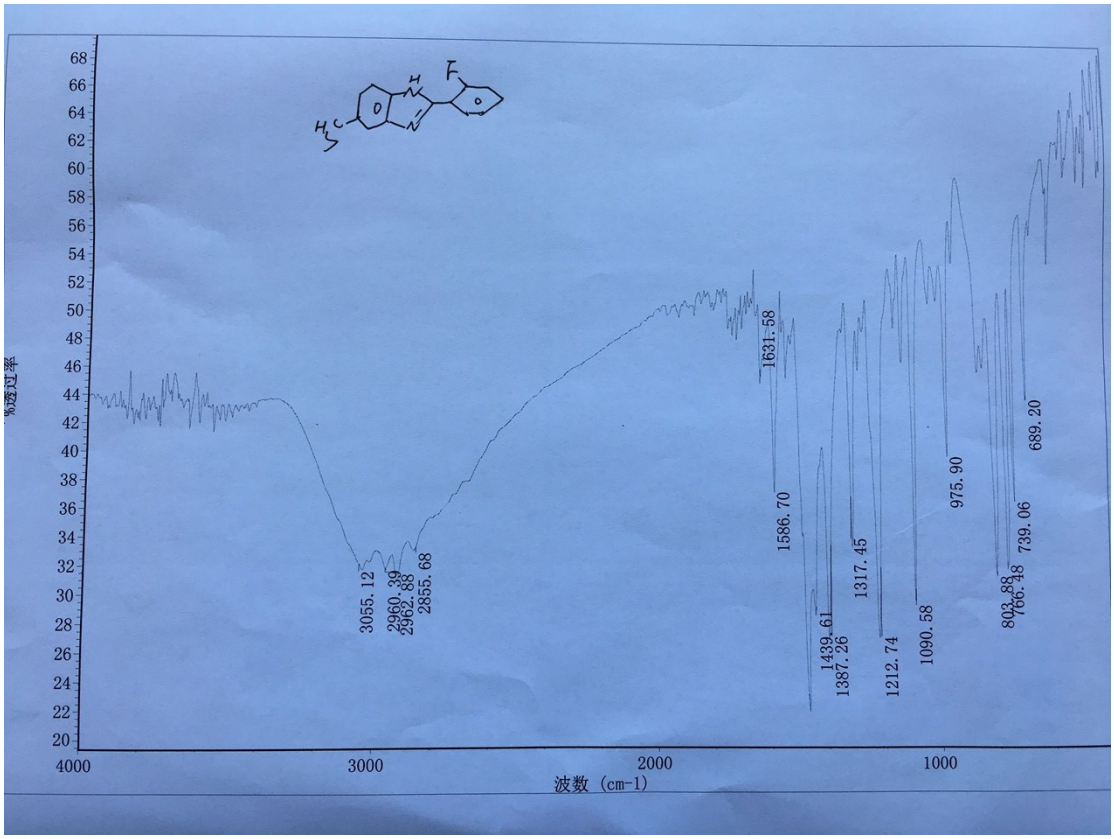



161.10
158.61
146.42
141.72
135.76
133.59
131.99
130.58
125.43
123.93
118.79
117.09
112.00
40.63
40.43
40.22
40.01
39.80
39.59
39.38
21.80
F
NH
N
H3C
f1 (ppm)

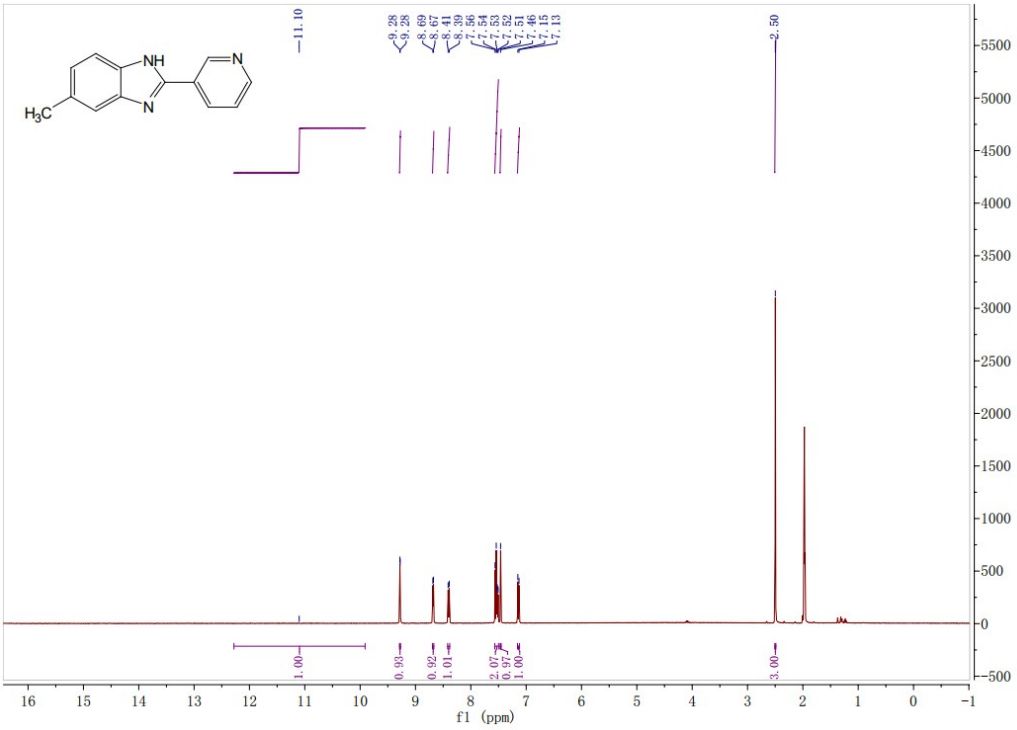
HRMS:

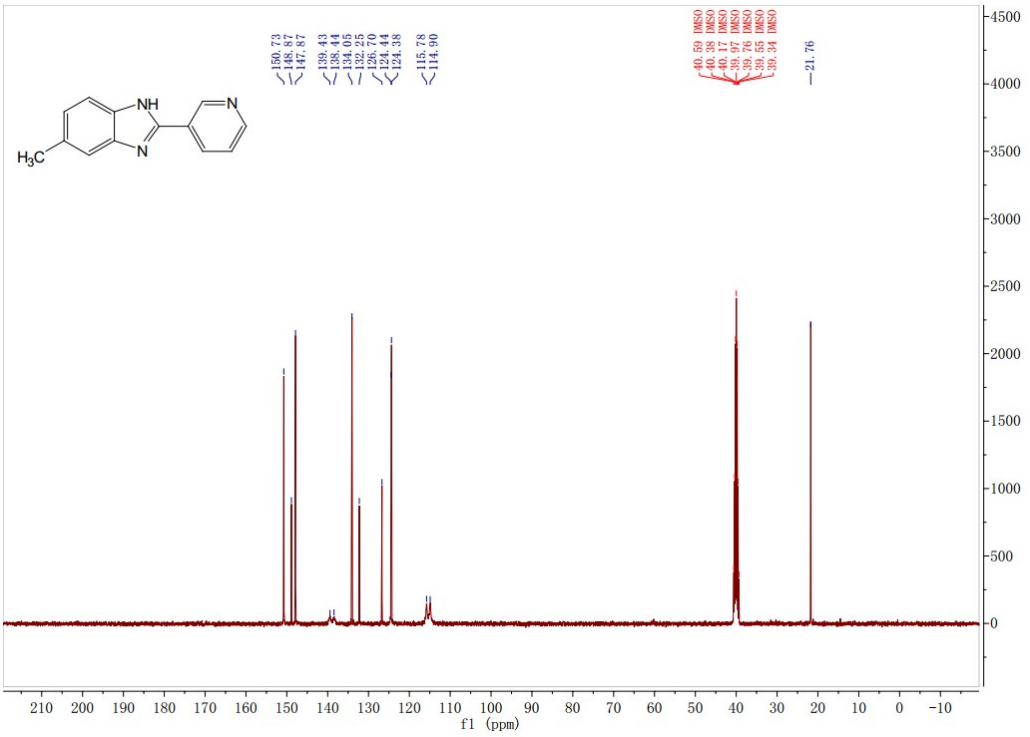

Mass Spectrum SmartFormula Report
Analysis Info
Analysis Name D:\Data\User_data\jinglinhai\qita\kf2.d
Method tune_50_1000.m
Sample Name kf2
Comment
Acquisition Date 10/6/2018 11:21:29 AM
Operator BDAL@CN
Instrument / Ser# micrOTOF-Q II 10429
Acquisition Parameter
Source Type ESI
Focus Active
Scan Begin 50 m/z
Scan End 800 m/z
Ion Polarity Positive
Set Capillary 4500 V
Set End Plate Offset -500 V
Set Collision Cell RF 300.0 Vpp
Set Nebulizer 0.4 Bar
Set Dry Heater 180 °C
Set Dry Gas 4.0 l/min
Set Divert Valve Waste
Intens.
x10^6
227.0985
+MS, 0.0-0.1min #(2-4)
m/z
m/z Res. S/N I FWHM
1 227.0985 18863 9437.3 1169624 0.0120

IR:

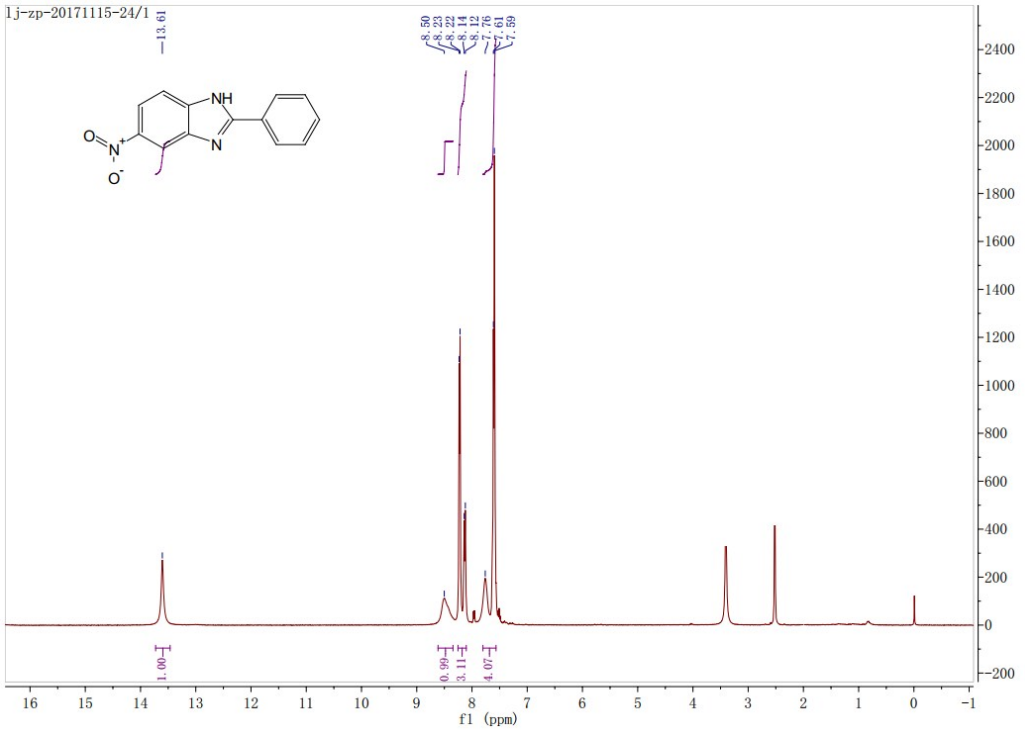


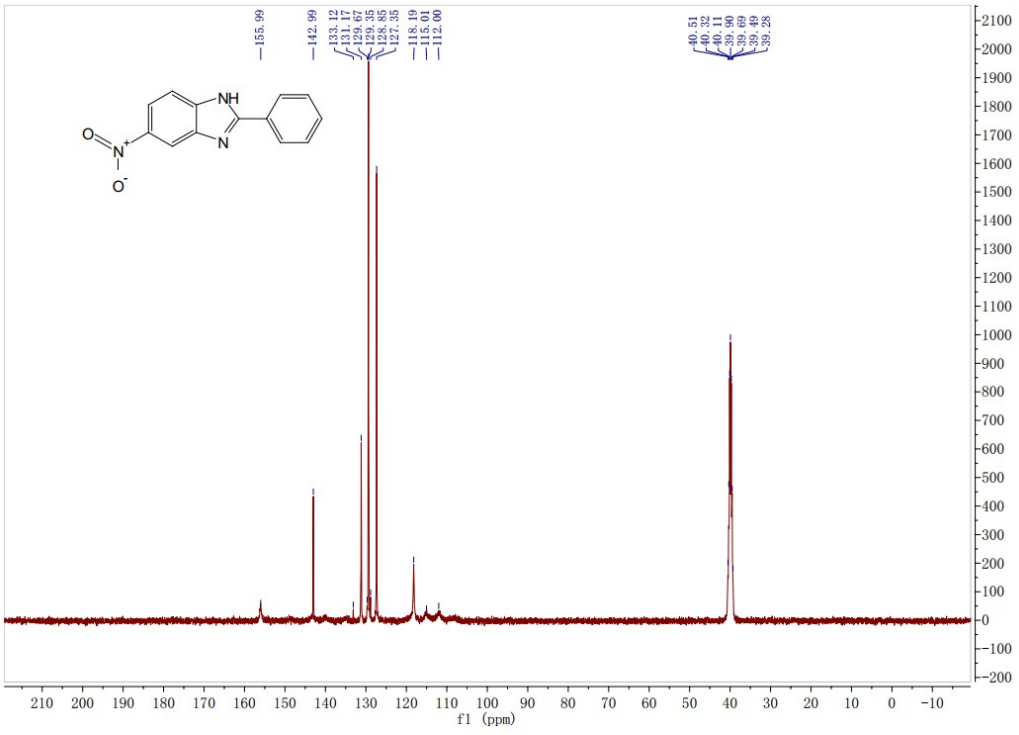
5-methyl-2-(pyridin-3-yl)-1H-benzo[d]imidazole[1]（Table 2, entry 5）



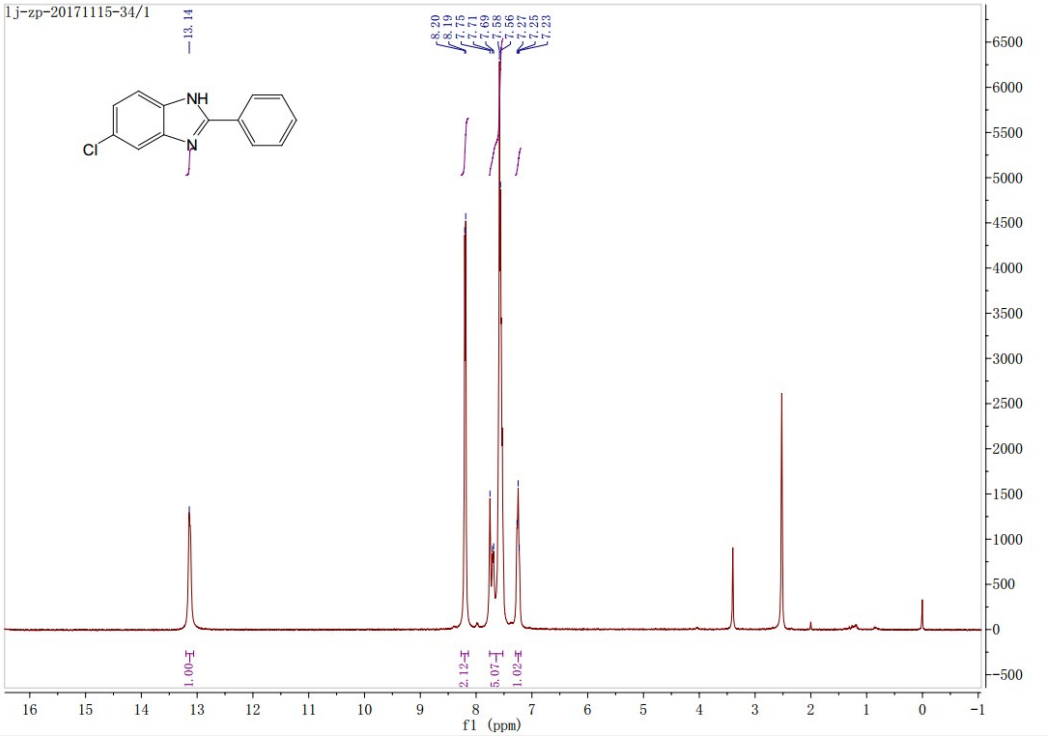


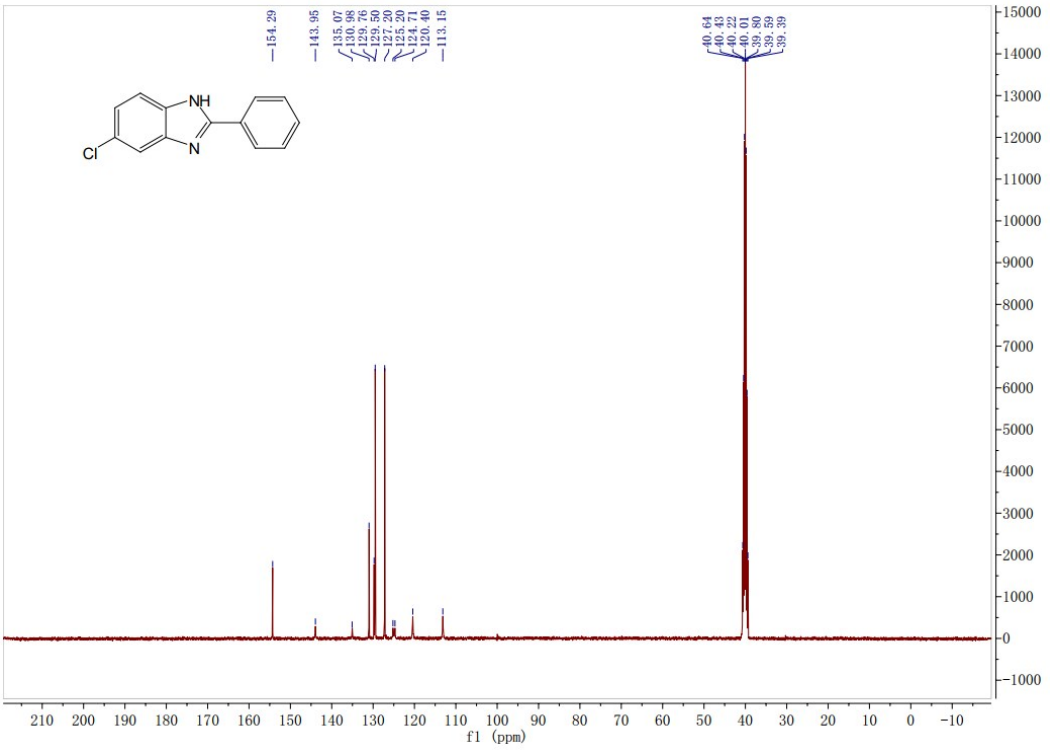
5-nitro-2-phenyl-1H-benzo[d]imidazole[8]（Table 2, entry 6）



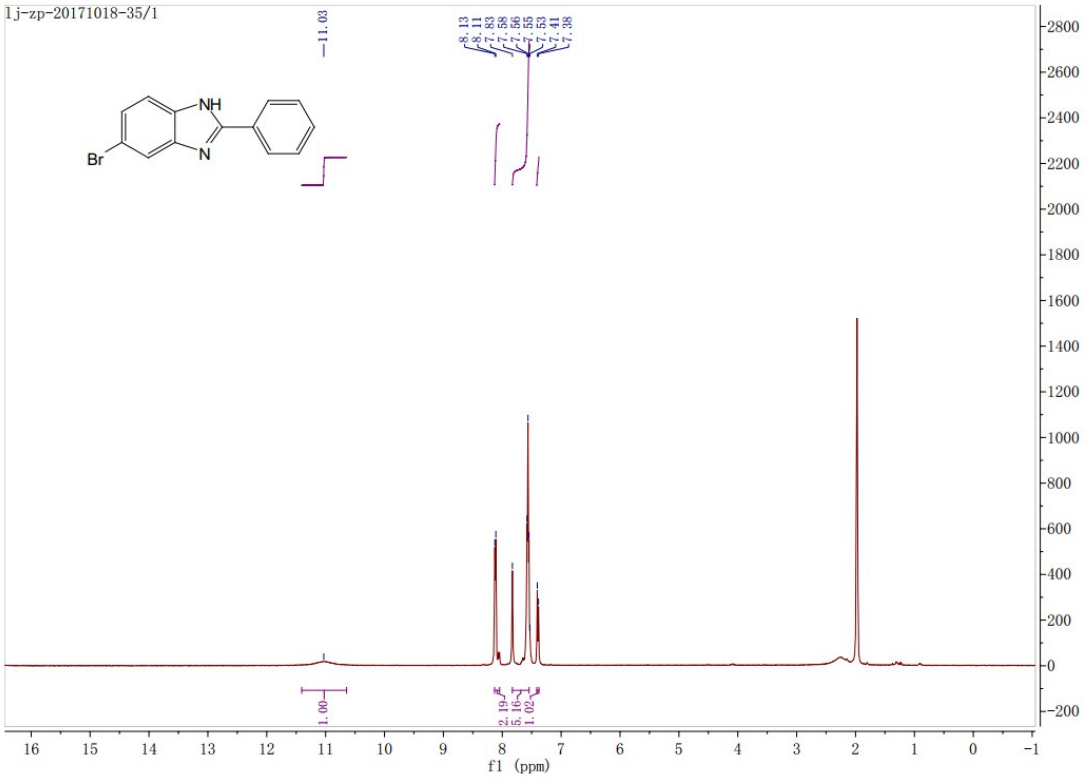


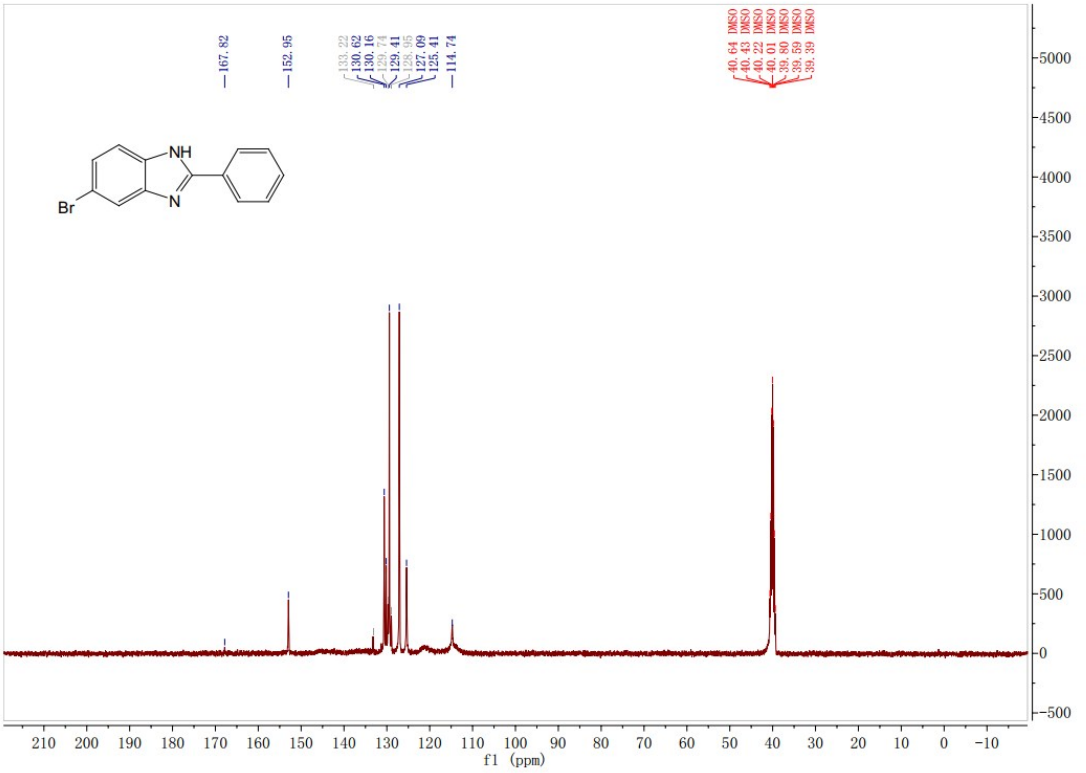
5-chloro-2-phenyl-1H-benzo[d]imidazole[1]（Table 2, entry 7）



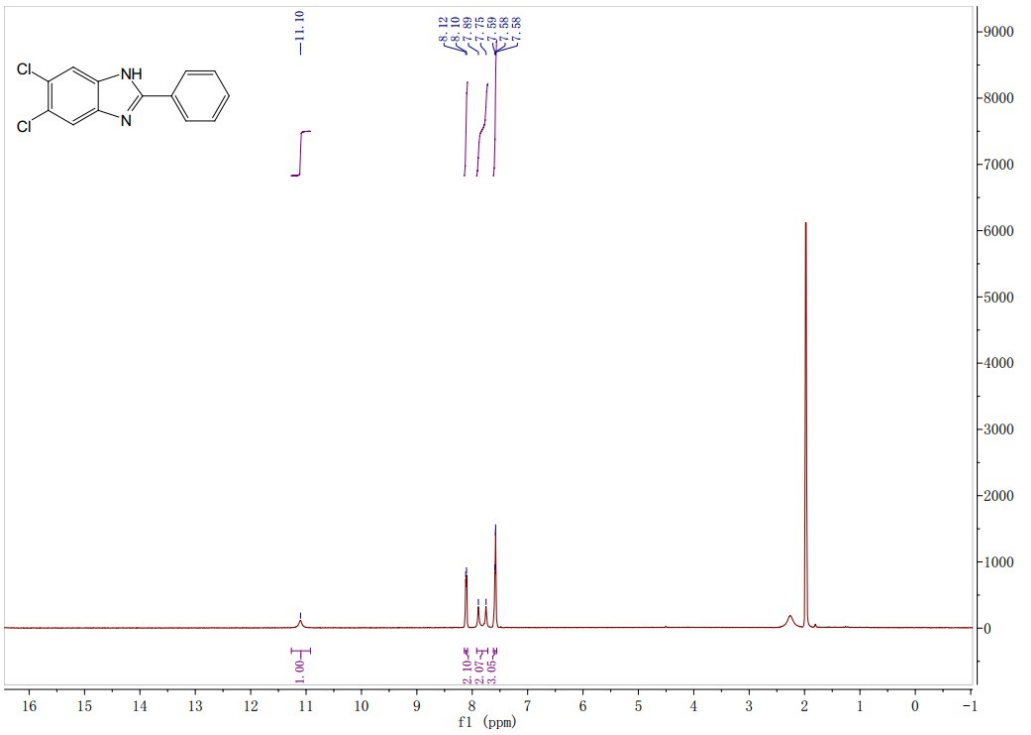


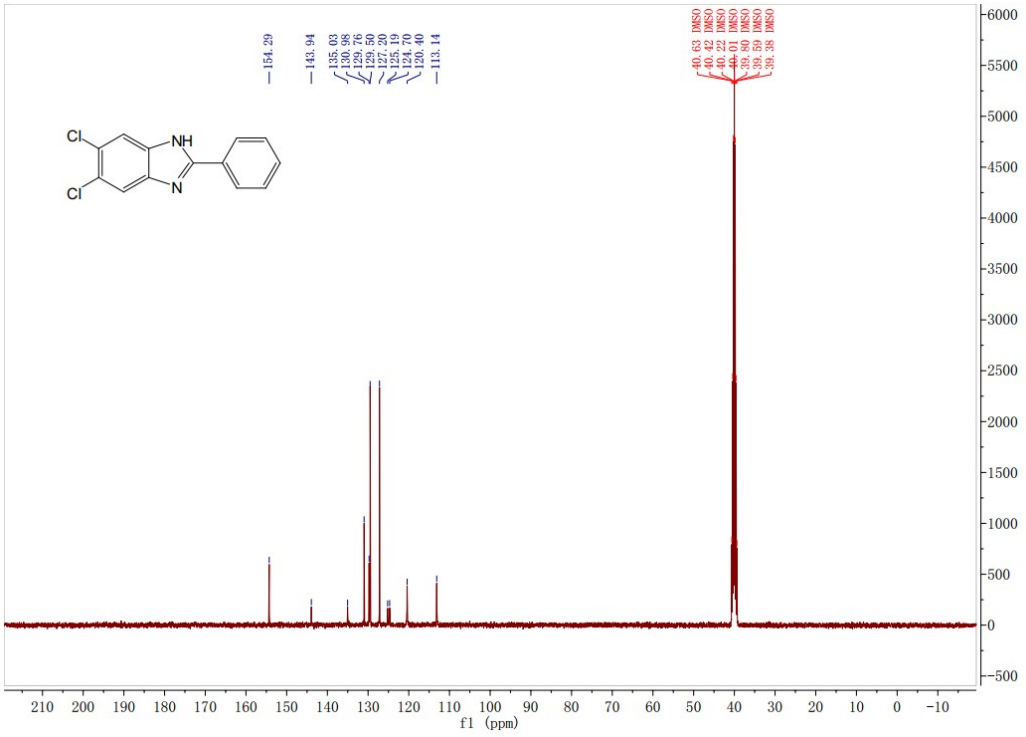
5-bromo-2-phenyl-1H-benzo[d]imidazole[1]（Table 2, entry 8）



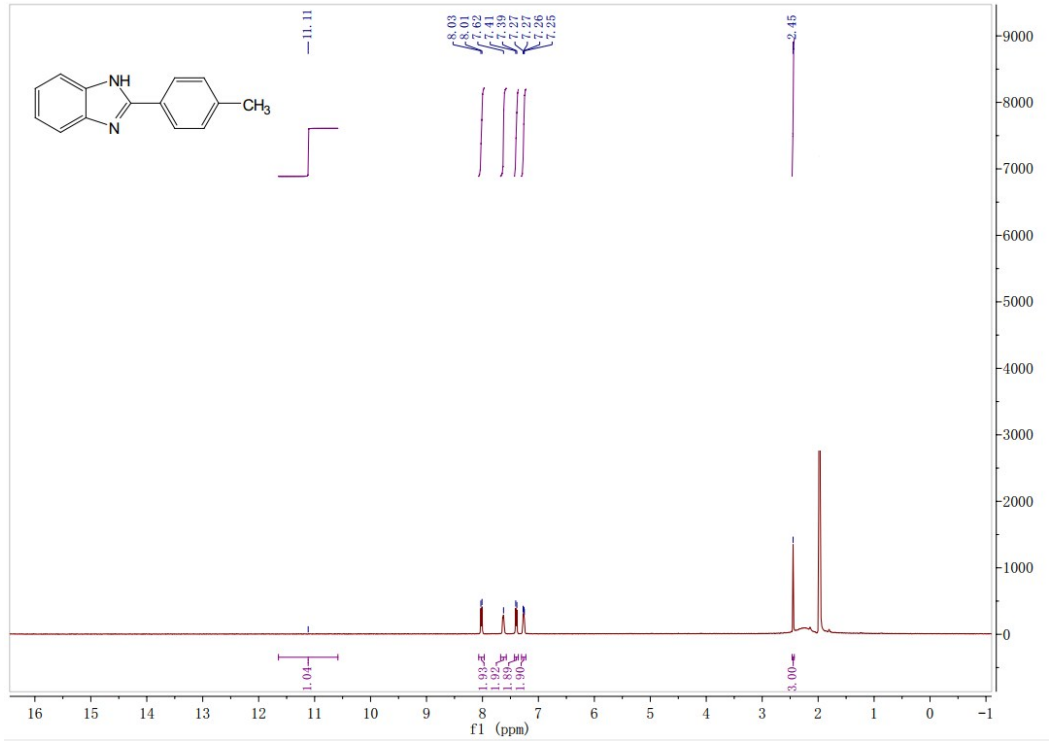


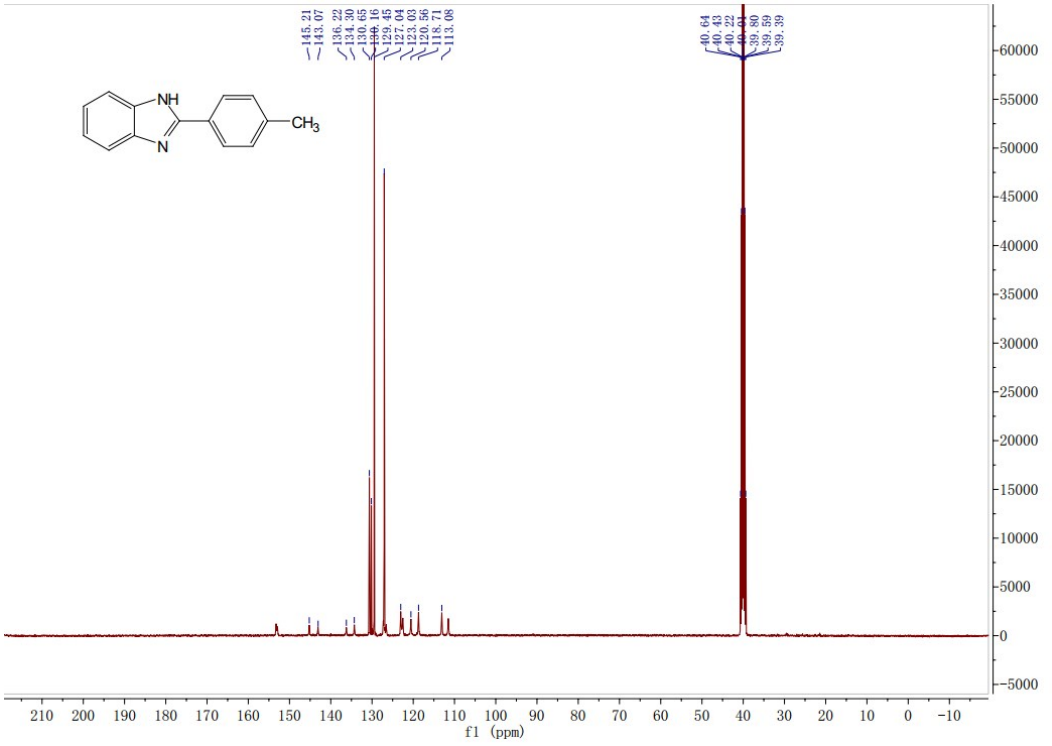
5,6-dichloro-2-phenyl-1H-benzo[d]imidazole[6]（Table 2, entry 9）



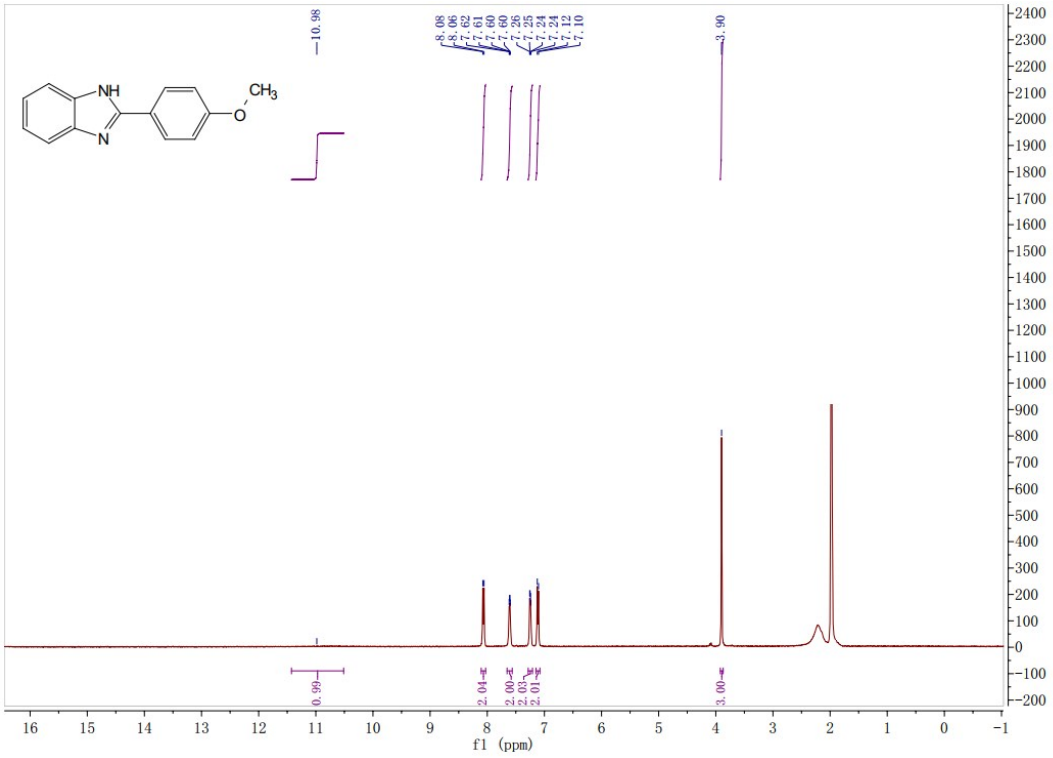


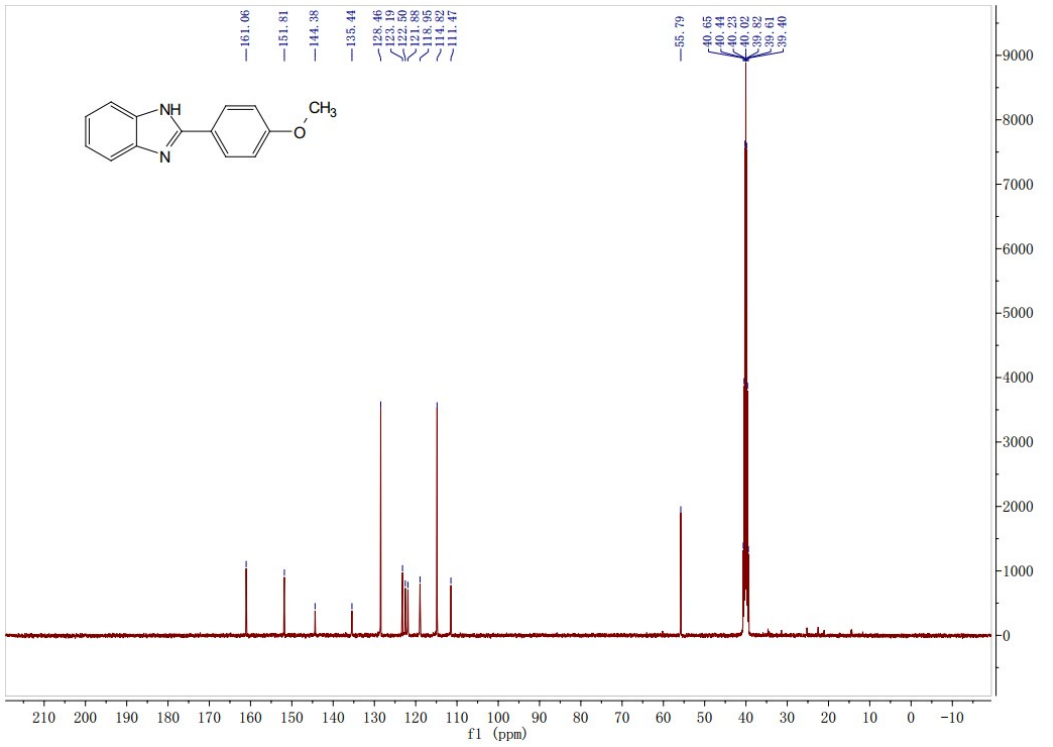
2-(p-tolyl)-1H-benzo[d]imidazole[1]（Table 2, entry 10）



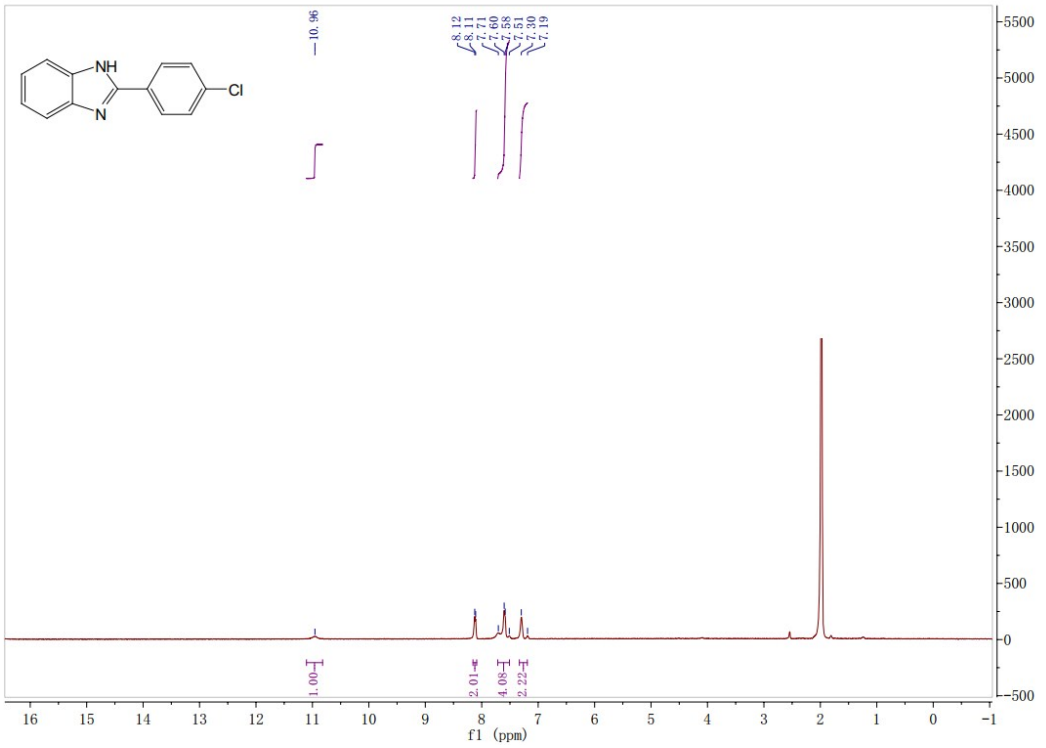


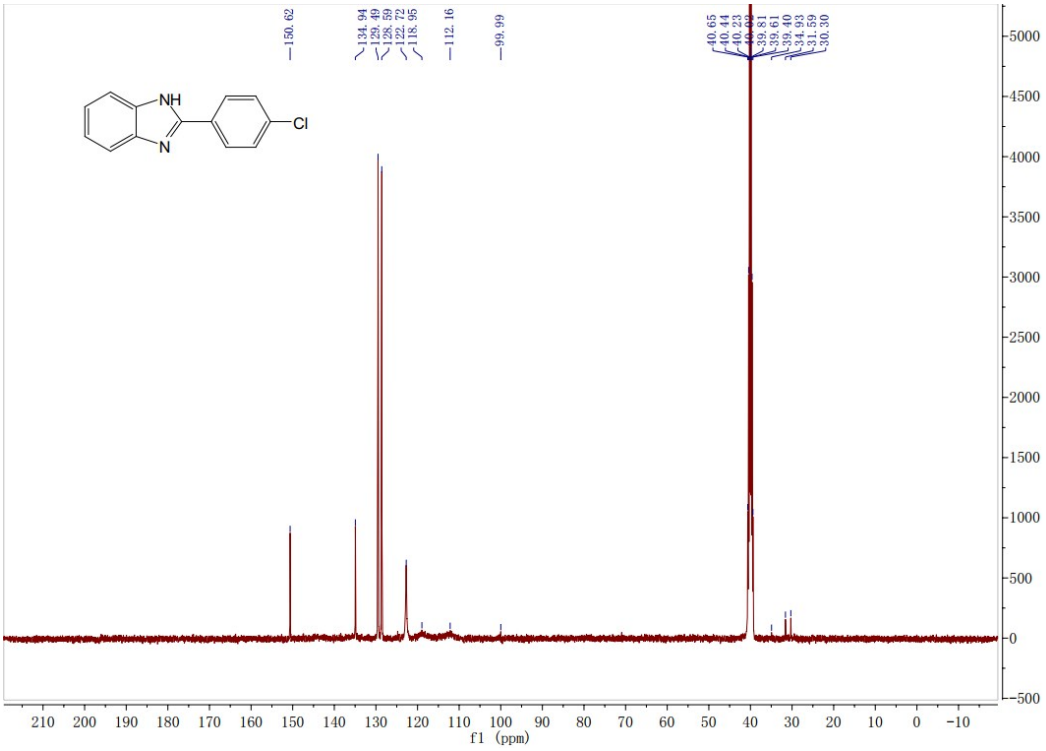
2-(4-methoxyphenyl)-1H-benzo[d]imidazole[1]（Table 2, entry 11）



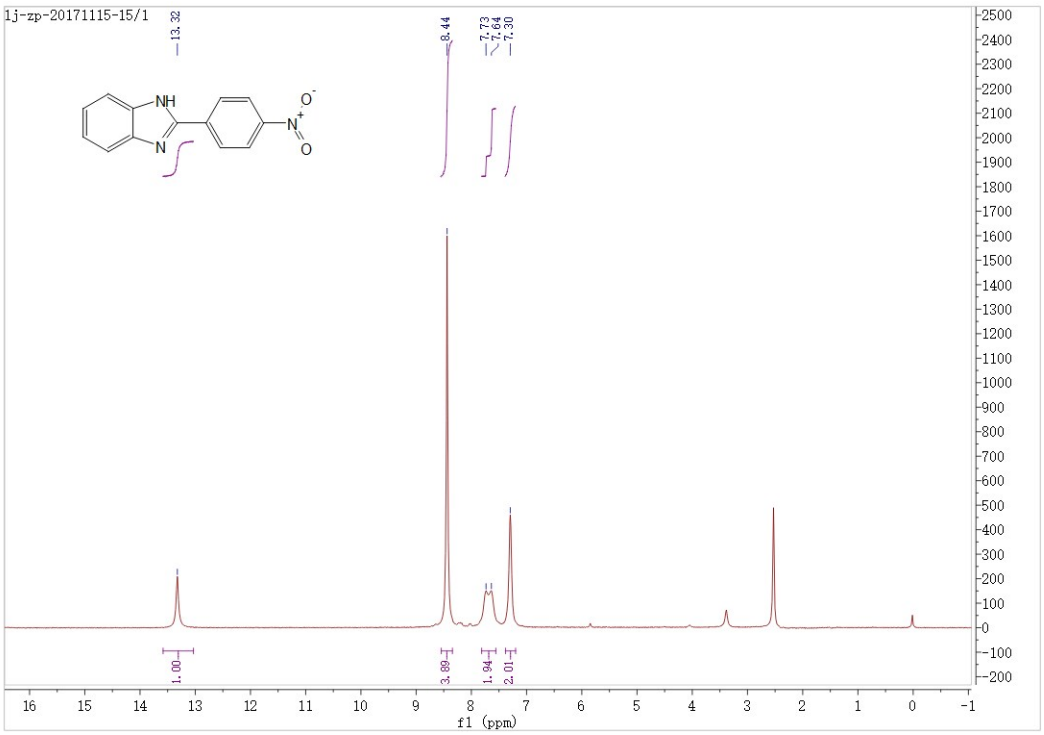


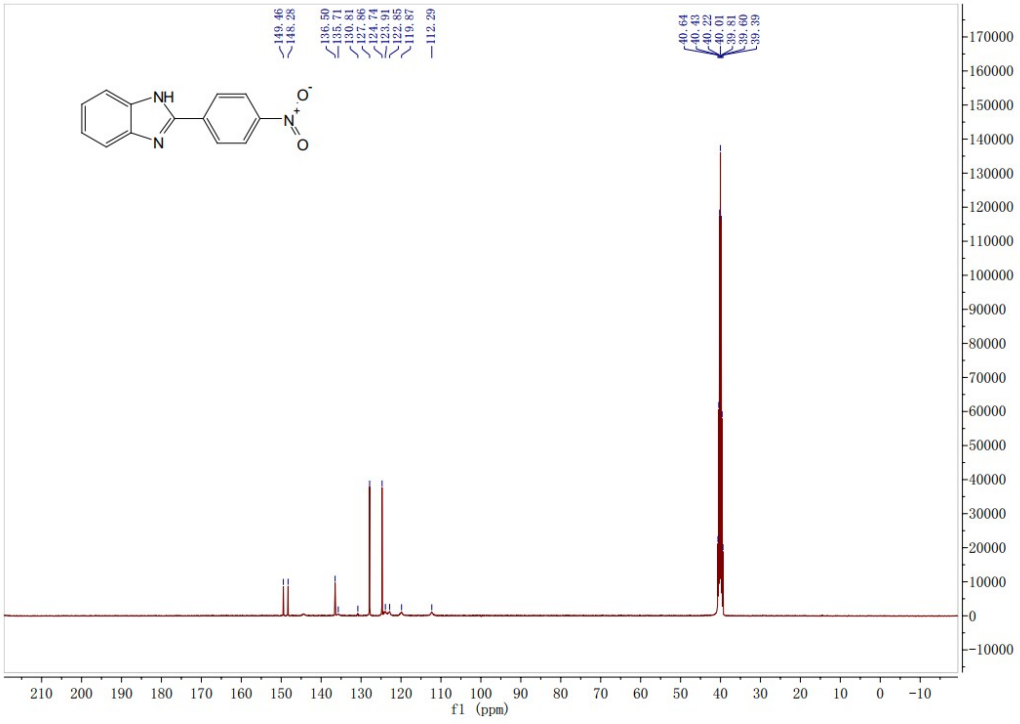
2-(4-chlorophenyl)-1H-benzo[d]imidazole[1] (Table 2, entry 12)



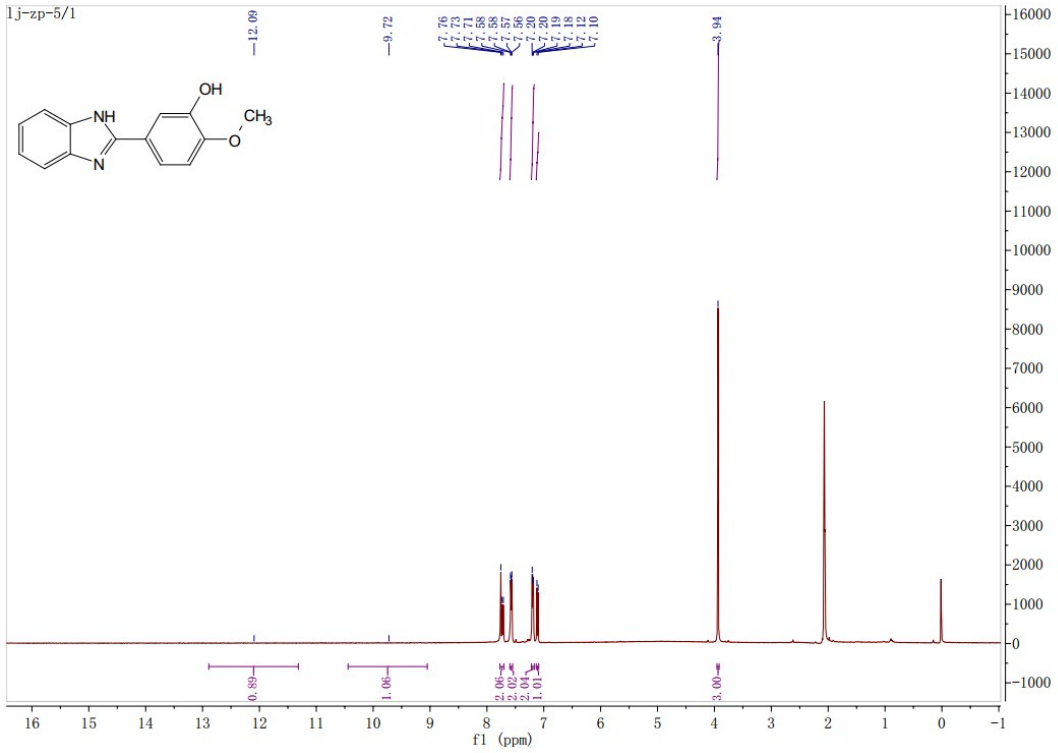


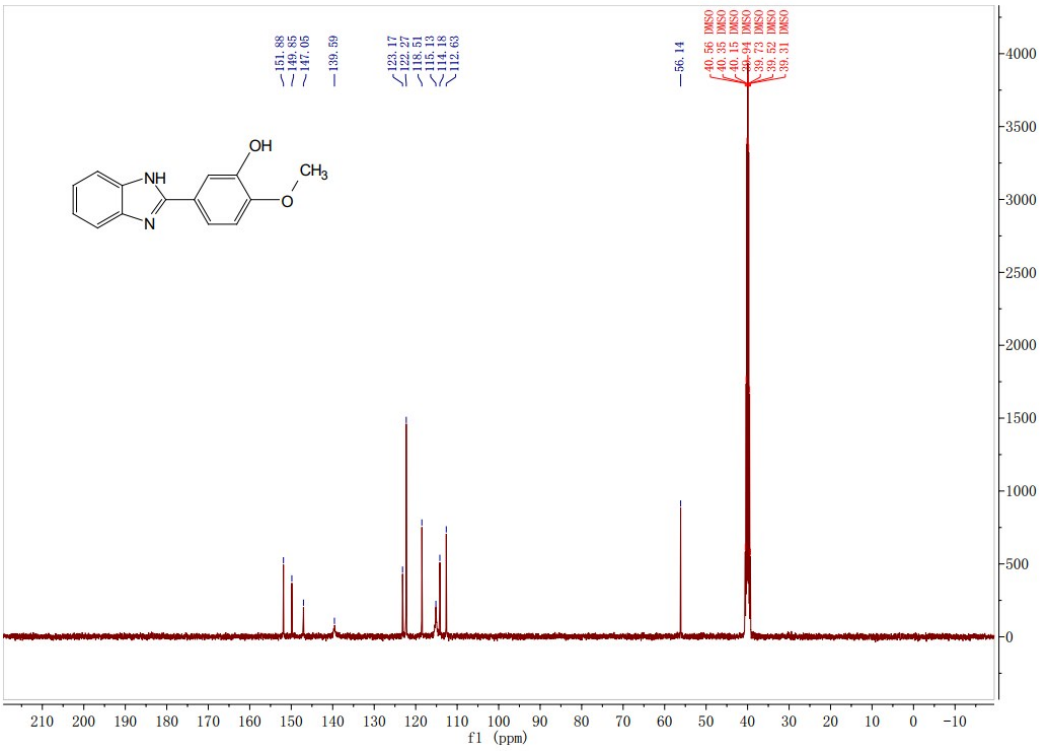
2-(4-nitrophenyl)-1H-benzo[d]imidazole[7]（Table 2, entry 13）



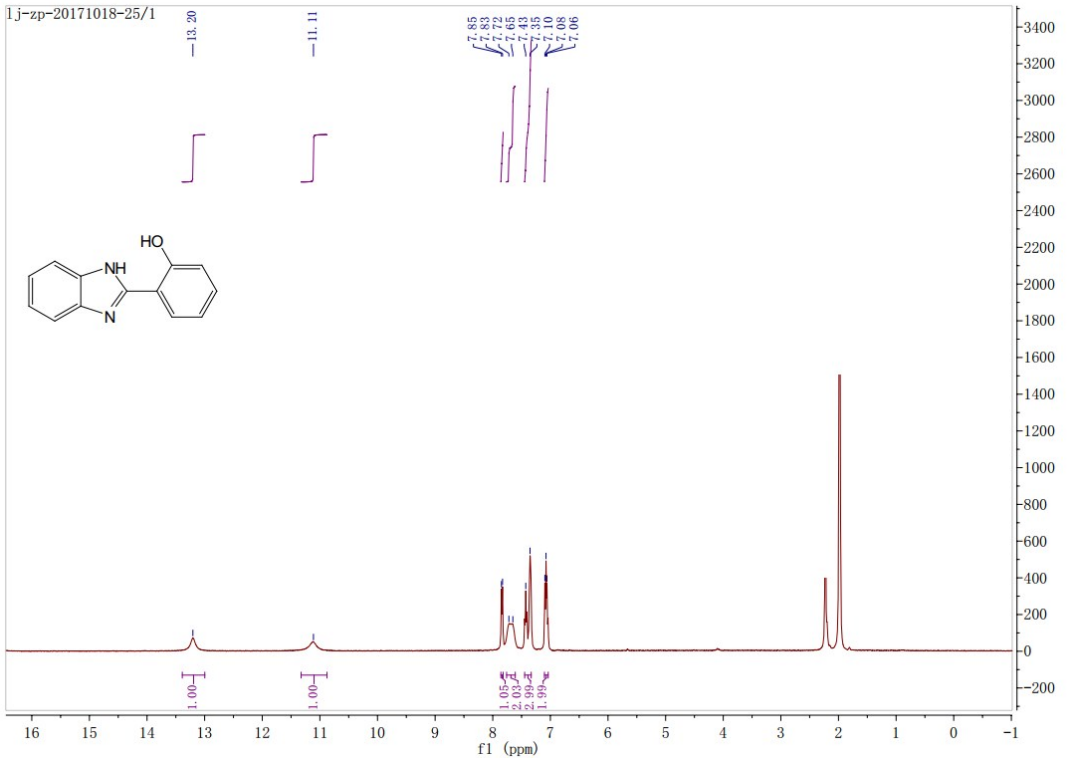


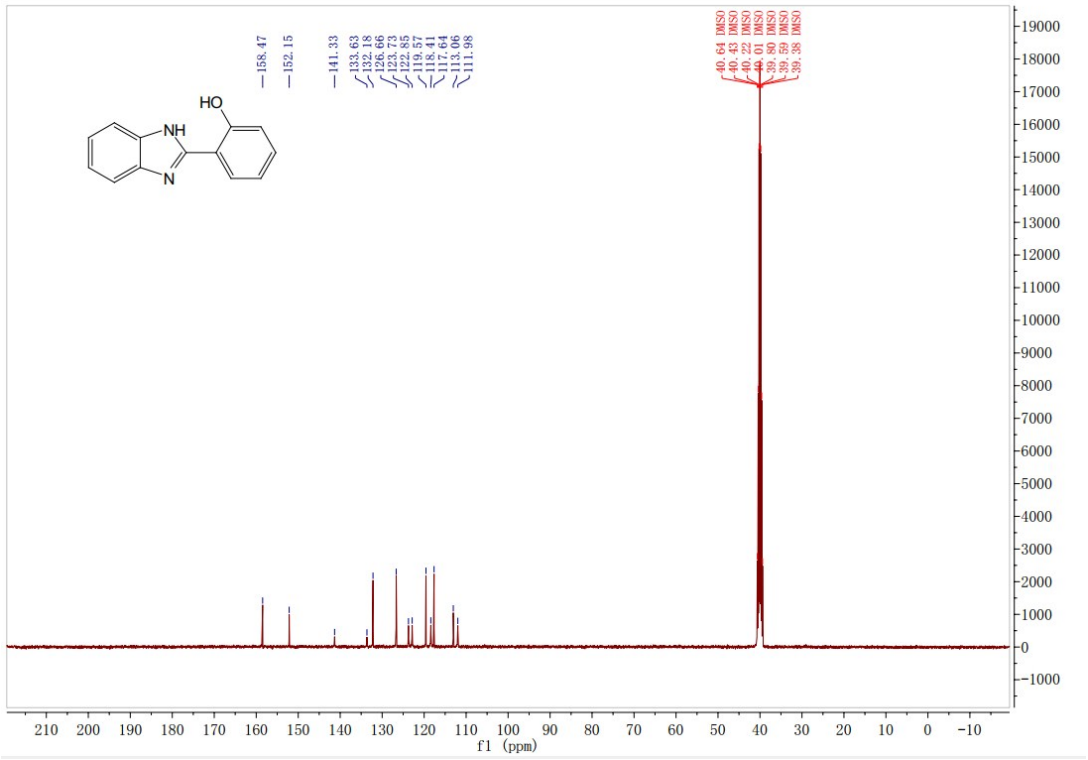
5-(1H-benzo[d]imidazol-2-yl)-2-methoxyphenol（Table 2, entry 14）



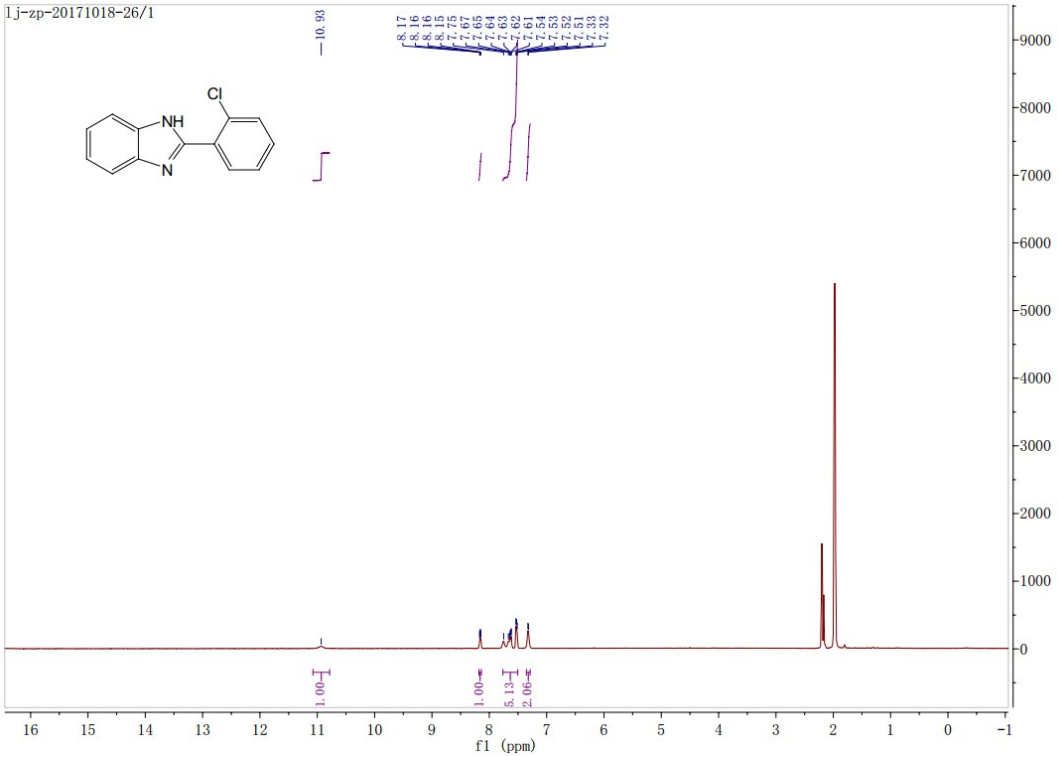


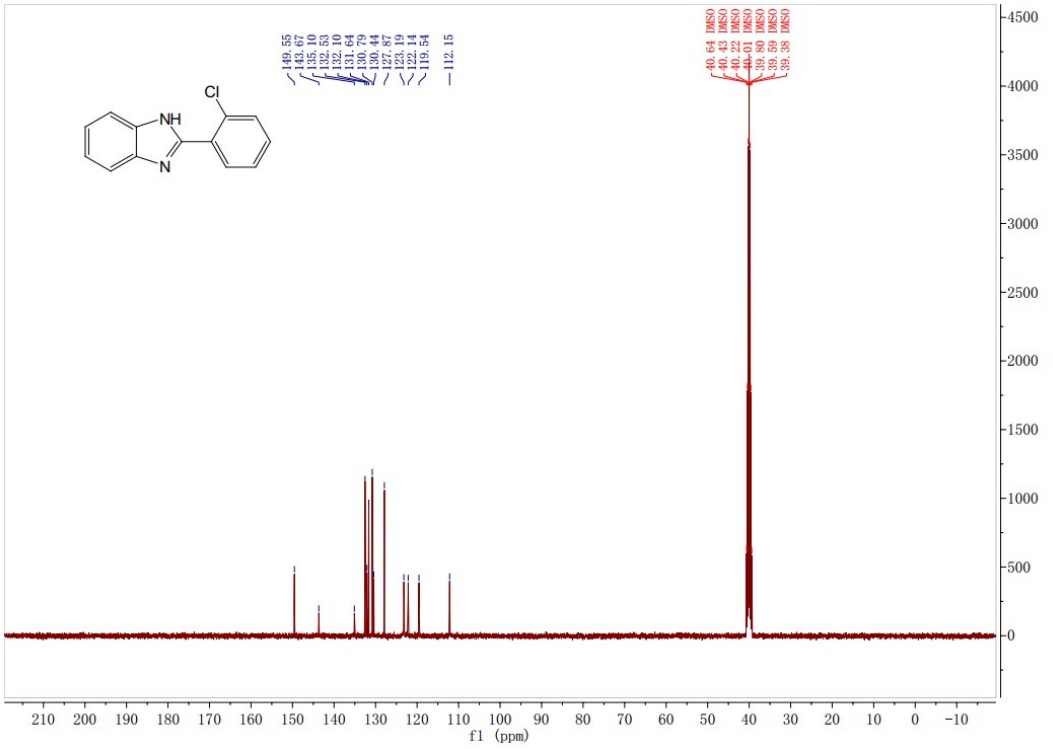
2-(1H-benzo[d]imidazol-2-yl)phenol[5]（Table 2, entry 15）



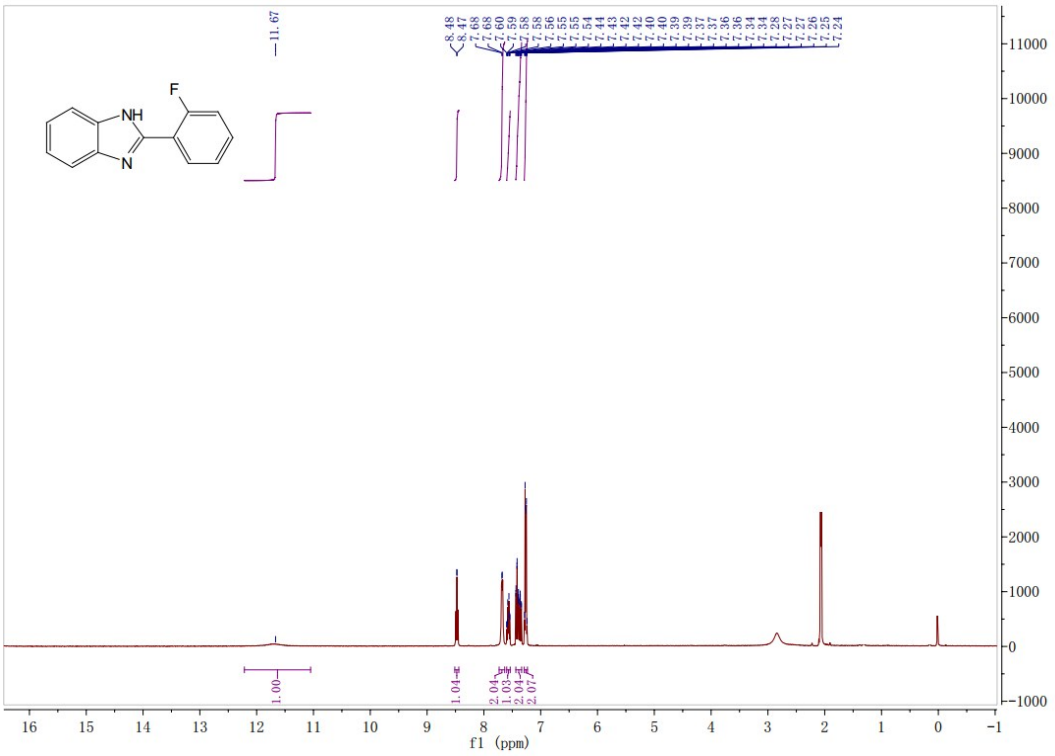


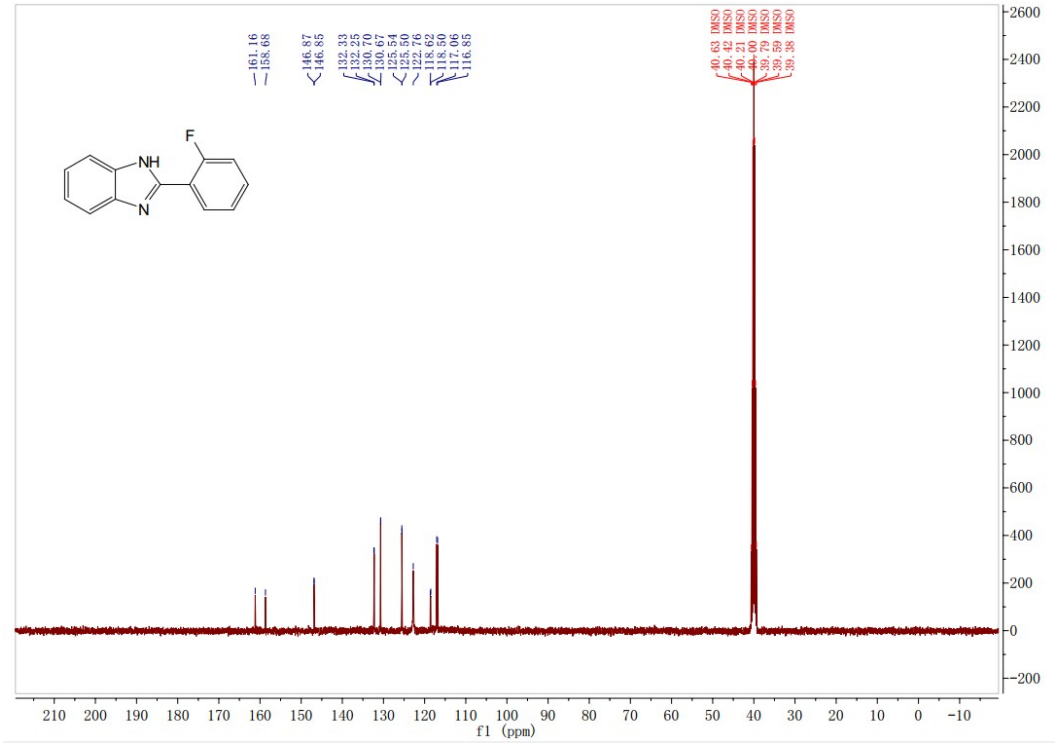
2-(2-chlorophenyl)-1H-benzo[d]imidazole[7]（Table 2, entry 16）



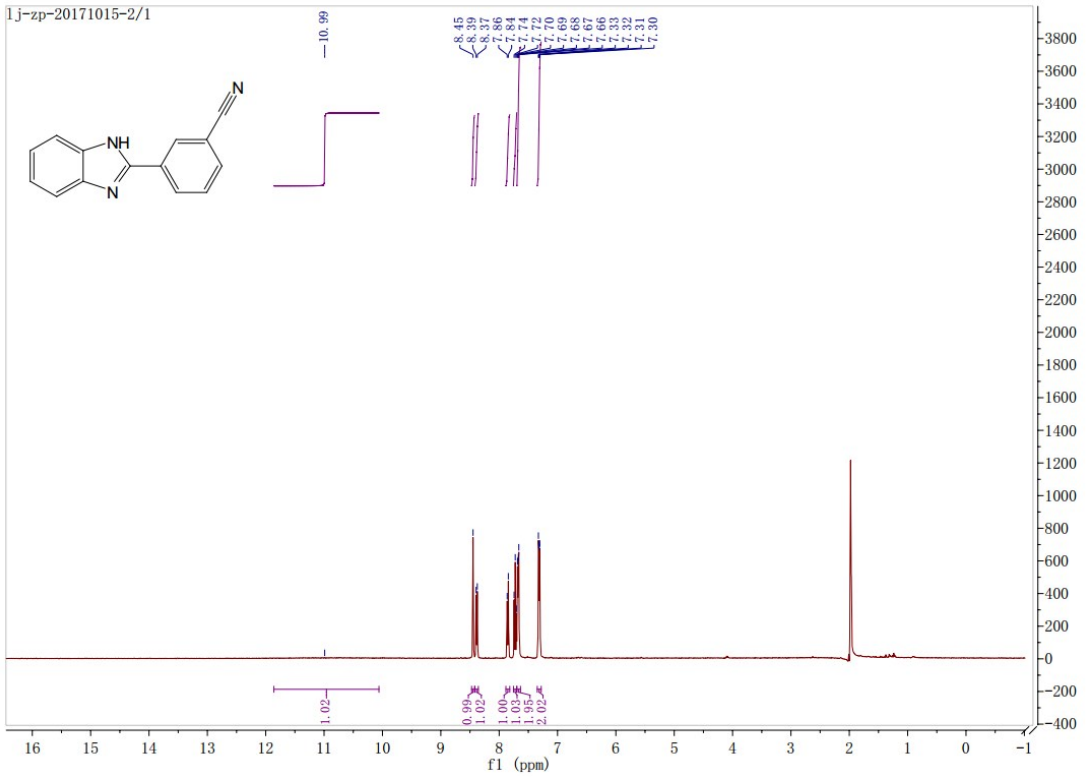


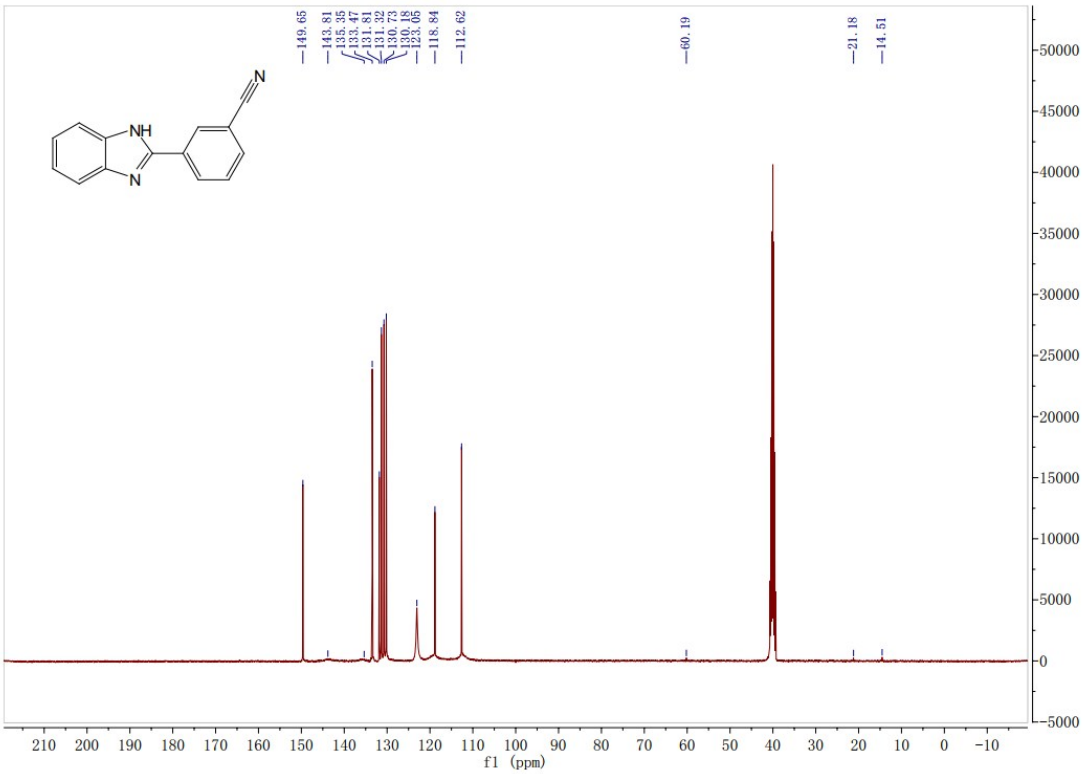
2-(2-fluorophenyl)-1H-benzo[d]imidazole[2]（Table 2, entry 17）



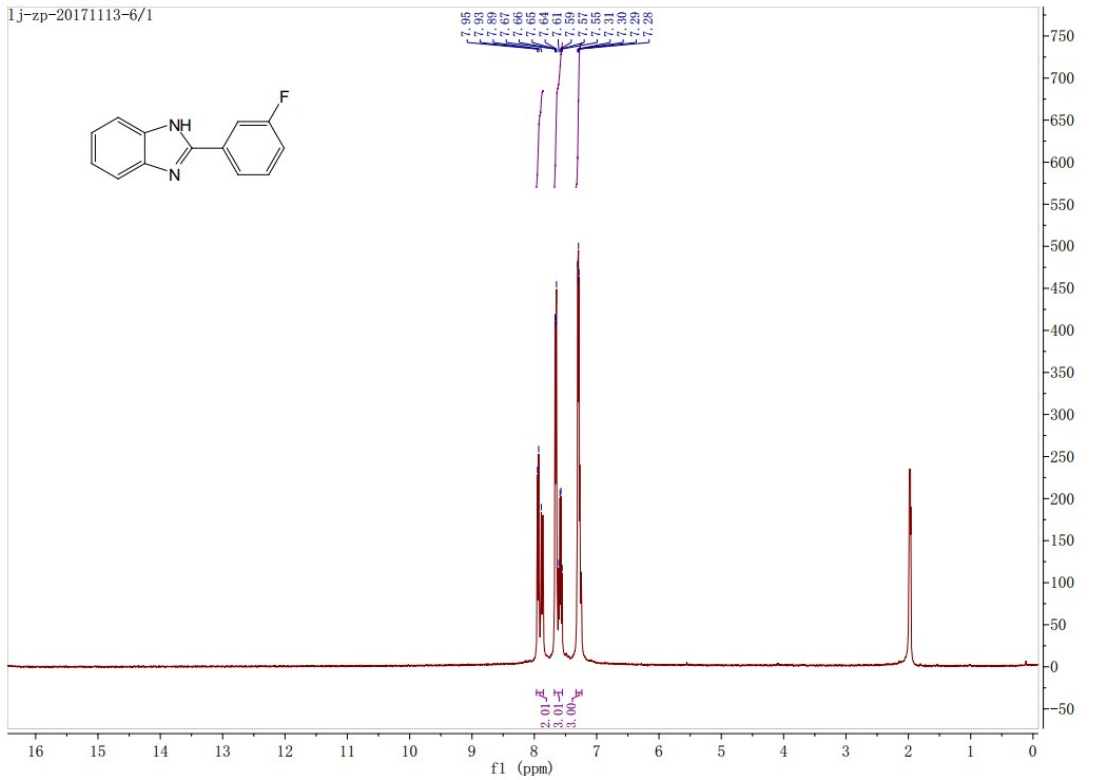


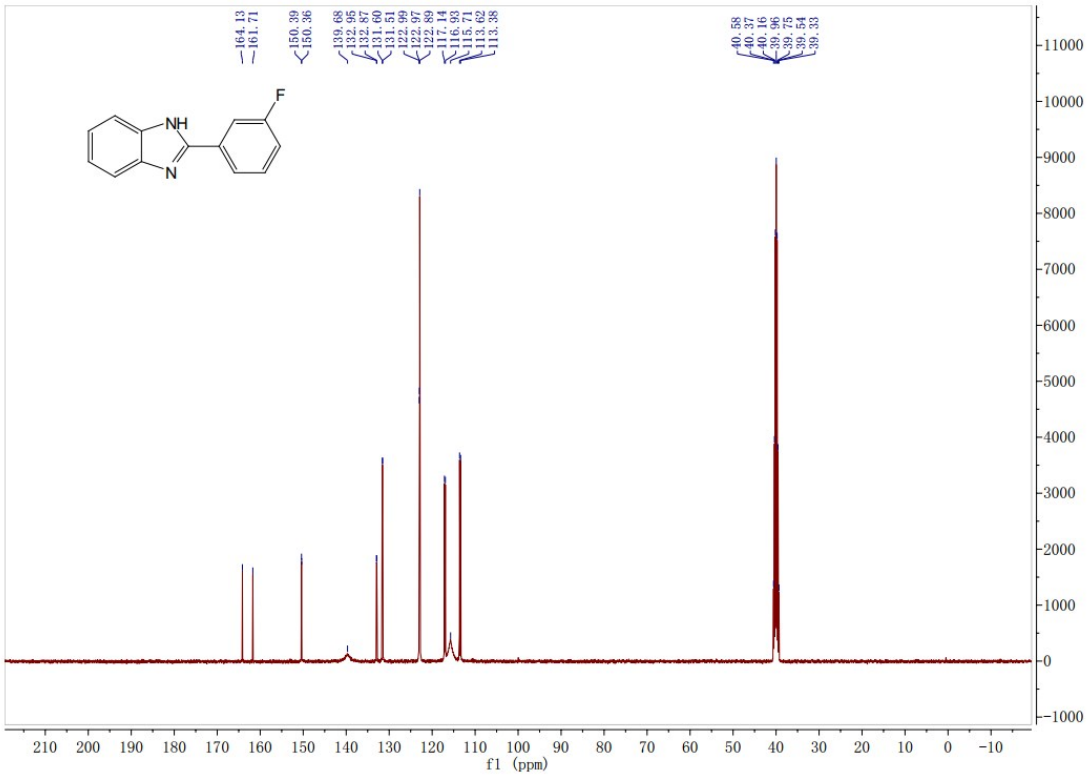
3-(1H-benzo[d]imidazol-2-yl)benzonitrile（Table 2, entry 18）



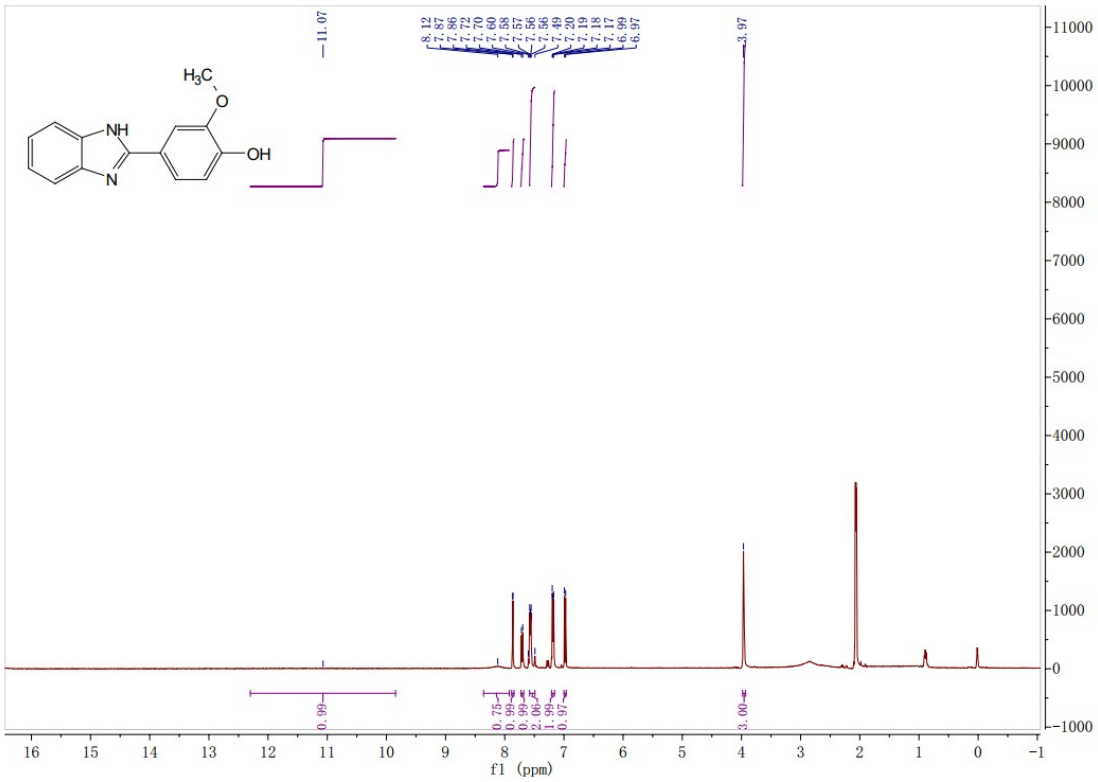


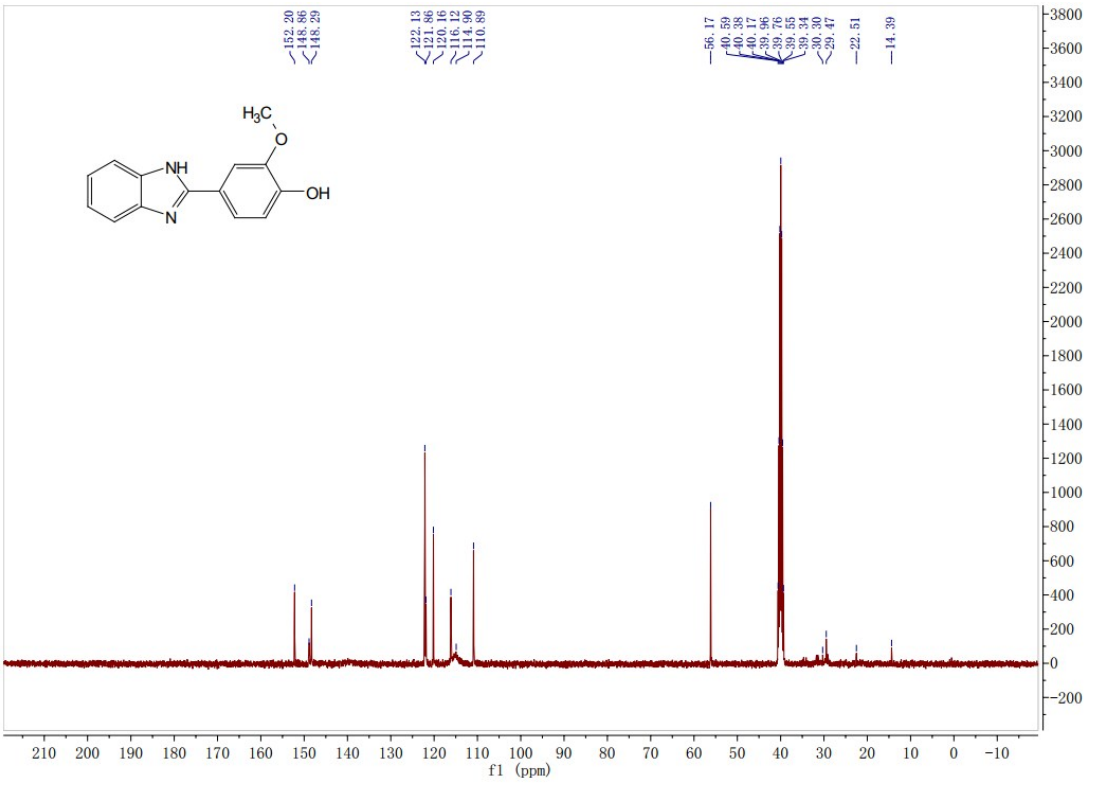
2-(3-fluorophenyl)-1H-benzo[d]imidazole（Table 2, entry 19）



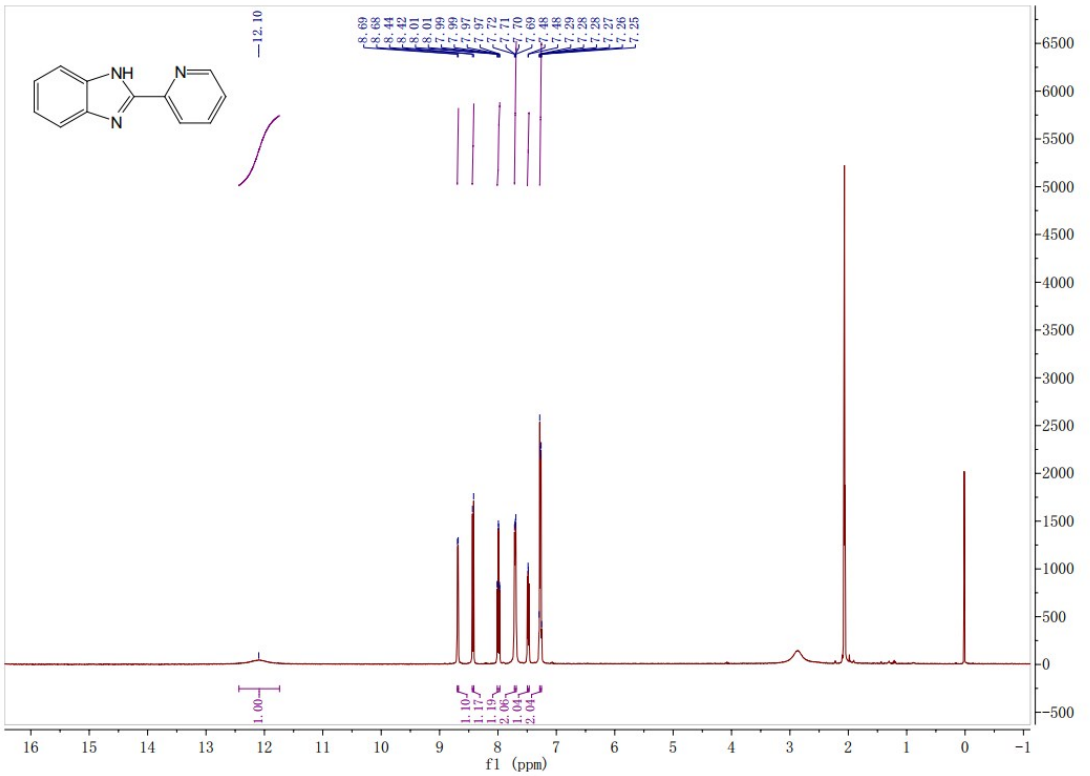


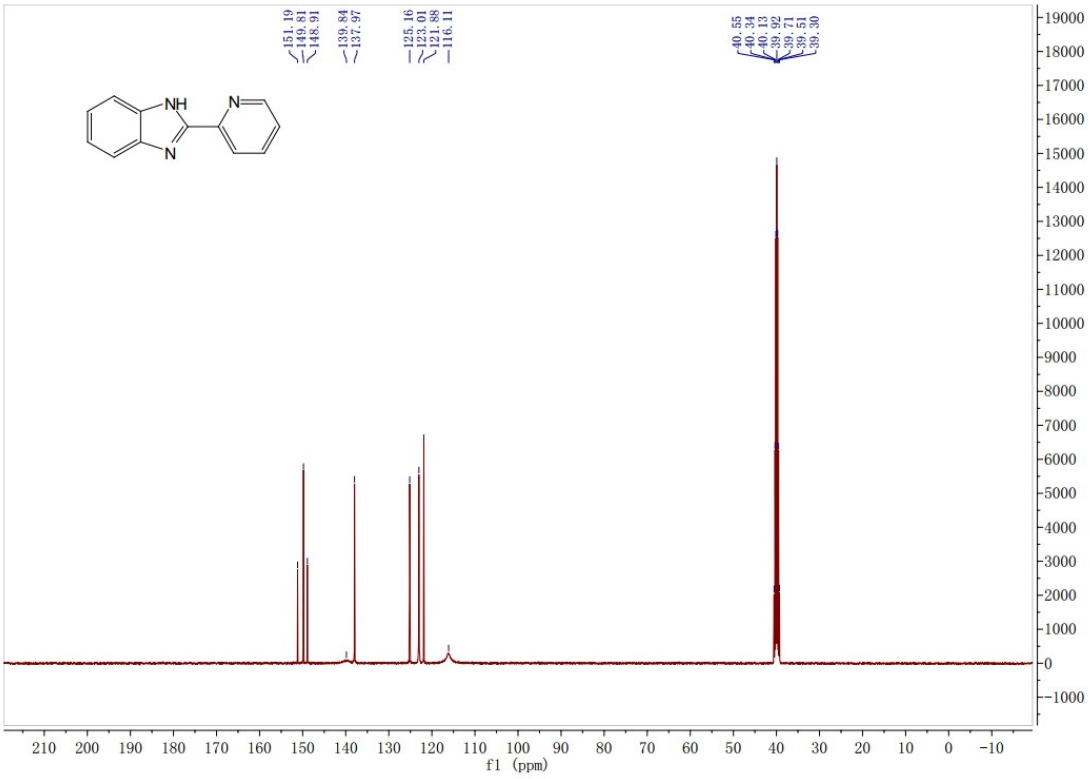
4-(1H-benzo[d]imidazol-2-yl)-2-methoxyphenol（Table 2, entry 20）



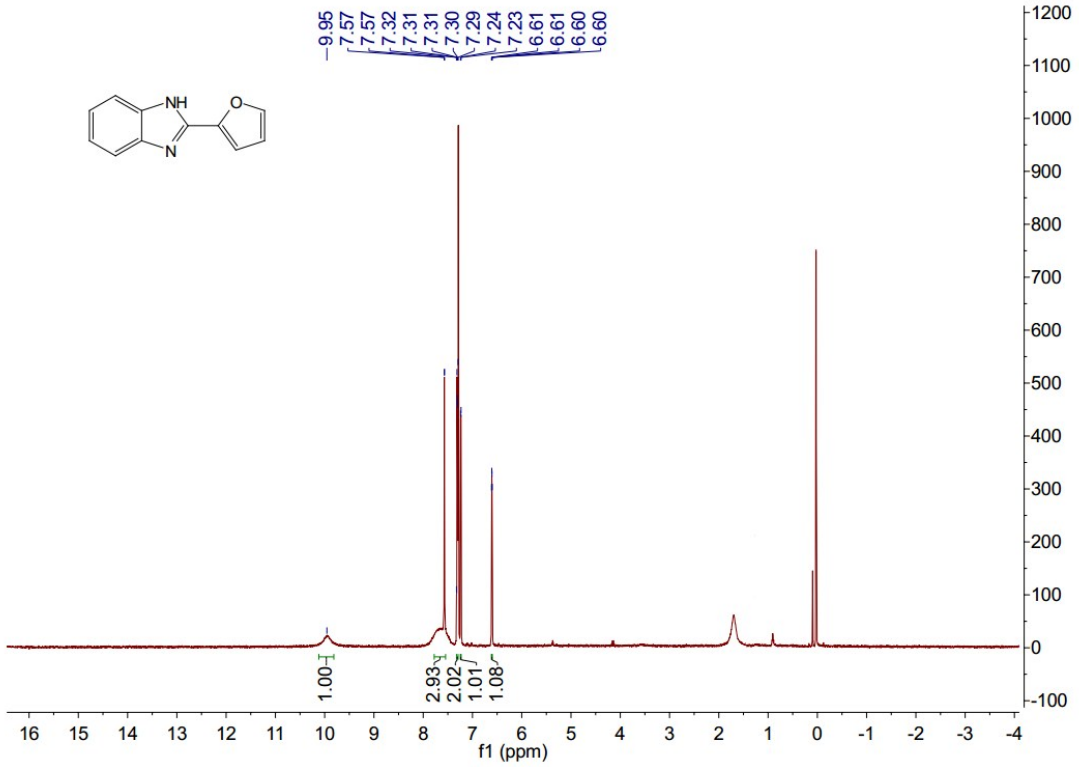


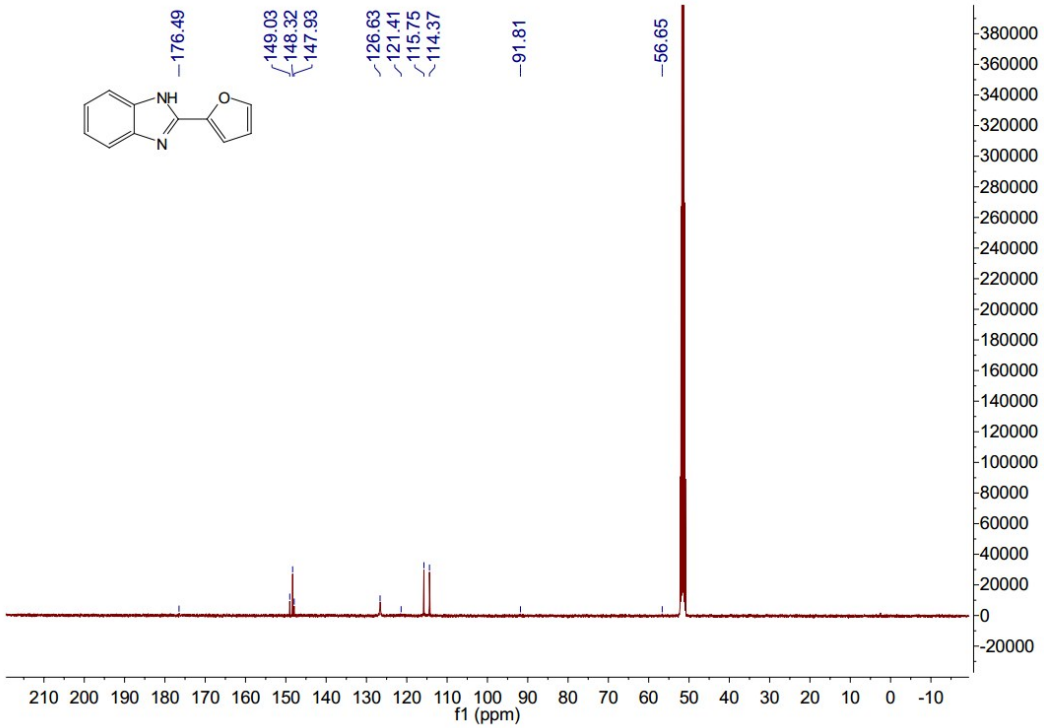
2-(pyridin-2-yl)-1H-benzo[d]imidazole[2] (Table 2, entry 21)



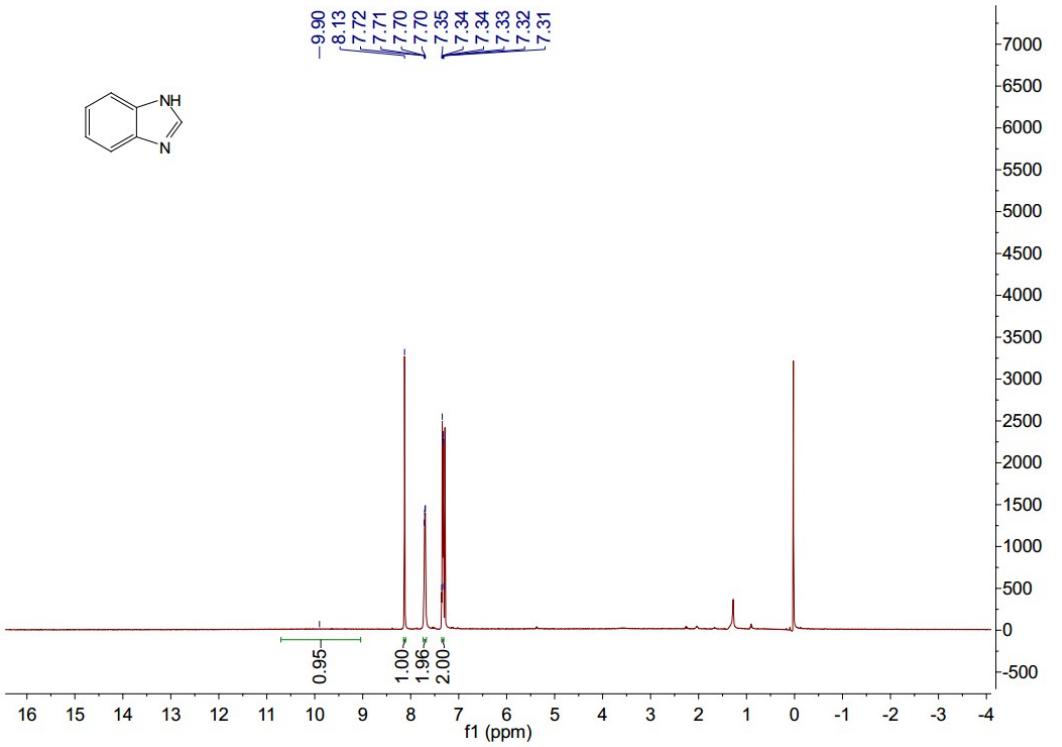


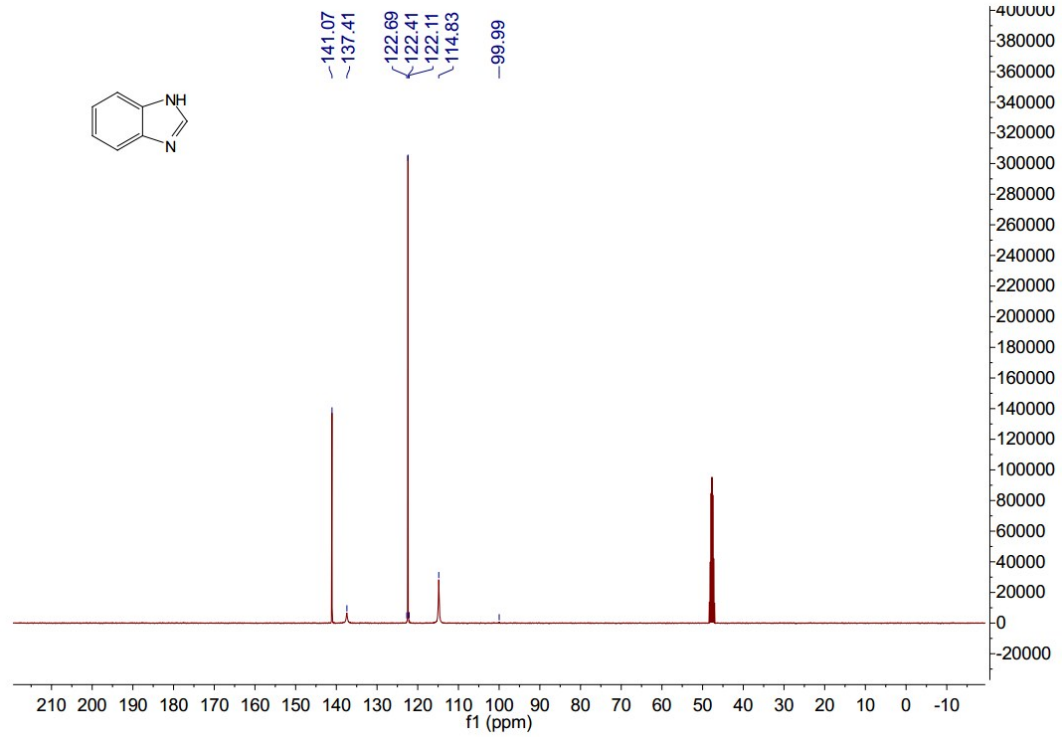
2-(furan-2-yl)-1H-benzo[d]imidazole[12]（Table 2, entry 22）:



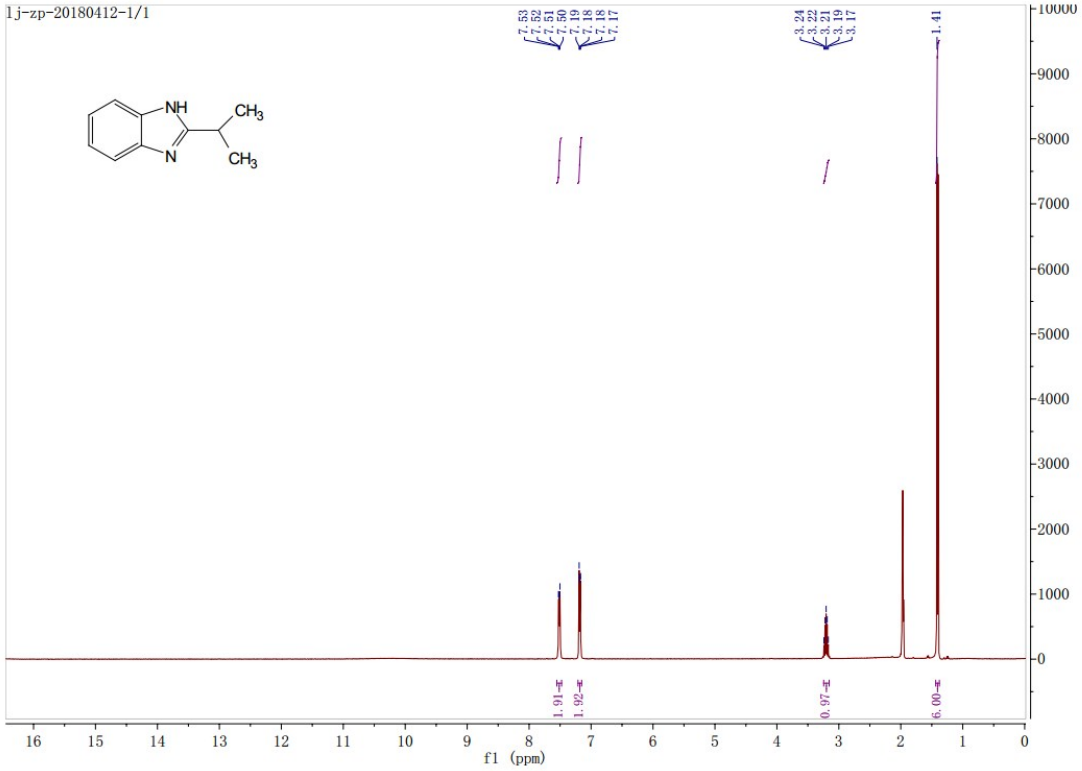


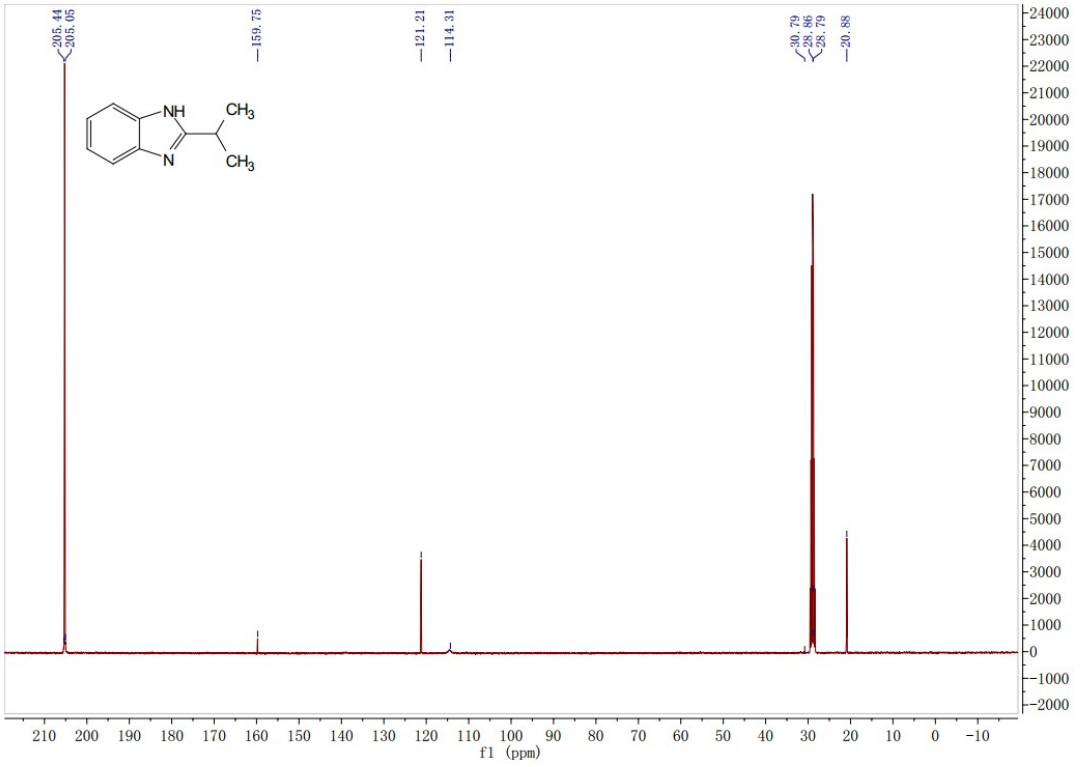
1H-benzo[d]imidazole[14] (Table 2, entry 23) :



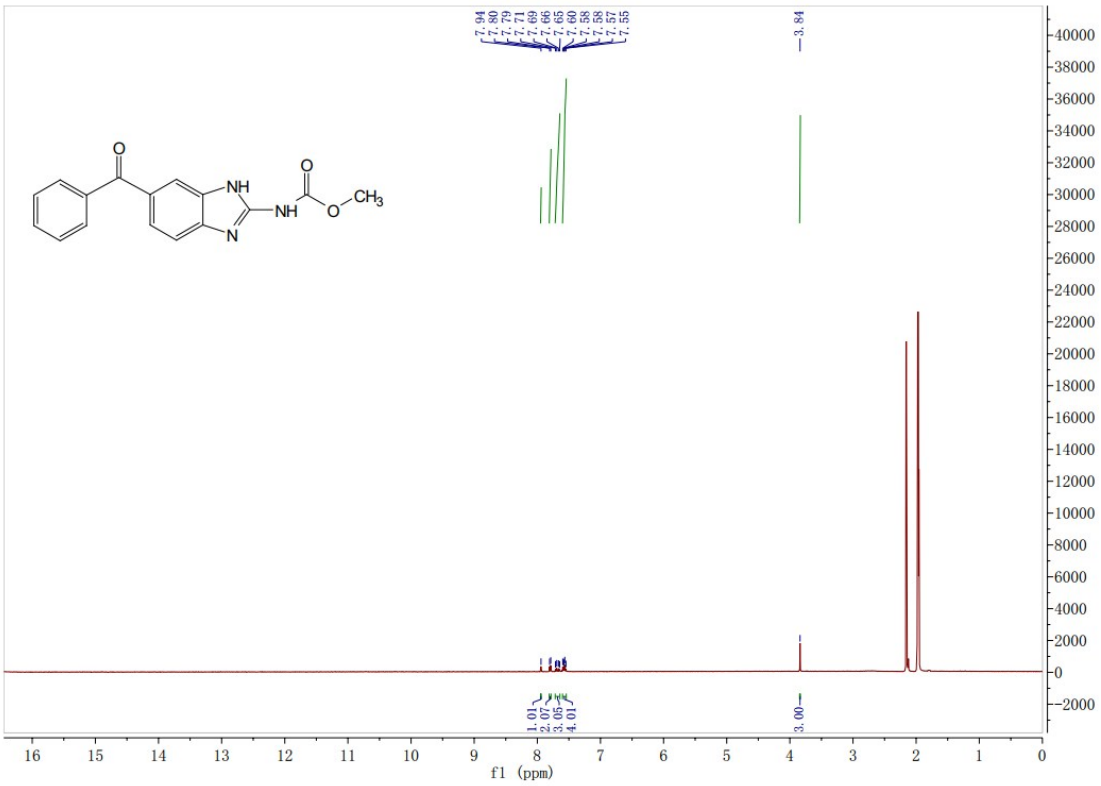


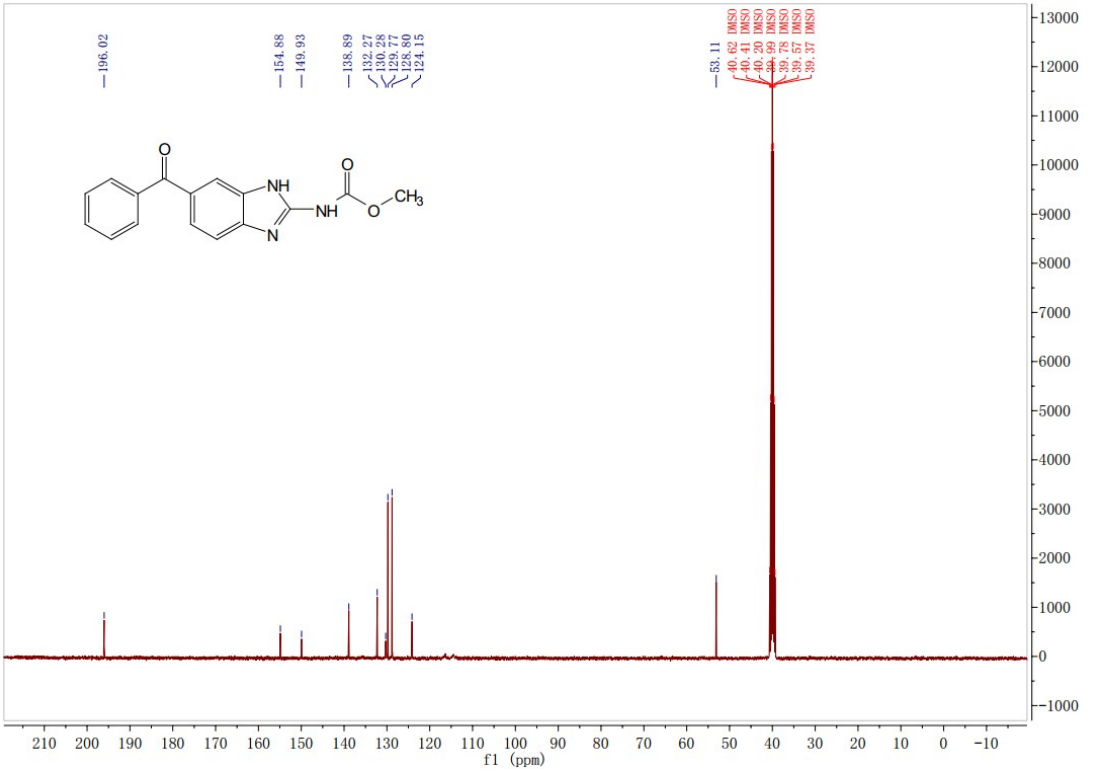
2-isopropyl-1H-benzo[d]imidazole[4] (Table 2, entry 24)





Mebendazole：


7.94
7.80
7.79
7.71
7.69
7.66
7.65
7.60
7.58
7.58
7.57
7.55
3.84
1.01
2.07
3.05
4.01
3.00
f1 (ppm)


196.02
154.88
149.93
138.89
132.27
130.28
129.77
128.80
124.15
53.11
40.62 DMSO
40.41 DMSO
40.20 DMSO
39.99 DMSO
39.78 DMSO
39.57 DMSO
39.37 DMSO
f1 (ppm)