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Nano CuO Catalyzed C–H Functionalization of 1, 3-Azoles with Bromoarenes and Bromoalkenes

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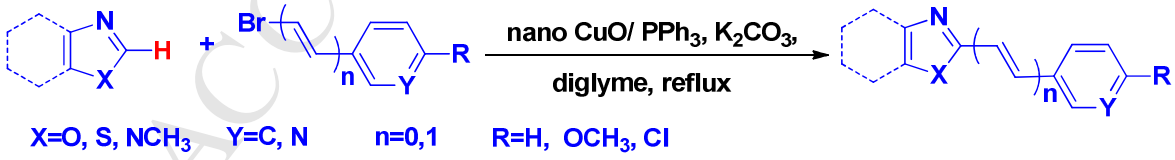
Abstract:

Copper oxide catalyzed direct C–H arylation and alkenylation of aromatic heterocycles using aryl and alkenyl bromides have been developed and has been applied to the C-H functionalization of a variety of 1,3-azoles like benzoxazole, benzothiazole, 1-methylbenzimidazole, and 1-methylimidazole, with moderate to excellent yields. The best performance has been achieved in the presence of PPh_3 when average size of CuO nanoparticles is 6.5 nm. This catalyst can be recovered and reused without significant decrease in its catalytic activity.

Keywords: CuO nanoparticles; C–H functionalization; 1, 3-azole; bromide

Graphical abstract



1. Introduction

1, 3-Azoles as important and ubiquitous structure motifs presented in many natural products, pharmaceutical active compounds, and organic functional materials (such as fluorescent dyes and liquid crystals),[1] have attracted great research efforts in their syntheses and further functionalization for various applications in drug discovery and organic synthesis.[2] The classical method for the preparation of this type of compounds is the transition metal-catalyzed coupling reaction, including palladium,[3] rhodium,[4] ruthenium,[5] and nickel [6] et al. Recently, the copper facilitated synthesis of heterocycle has attracted increasing research interests due to their relatively low cost and high efficiency.[7] Among those, the copper-catalyzed direct C–H functionalization is effective and straightforward and can avoid the preparation of organometallic intermediates as coupling partners.[8] Pioneering work in this field has been performed by Do and Daugulis in the CuI-catalyzed arylation of oxazoles,[9] by Miura in the CuI/PPh_3 catalyzed direct arylation of benzoazoles,[10] by You in the CuI-catalyzed arylation of heterocycles using 1, 10-phenanthroline as ligand,[11] and by Piguel in the CuI-catalyzed direct alkenylation of 5-phenyloxazoles using *trans*-N, N'-dimethylcyclohexane-1, 2-diamine as ligand.[12] However, the separation and recycle of these catalyst remains a problem. Therefore, it is very necessary to develop novel copper catalyzed system that can be easily separated and recycled after the reactions.

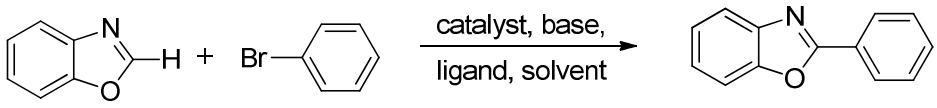
Nanoparticles have emerged as high surface area heterogeneous catalysts which increase the exposed surface area of the active component.[13] Meanwhile, their

insolubility in reaction solvents renders them easily separable from the reaction mixture. Recently, Copper nanoparticles have been used to catalyze the carbon-carbon and carbon-heteroatom bond formation due to their stability and wild availability.[14] Previously, we already developed CuO nanospindles-catalyzed directed arylation of heterocycles with aryl iodides.[15] It is well known that the reactivity of aromatic iodides is far superior to that of aromatic bromides. Herein we report the CuO nanoparticles catalyzed C−H functionalization of heterocycles using aromatic bromides.

2. Results and discussion

Our initial investigations were focused on the nanometer CuO catalyzed direct arylation of benzoxazole **1a** with bromobenzene **2a**. Catalysts, bases, ligands, solvents, reaction temperature, and reaction time were screened, and the results are summarized in Table 1. Under our previously reported condition for the arylation of heterocycle with aryl iodide[15]: the substrates were refluxed with CuO nanospindles (10 mol %) at reflux in diglyme in the presence of K_2CO_3 under stir (Table 1, entry1), no desired product **3a** was obtained. To our delight, the addition of PPh_3 (30 mol %) led to the formation of **3a** in 55% yield (Table 1, entry 2). This promoted us to further investigate the catalytical performance of the particle size and different shape of nano CuO in the reaction.

Table 1. Optimization of the direct arylation of benzoxazole and bromobenzene[a]



1a **2a** **3a**

entry	catalyst	base	ligand	solvent	yield(%)[b]
1	CuO nanospindles (10 mol %)	K_2CO_3	—	diglyme	—
2	CuO nanospindles (10 mol %)	K_2CO_3	PPh_3	diglyme	55
3	CuO (200 mesh) (10 mol %)	K_2CO_3	PPh_3	diglyme	—
4	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	diglyme	95
5	CuO nanobelts (10 mol %)	K_2CO_3	PPh_3	diglyme	40
6	CuO nanosheets (10 mol %)	K_2CO_3	PPh_3	diglyme	trace
7	CuO nanoparticles (5 mol %)	K_2CO_3	PPh_3	diglyme	85
8	CuO nanoparticles (20 mol %)	K_2CO_3	PPh_3	diglyme	98
9	CuO nanoparticles (10 mol %)	K_2CO_3	Phen	diglyme	34
10	CuO nanoparticles (10 mol %)	K_2CO_3	DMEDA	diglyme	—
11	CuO nanoparticles (10 mol %)	K_2CO_3	dipyridine	diglyme	—
12	CuO nanoparticles (10 mol %)	Na_2CO_3	PPh_3	diglyme	84
13	CuO nanoparticles (10 mol %)	NaOAc	PPh_3	diglyme	73
14	CuO nanoparticles (10 mol %)	NEt_3	PPh_3	diglyme	67
15	CuO nanoparticles (10 mol %)	Cs_2CO_3	PPh_3	diglyme	—
16	CuO nanoparticles (10 mol %)	K_3PO_4	PPh_3	diglyme	—
17	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	DMSO	41
18	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	DMF	78
19	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	dioxane	32
20	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	toluene	trace
21[c]	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	diglyme	60
22[d]	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	diglyme	—
23[e]	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	diglyme	98
24[f]	CuO nanoparticles (10 mol %)	K_2CO_3	PPh_3	diglyme	76

[a]Reaction conditions: benzoxazole (1 equiv), bromobenzene (2 equiv), base (2 equiv), CuO nanoparticles (10 mol%), ligand (30 mol%), solvent (2 mL), under reflux in argon for 5h. [b] Isolated yields. [c]150 °C. [d]140 °C. [e] 8 h. [f] 3 h.

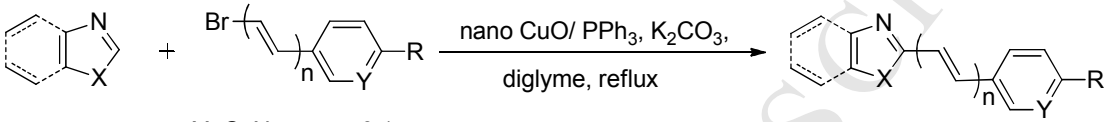
The particle size and shape is critical in this reaction, with the best performance achieved when the CuO with 6.5 nm in average diameter was used, from which the desired product was obtained in 95% yield (Table 1, entries 2–6)). By contrast, no product was obtained when commercial CuO powder (about 200 mesh) was used.

Reduing the catalyst loading from 10 to 5 mol % resulted in a decrease of the reaction yield from 95% to 85% (Table 1, entry 7), no significant improvement in the yield was observed when the catalyst loading was increased to 20 mol % (Table 1, entry 8). Among several ligands investigated, including PPh_3, phen, DMEDA, and α, α′-dipyridine, the addition of PPh_3 is crucial to the copper-catalyzed arylation (Table 1, entries 4, 9-11), which stabilize and activate the CuO nanoparticles. Both organic and inorganic bases, including Na_2CO_3, NaOAc and NEt_3 were found to promote the reaction, with the best performance achieved from K_2CO_3 (Table 1, entries 12-16). Among various solvent studied, diglyme gave the best result (Table 1, entries 17–20). In addition, variation of the temperature, and reaction time were also explored (Table 1, entries 21-24). The best results were obtained in diglyme at reflux for 5 h using two equivalents of K_2CO_3 as the base in the presence of CuO nanoparticles /PPh_3 catalyst system.

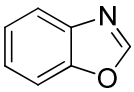
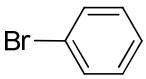
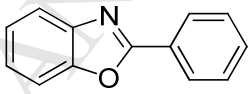
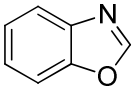
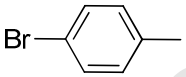
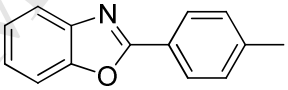
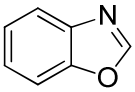
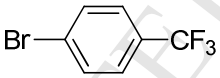
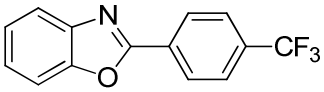
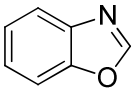
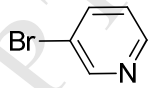
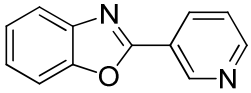
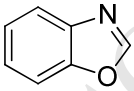
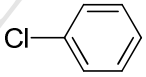
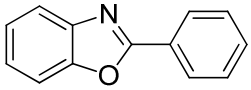
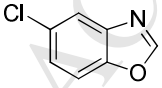
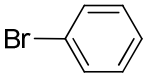
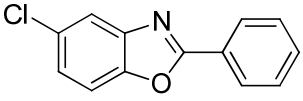
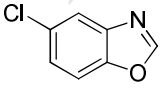
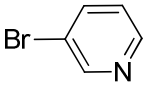
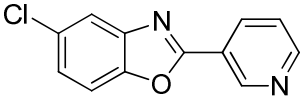
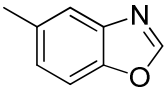
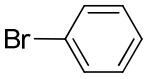
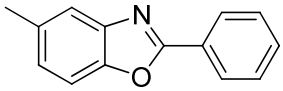
With this optimized reaction conditions in hand, the scope of this nano CuO-catalyzed C–H functionalization was further investigated and the results are summarized in Table 2. In the arylation of benzoxazole, higher yields were obtained in the presence of electron-withdrawing groups on aryl bromides comparison to those with electron-donating groups (Table 2, entries 1–3). Heteroaryl bromides are also suitable for this reaction and provide the corresponding product in excellent yields (entry 4). By contrast, no reaction was observed when aryl chloride was used for this reaction (entry 5). Both electron-poor (entries 6-7) and electron-rich (entry 8) benzoxazoles were efficiently arylated under this reaction conditions. In addition,

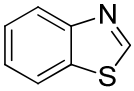
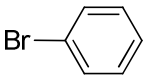
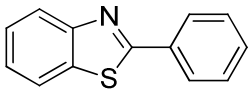
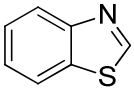
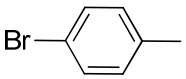
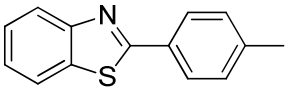
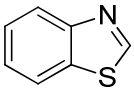
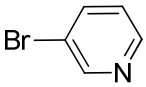
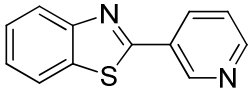
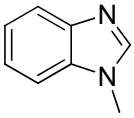
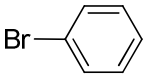
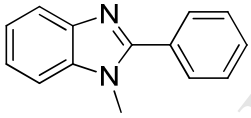
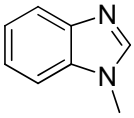
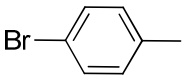
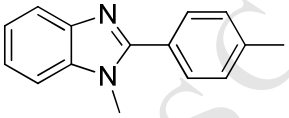
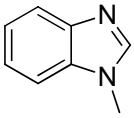
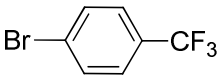
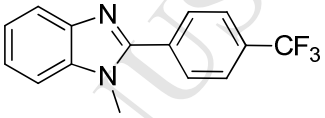
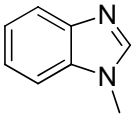
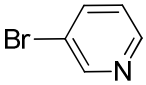
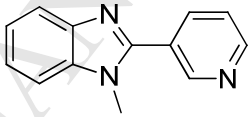
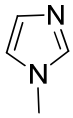
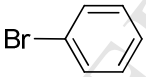
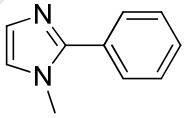
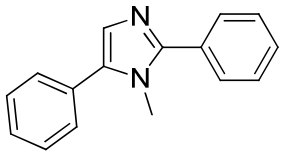
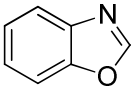
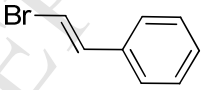
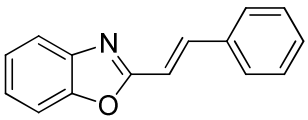
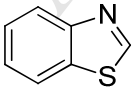
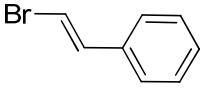
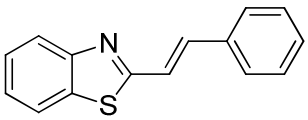
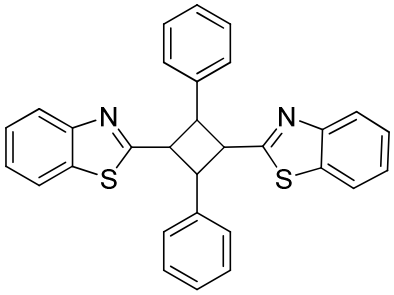
heterocycles, like benzothiazole and benzimidazole also applicable for this reaction with moderate to high yields (entries 9-15), with the lowest yields observed for the reaction of benzothiazole with aryl bromide, which is in accordance with our previous reported result. Imidazole can be monoarylated in 43% yield, with 35 % of the diarylated product isolated (entry 16).

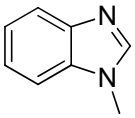
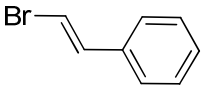
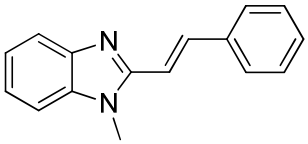
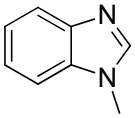
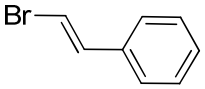
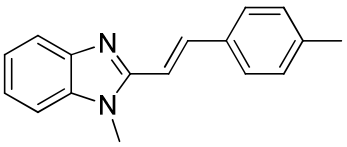
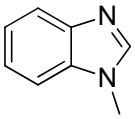
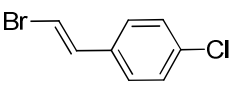
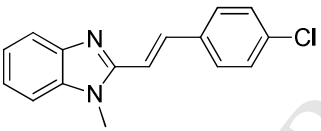
Table 2. Functionalization scope with respect to Aryl/Allyl bromides and heterocycles[a]



X=O, S, NCH_3 Y=C, N n=0,1 R=H, OCH_3

entry	heterocycle	ArX	product	time, h	yield (%)
1				5	95
2				5	79
3				5	83
4				5	92
5				5	—
6				5	59
7				5	73
8				5	76

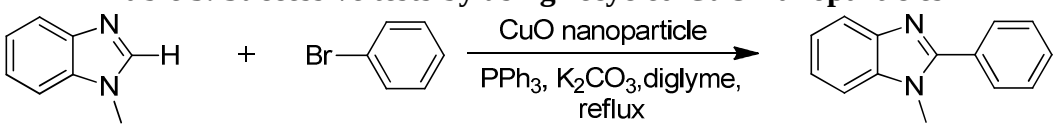
9				24	70
10				24	51
11				24	92
12				24	88
13				24	75
14				24	85
15				24	95
16			 	21	43 35
17				8	54
18			 	15	40 15

19				18	52
20				24	46
21				24	86

[a] The reactions were carried out using heterocycle (0.25 mmol), bromobenzene (0. 5 mmol), CuO (0.025 mmol), base (0. 5 mmol), ligand(0. 075 mmol) in diglyme (2 mL) under reflux in argon for 5h. [b]Isolated yields.

This catalytic condition was also successfully applied to the alkenylation of azoles with (*E*)-*β*-bromostyrene, and the results were shown in Table 2 (entries 17-21). Both electron-rich and electron-deficient *β*-bromostyrene reacted with benzimidazole to give the desired product in moderate to good yields. In general, the presence of electron-withdrawing groups on *β*-bromostyrene leads to higher yields in comparison to those with electron-donating groups. The *E*-isomers were obtained exclusively. Surprisingly, a new product was separated from the reaction mixture of benzothiazole and (*E*)-*β*-bromostyrene, and further characterization shows that it was a [2+2] cycloaddition product. The detailed [2+2] cycloaddition process in this reaction is still under investigation.

Table 3. Successive tests by using recycled CuO nanoparticles[a]



test	yield
1	88
2	85

[a] Reaction conditions: 1-methylbenzimidazole (1 equiv), bromobenzene (2 equiv), 10 mol % CuO nanoparticles, 30 mol % PPh_3, K_2CO_3 (2 equiv), diglyme (2 mL), under reflux in argon for 24h.

To test the potential applications of this reaction in industrial and pharmaceutical areas, the reusability of the CuO nanoparticles was investigated. As shown in Table 3, no significant decrease in the catalytic activity for the arylation of 1-methylbenzimidazole with bromobenzene was observed for the recovered CuO nanoparticles.

To examine whether the observed catalysis is derived from CuO nanoparticles or the leached copper species, the arylation of benzoxazole was carried out under the optimized conditions and the catalyst was removed from the mixture by centrifugation after 2 hours. The “catalyst-free” solution was then kept on the reaction under the same conditions. However, no further progress of reaction was observed even after 5 hours. The leaching of the copper from the CuO nanoparticles during reaction was examined by AAS analysis, and a slight leaching (< 1 ppm) is observed. We thus believe that the reaction may undergo through an oxidative addition, anion substitution, and then a reductive elimination process on the surface of the CuO nanoparticles which was stabilized by PPh_3 via a heterogeneous process. The mechanism of the reaction is similar to our reported work.[15]

3. Conclusion

In conclusion, we have developed a practical and effective CuO nanoparticles catalyzed C–H functionalization of heterocycles, such as benzoxazole, benzothiazole and 1-methylbenzimidazole with aryl bromides and alkenyl bromides in moderate to

excellent yields. The CuO nanoparticles catalyst can be recycled and reused without any significant decrease in the catalytic activity.

4. Experimental section

4.1 General

All starting materials and reagents were commercially available and used without further purification. The CuO nanospindles, nanoparticles, nanobelts and nanosheets were prepared according to reference.[16] The prepared CuO were characterized by X-ray powder diffraction with graphite monochromatized Cu-Kα radiation (λ = 0.154060 nm) in the 2θ range from 10° to 80°. The field-emission scanning electron microscopy (FE-SEM) images were obtained on an S-4800 field-emission scanning electron microscope with an accelerating voltage of 5 kV. Brunauer-Emmett-Teller (BET) nitrogen adsorption-desorption was measured by using a Micromeritics ASAP 2020 accelerated surface area and porosimetry system. NMR spectra were obtained at 25 °C on a Bruker Avance-300 at 300 MHz for ^{1}H, and at 75 MHz for ^{13}C NMR, chemical shifts for ^{1}H and ^{13}C were both referenced to $CDCl_3$. High resolution mass spectral (HRMS) data were obtained with an ionization mode of ESI on Agilent 6200 LC/MS TOF.

4.2 Catalysts characterization

The obtained CuO nanoparticles were characterized by X-ray powder diffraction analysis (XRD). Figure 1 presents a typical XRD pattern of the as-prepared sample. All of the detectable diffraction peaks can be indexed to (-111), (111), (-202), (202), (-113), (-311), (220) and (-222) reflections of the monoclinic phase CuO, in good

agreement with the standard value (JCPDS card NO. 80-1916). The mean crystalline size of the sample, estimated from Sherrer formula, is about 6.5 nm. The morphology of the as-synthesized CuO catalyst was studied by SEM. Figure 2a shows that the as-prepared sample is mainly composed of aggregated spherical particles with average diameter of about 6.5 nm, which is coincident with the result of HRTEM as shown in Figure 2b. In addition, the results of nitrogen adsorption experiments illustrate that the CuO catalyst has BET (Brunauer–Emmett–Teller) surface areas of 89.33 m^2g^{-1}.

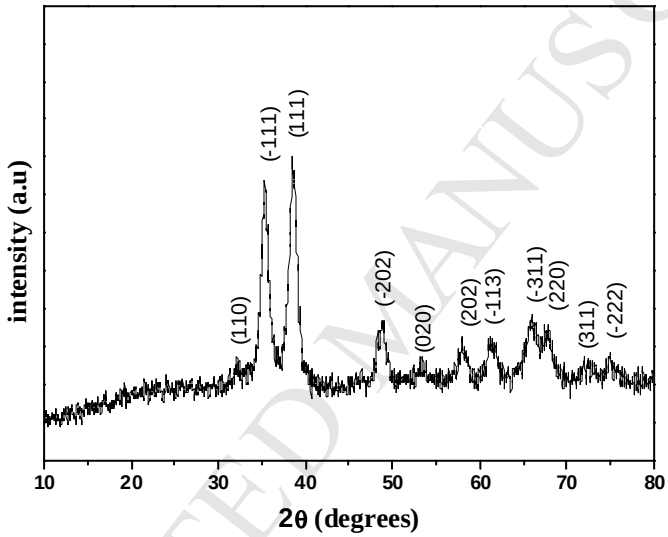


Figure 1. XRD pattern of the prepared sample.

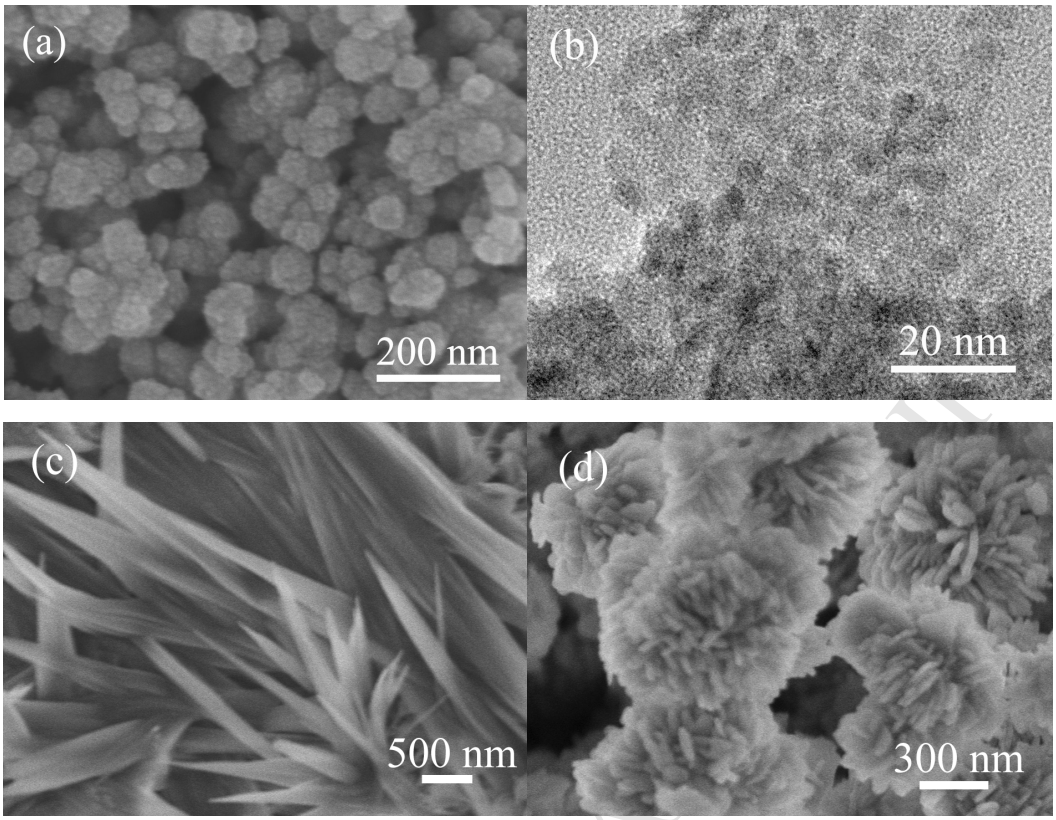


Figure 2. (a) FE-SEM image of the as-prepared CuO nanoparticles; (b) HRTEM image of the as-prepared CuO nanoparticles; (c) FE-SEM image of the as-prepared CuO nanobelts; (d) FE-SEM image of the as-prepared CuO nanosheets.

4.3 General procedure for CuO catalyzed arylation and alkenylation of 1, 3-azole

Under argon, 0.5 mmol of the bromobenzene or bromoalkenes were added to the reaction mixture containing 0.25 mmol of the benzoxazole and 0.5 mmol K_2CO_3, 0.025 mmol CuO, 0. 075 mmol PPh_3, 2 mL dry diglyme was added to the reaction vessel followed. The sealed reaction tube was stirred at 160 °C for 5-24 h. After cooling, the reaction mixture was centrifuged to remove solid and separated the organic phase. Then, organic phase was extracted and dried over anhydrous $MgSO_4$,

and concentrated under reduced pressure after filtered. The residue was purified by column chromatography on silica gel eluted to afford corresponding product.

4.4 Recycling procedure of the catalysts

The separated precipitates in the above procedure was washed sufficiently with de-ionized water and ethanol for three times each, and then dried under vacuum at 50 °C for 8 h. After that the CuO nanoparticles were recovered.

4.5 Characterization data of the desired products

4.5.1 2-Phenylbenzo[d]oxazole. White solid; m.p. 102–103 °C (lit., 96-97 °C) [2b]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27–8.25(m, 2H), 7.81–7.77(m, 1H), 7.60–7.57(m, 1H), 7.54–7.49(m, 3H), 7.38–7.33(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.0, 150.8, 142.1, 131.5, 128.9, 127.6, 127.2, 125.1, 124.6, 120.0, 110.6.

4.5.2 2-(p-Tolyl)benzo[d]oxazole. White solid; m.p. 113–114 °C (lit., 114-115 °C) [5a]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07(d, *J* = 7.5 Hz, 2H), 7.69–7.67(m, 1H), 7.50–7.48(m, 1H), 7.26–7.24(m, 4H), 2.36(s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3, 150.7, 142.2, 142.1, 129.7, 127.6, 124.5, 124.4, 119.9, 110.5, 21.6.

4.5.3 2-(4-(trifluoromethyl)phenyl)benzo[d]oxazole. White solid; m.p. 138–139°C (lit., 143-145 °C) [4d]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.38(d, *J* = 7.5 Hz, 2H), 7.80–7.78(m, 3H), 7.63–7.60 (m, 1H), 7.41–7.39(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.8, 151.2, 142.2, 130.8, 128.2, 126.3, 126.3, 126.2, 125.3, 122.3, 120.8, 111.2.

4.5.4 2-(pyridin-3-yl)benzo[d]oxazole. White solid; m.p. 107–109 °C (lit., 109-110 °C) [17a]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.44(s, 1H), 8.73(d, *J* =3.5 Hz, 1H), 8.46(d, *J* =7.7 Hz, 1H), 7.77–7.76(m, 1H), 7.57–7.56(m, 1H), 7.44–7.40(m, 1H), 7.36–7.35(m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.6, 152.0, 150.7, 148.7, 141.7, 134.7, 125.7, 124.9, 123.7, 123.5, 120.3, 110.7.

4.5.5 5-chloro-2-phenylbenzo[d]oxazole. White solid; m.p. 100–102 °C (lit., 104-106 °C) [3a]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25–8.23(m, 2H), 7.75(s, 1H), 7.55–7.48(m, 4H), 7.34–7.31(m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 149.4, 143.3, 131.9, 130.0, 129.0, 127.8, 126.7, 125.4, 120.0, 111.3.

4.5.6 5-chloro-2-(pyridin-3-yl)benzo[d]oxazole. White solid; m.p. 151–153°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.53(s, 1H), 8.86(d, *J* = 1.5 Hz, 1H), 8.57(d, *J* = 7.2 Hz, 1H), 7.85(s, 1H), 7.63–7.56(m, 2H), 7.46–7.43(m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 152.4, 149.4, 148.9, 142.9, 134.9, 130.5, 126.0, 123.7, 123.1, 120.3, 111.5. HRMS (ESI) calcd for $C_{12}H_8N_2OCl$ ($[M + H]^+$) 231.0325, found 231.0324.

4.5.7 5-methyl-2-phenylbenzo[d]oxazole White solid; m.p. 105–106°C (lit., 105-106 °C) [5a]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27–8.26(m, 2H), 7.58–7.55(m, 4H), 7.47(d, *J* = 8.4 Hz, 1H) 7.18(d, *J* = 8.1 Hz, 1H), 2.51(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 149.0, 142.3, 134.4, 131.4, 128.9, 127.5, 127.3, 126.2, 119.9, 109.9, 21.5.

4.5.8 2-Phenylbenzo[d]thiazole. White solid; m.p. 114–115 °C (lit., 111-112°C)[2b]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12–8.09(m, 3H), 7.88(d, *J* = 7.8 Hz, 1H), 7.52–7.48(m, 4H), 7.38(t, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 154.1, 135.1, 133.6, 131.0, 129.0, 127.6, 126.3, 125.2, 123.2, 121.7.

4.5.9 2-(p-Tolyl)benzo[d]thiazole. White solid; m.p. 79–81 °C (lit., 80-82 °C) [5a]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06(d, *J* = 8.1 Hz, 1H), 7.99(d, *J* = 7.5 Hz, 2H), 7.89(d, *J* = 7.5 Hz, 1H), 7.48(t, *J* = 6.6 Hz, 1H), 7.39–7.37(m, 1H), 7.30(d, *J* = 7.2 Hz, 2H), 2.42(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 154.2, 141.4, 134.9, 131.0, 129.7, 127.5, 126.2, 125.0, 123.0, 121.6, 21.5.

4.5.10 2-(pyridin-3-yl)benzo[d]thiazole. White solid; m.p. 126–127 °C (lit., 134 °C) [17b]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.23(s, 1H), 8.64(d, *J* = 1.2 Hz, 1H), 8.27(d, *J* = 7.2 Hz, 1H), 8.03(d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.44(t, *J* = 7.2 Hz, 1H),

7.33–7.31(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 153.9, 151.5, 148.5, 134.9, 134.5, 129.6, 126.6, 125.7, 123.7, 123.5, 121.7.

4.5.11 1-Methyl-2-phenyl-1H-benzo[d]imidazole. White solid; m.p. 89–91 °C (lit., 92-94 °C) [4d]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86–7.82(m, 1H), 7.75–7.73(m, 2H), 7.53–7.48(m, 3H), 7.37–7.28(m, 3H), 3.80(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 142.9, 136.5, 130.1, 129.8, 129.5, 128.7, 122.8, 122.5, 119.8, 109.6, 31.7.

4.5.12 1-Methyl-2-(p-tolyl)-1H-benzo[d]imidazole. White solid; m.p. 125–127 °C (lit., 127-128 °C) [15]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84–7.81(m, 1H), 7.64(d, *J* = 8.1 Hz, 2H), 7.36–7.27(m, 5H), 3.80(s, 3H), 2.42(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 143.0, 139.9, 136.6, 129.4, 129.3, 127.3, 122.6, 122.3, 119.7, 109.6, 31.7, 21.4.

4.5.13 1-methyl-2-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazole. White solid; m.p. 121–123°C (lit., 122-124 °C) [15]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93(d, *J* = 7.8 Hz, 2H), 7.87–7.80(m, 3H), 7.45–7.35(m, 3H), 3.91(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.1, 142.9, 136.6, 133.8, 129.8, 125.7(q, *J* = 3.6), 123.4, 122.8, 120.1, 109.8, 31.8.

4.5.14 1-methyl-2-(pyridin-3-yl)-1H-benzo[d]imidazole. Pale yellow solid; m.p. 142–143 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.02(s, 1H), 8.76-8.74(m, 1H), 8.14(d, *J* = 8.1 Hz, 1H), 7.84(d, *J* = 7.2 Hz, 1H), 7.51–7.31(m, 4H), 3.90(s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 149.8, 143.0, 136.9, 136.6, 126.6, 123.6, 123.3, 122.8, 120.0, 109.8, 31.7. HRMS (ESI) calcd for $C_{13}H_{12}N_3$ ($[M + H]^+$) 210.1031, found 210.1030.

4.5.15 1-methyl-2-phenyl-1H-imidazole. Light yellow oil; [17c] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64(d, *J* = 6.6 Hz, 2H), 7.46–7.44(m, 3H), 7.13(s, 1H), 6.98(s, 1H), 3.75(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 130.6, 128.6, 128.6, 128.5, 128.4, 122.3, 34.5.

4.5.16 1-methyl-2,5-diphenyl-1H-imidazole. White solid; m.p. 165-166°C (lit., 172–174°C)[17c]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70(d, *J* = 6.6 Hz, 2H), 7.46–7.40(m,

8H), 7.21(s, 1H), 3.68(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.4, 135.4, 130.9, 130.3, 128.8, 128.8, 128.7, 128.7,128.6, 127.9, 127.5, 33.8.

4.5.17 (E)-2-styrylbenzo[d]oxazole. Light yellow solid; m.p. 80–81 °C (lit., 85-86 °C) [2b] ; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 16.4 Hz, 1H), 7.72(m, 1H), 7.61–7.52 (m, 3H), 7.42–7.33(m, 5H), 7.09 (d, *J* = 16.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.8, 150.4, 142.2, 139.5, 135.2, 129.8, 129.0, 127.6, 125.2, 124.5, 119.9, 114.0, 110.3.

4.5.18 (E)-2-styrylbenzo[d]thiazole. Light yellow solid: m.p. 106–108 °C (lit., 106-108 °C) [13]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98(d, *J* = 7.8 Hz, 1H), 7.84(d, *J* = 7.8 Hz, 1H), 7.58–7.56(m, 2H), 7.49–7.37 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 153.9, 137.7, 135.4, 134.4, 129.5, 129.0, 127.4, 126.3, 125.4, 123.0, 122.1, 121.5.

4.5.19 2,2'-(2,4-diphenylcyclobutane-1,3-diyl)bis(benzo[d]thiazole. Light yellow solid, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03(d, *J* = 7.8 Hz, 2H), 7.77(d, *J* = 7.8 Hz, 2H), 7.50–7.34(m, 10H), 7.24–7.13(m, 4H)，5.16–5.08(m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 153.0, 138.0, 135.4, 128.3, 128.0, 126.9, 125.7, 124.6, 122.8, 121.4, 47.8, 46.3. HRMS (ESI) calcd for $C_{32}H_{22}N_2S_2$ ($[M + H]^+$) 475.1302, found 475.1299.

4.5.20 (E)-1-methyl-2-styryl-1H-benzo[d]imidazole. Yellow solid; m.p. 107–109 °C (lit.,114 °C)[17d]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97(d, *J* = 15.9 Hz, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.62(d, *J* = 6.9 Hz, 2H), 7.43–7.29 (m, 6H), 7.10(d, *J* = 15.9 Hz, 1H), 3.85(s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.1, 143.1, 137.3, .136.0, 129.1, 128.9, 127.3, 122.7, 122.6, 119.3, 112.9, 109.2, 29.8.

4.5.21 (E)-1-methyl-2-(4-methylstyryl)-1H-benzo[d]imidazole. White solid; m.p. 136–139° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96(d, *J* = 15.9, 1H), 7.78(d, *J* = 6.3 Hz, 1H), 7.52(d, *J* = 7.8 Hz, 2H), 7.29–7.28(m, 3H), 7.21(d, *J* = 7.8 Hz, 2H), 7.04(d, *J* = 15.9, 1H), 3.82(s, 3H), 2.39(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.3, 143.1, 137.3, 136.0, 133.3, 129.6, 127.2, 122.6, 122.4, 119.2, 111.9, 109.1, 29.7, 21.4.

HRMS (ESI) calcd for $C_{17}H_{17}N_2$ ($[M + H]^+$)249.1392, found 249.1388.

4.5.22 (E)-2-(4-chlorostyryl)-1-methyl-1H-benzo[d]imidazole. White solid; m.p. 145–146^o C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91(d, *J* = 15.6 Hz, 1H), 7.78–7.76 (m, 1H), 7.52(d, *J* = 8.1 Hz, 2H), 7.36(d, *J* = 8.4 Hz, 2H), 7.30–7.27 (m, 3H), 7.05(d, *J* = 15.9 Hz, 1H), 3.84(s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.7, 143.0, 136.0, 135.8, 134.8, 134.4, 129.3, 129.1, 128.5, 128.4, 122.8, 122.7, 119.3, 113.4, 109.3, 29.8. HRMS (ESI) calcd for $C_{16}H_{14}N_2Cl$ ($[M + H]^+$)269.0845, found 269.0840.

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Supplementary data

Supplementary data related to this article can be found at

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Supporting Information

Nano CuO Catalyzed C–H Functionalization of 1, 3-Azoles with Bromoarenes and Bromoalkenes

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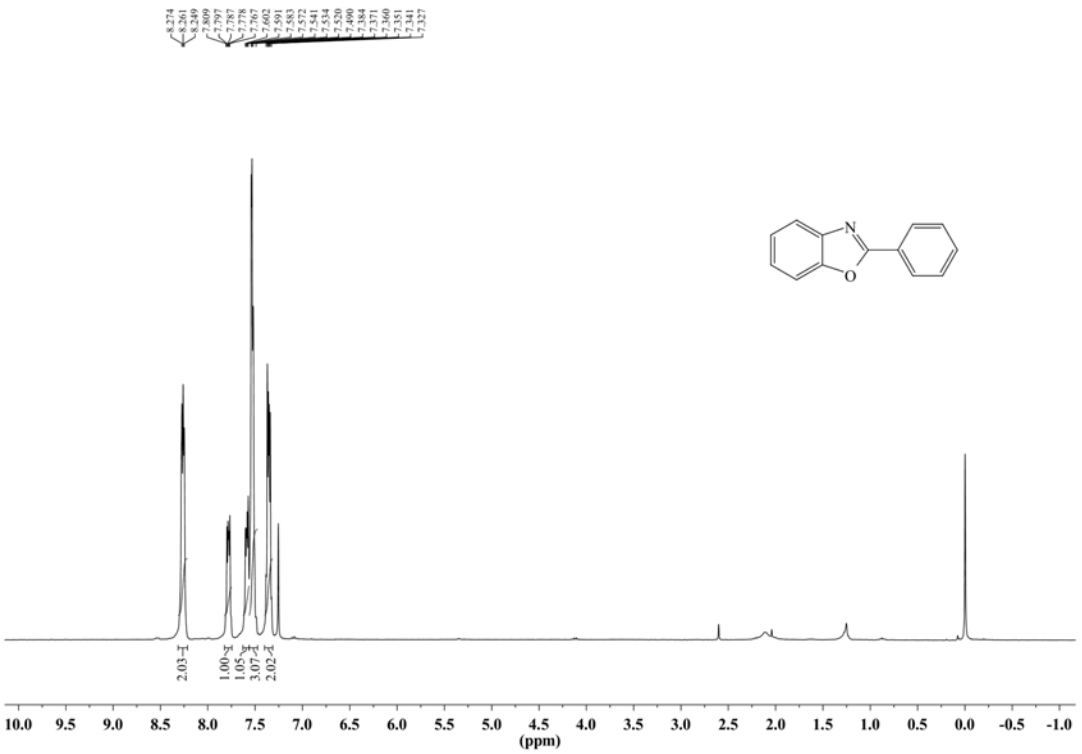
Contents

2-Phenylbenzo[d]oxazole（^{1}H NMR 300 MHz, $CDCl_3$)



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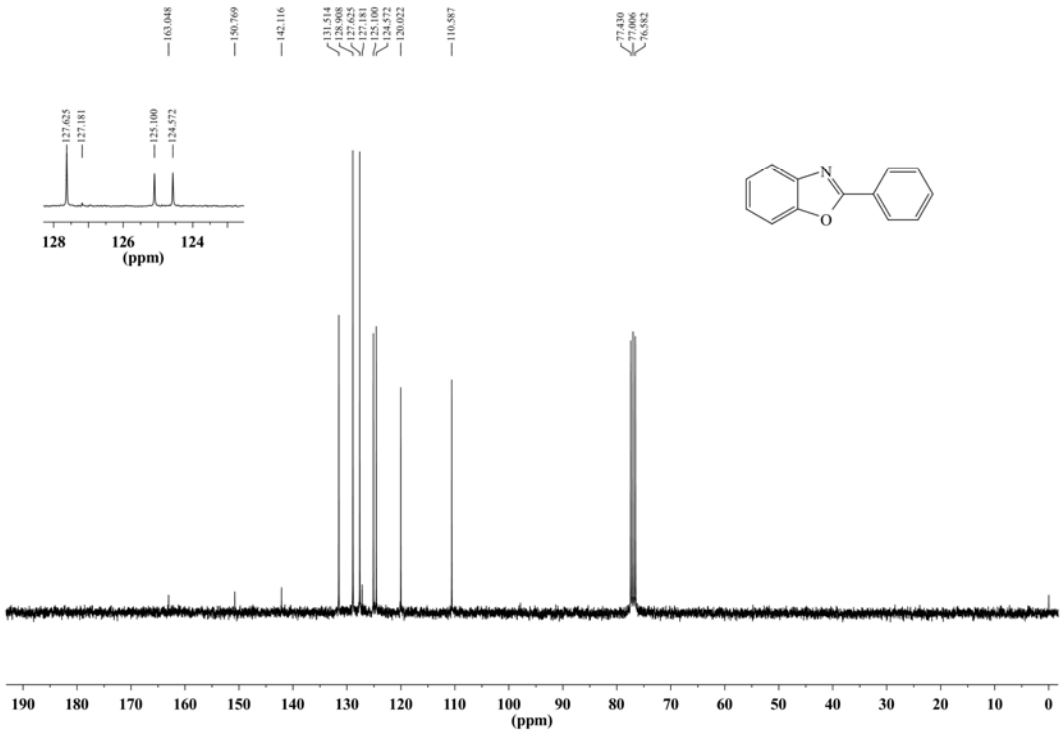

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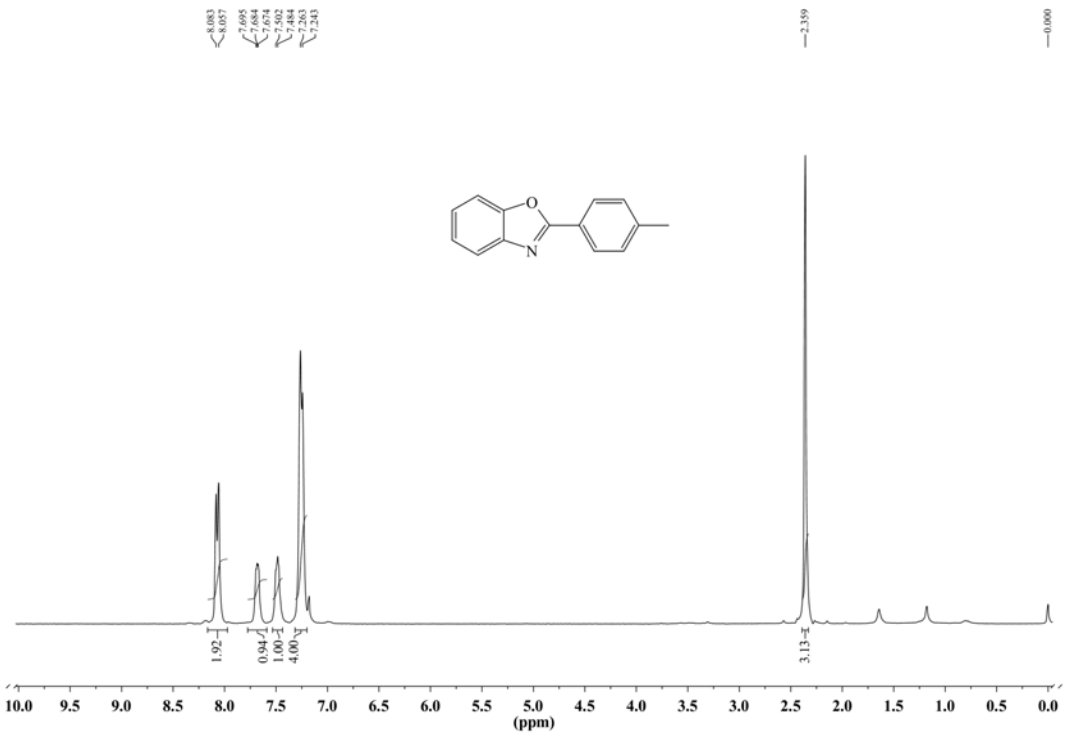

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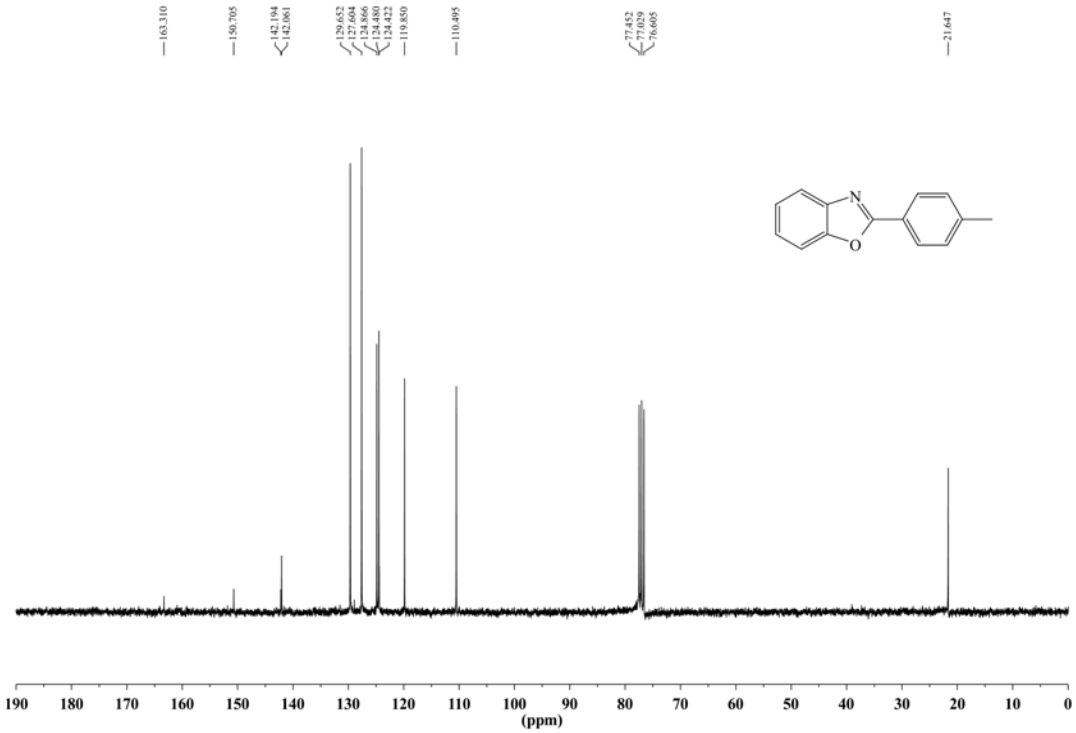

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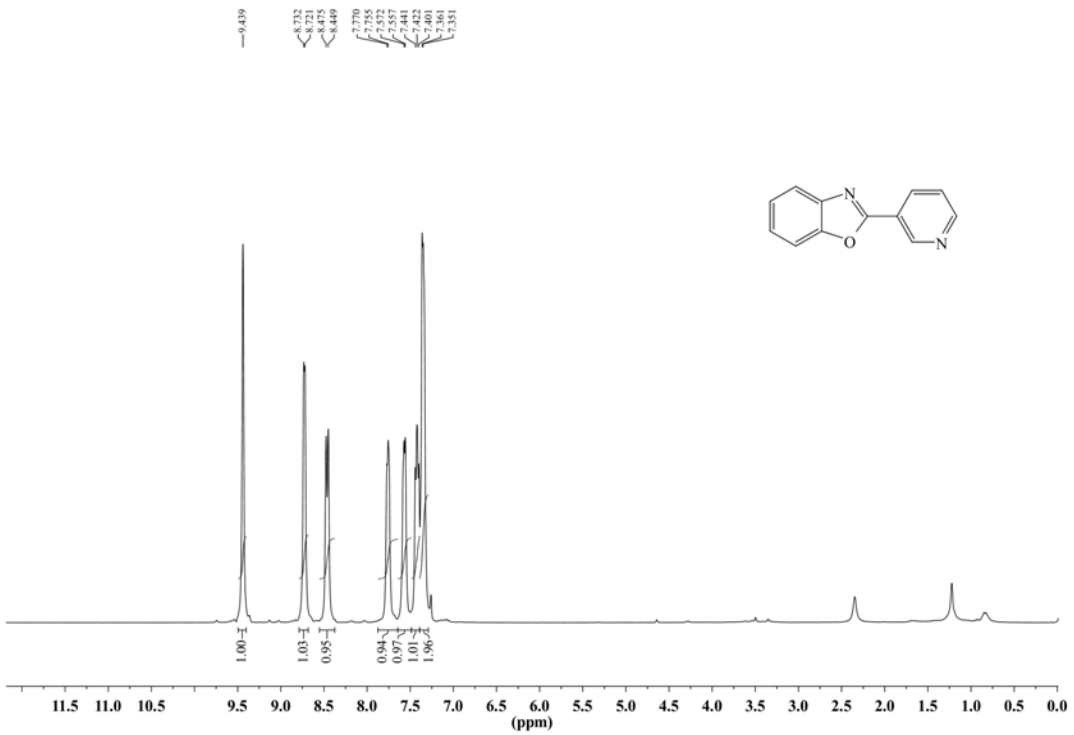

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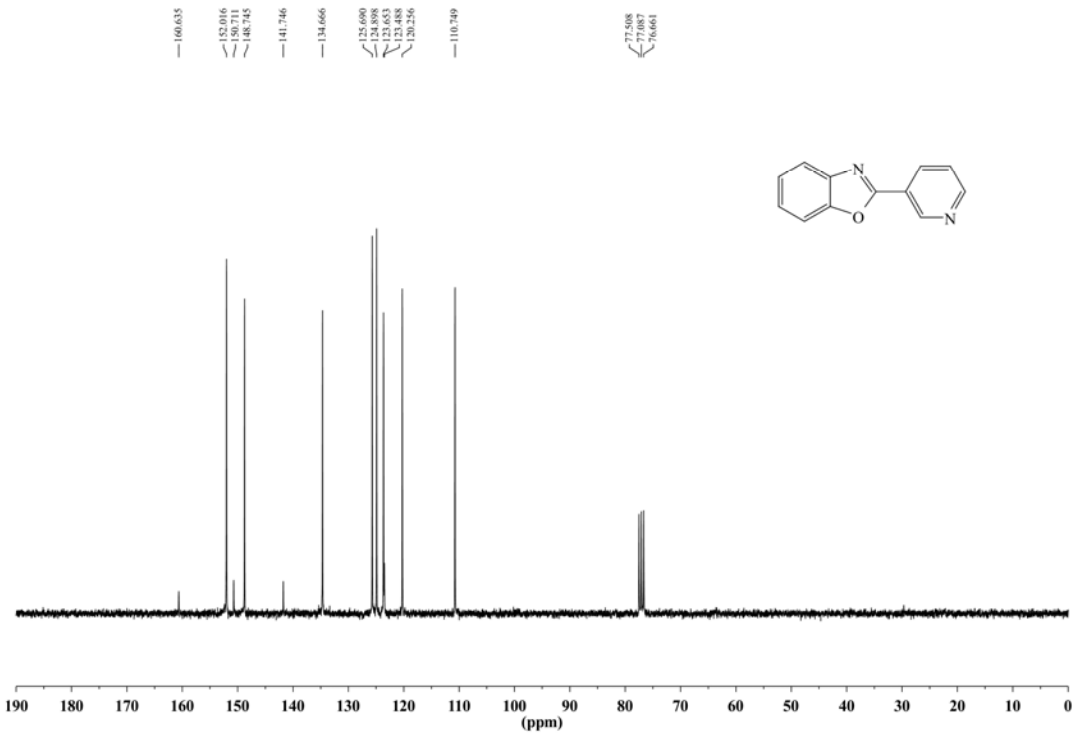

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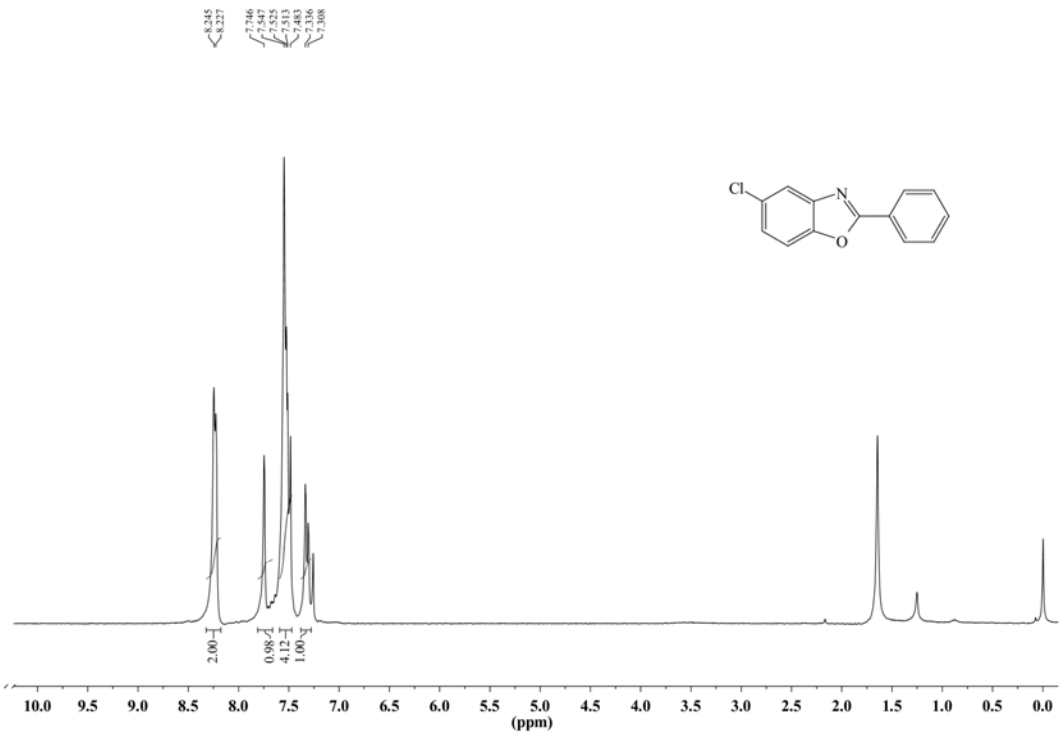

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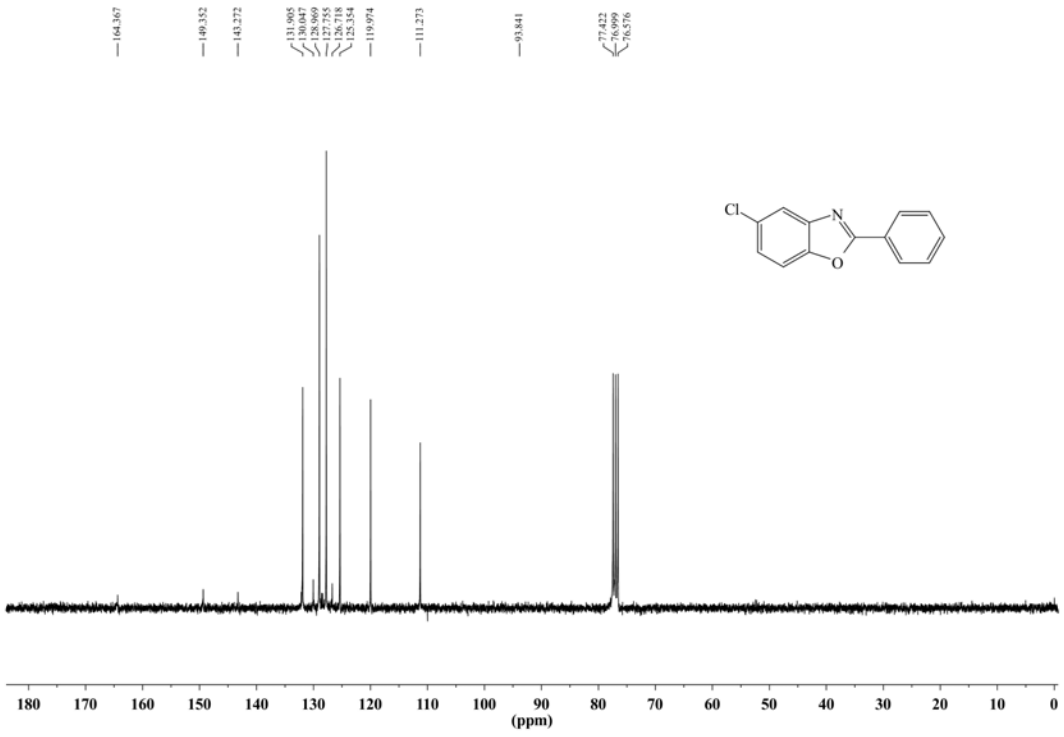

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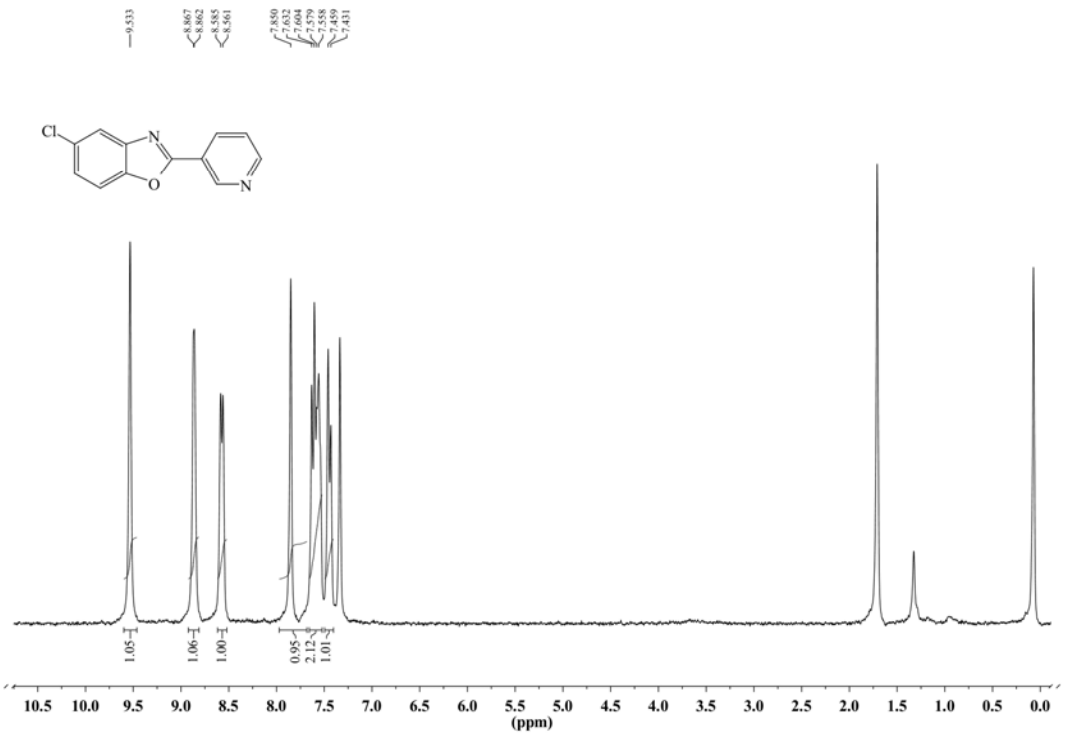

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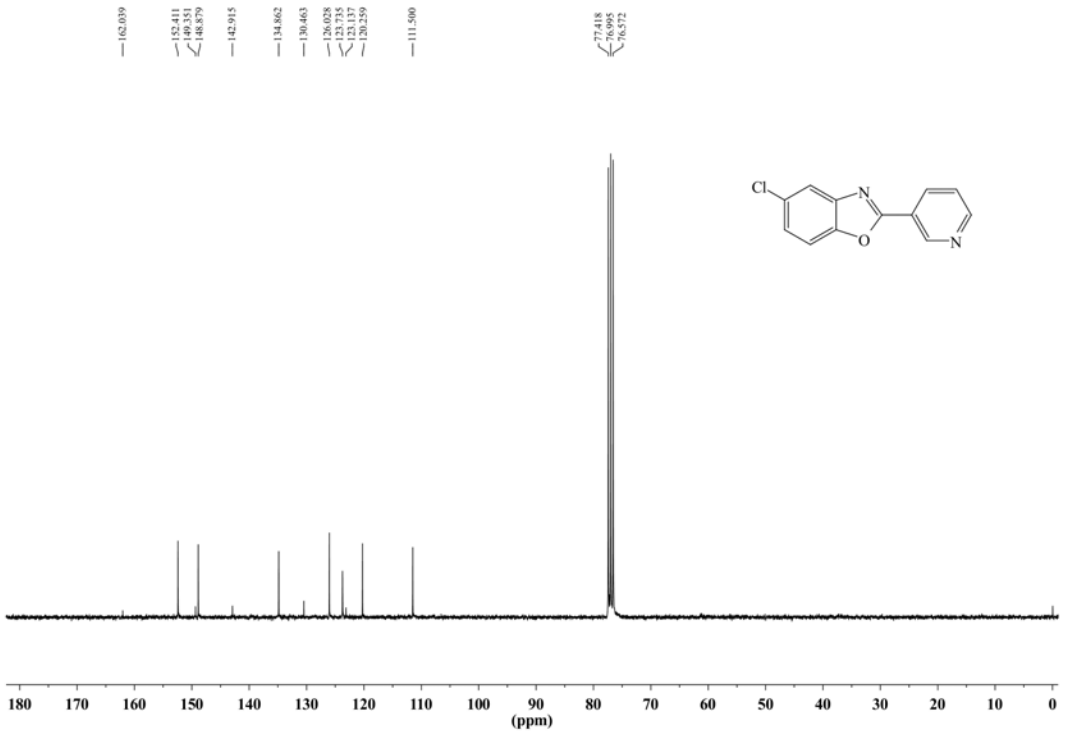

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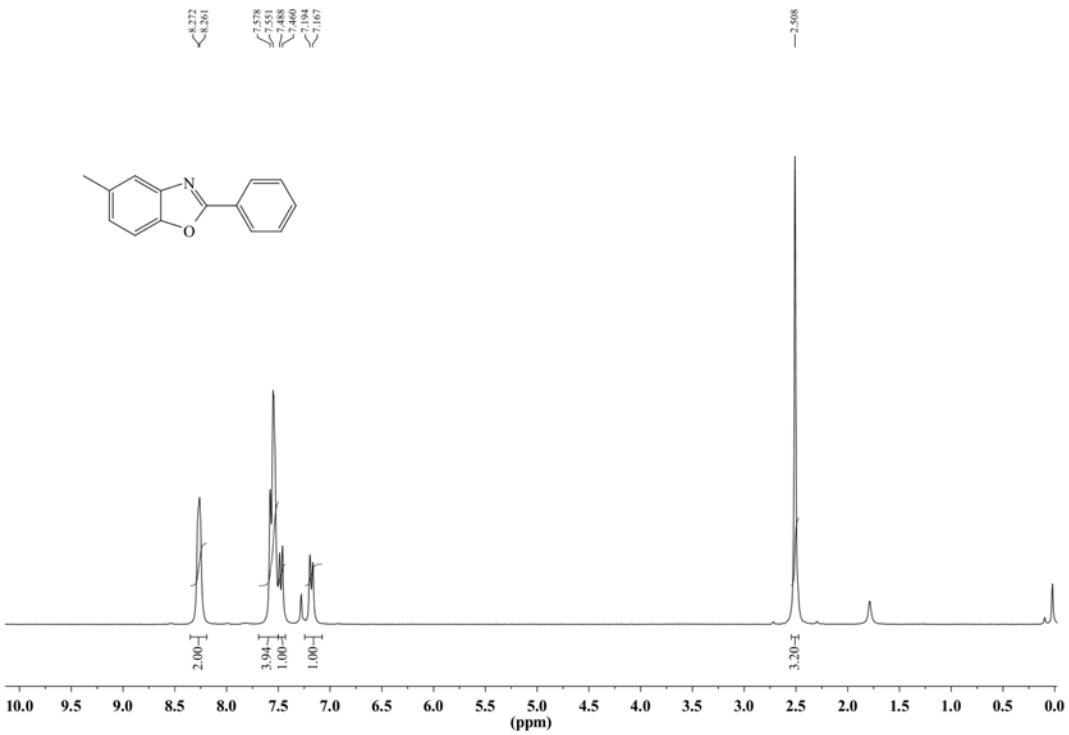

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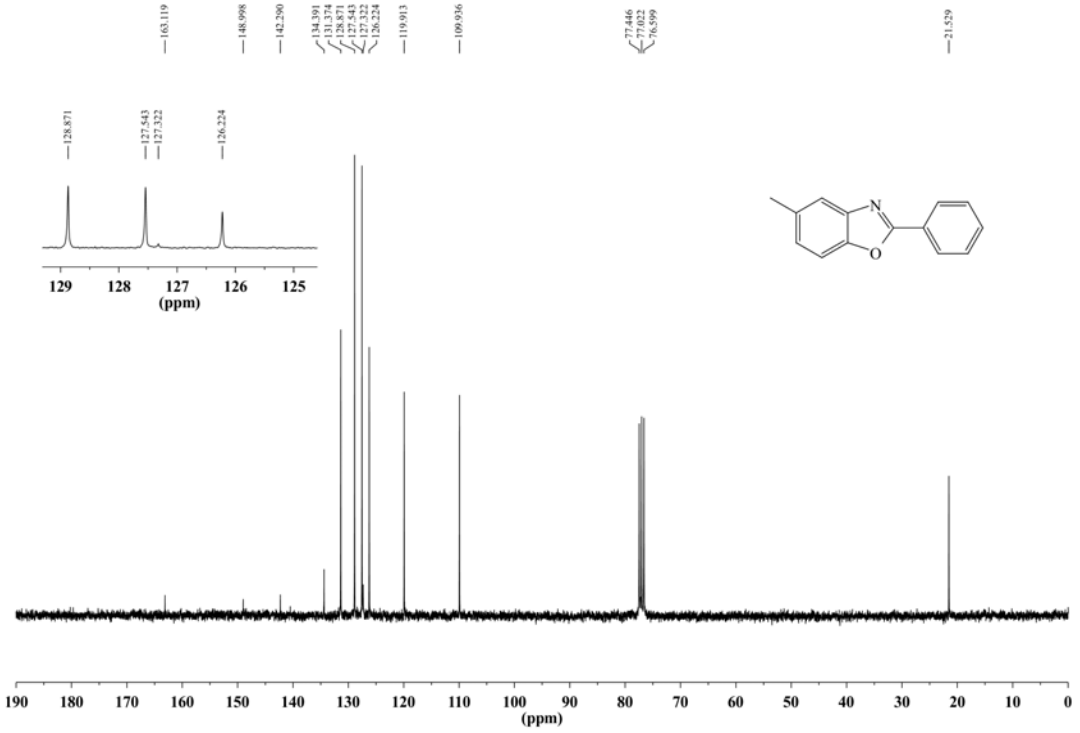

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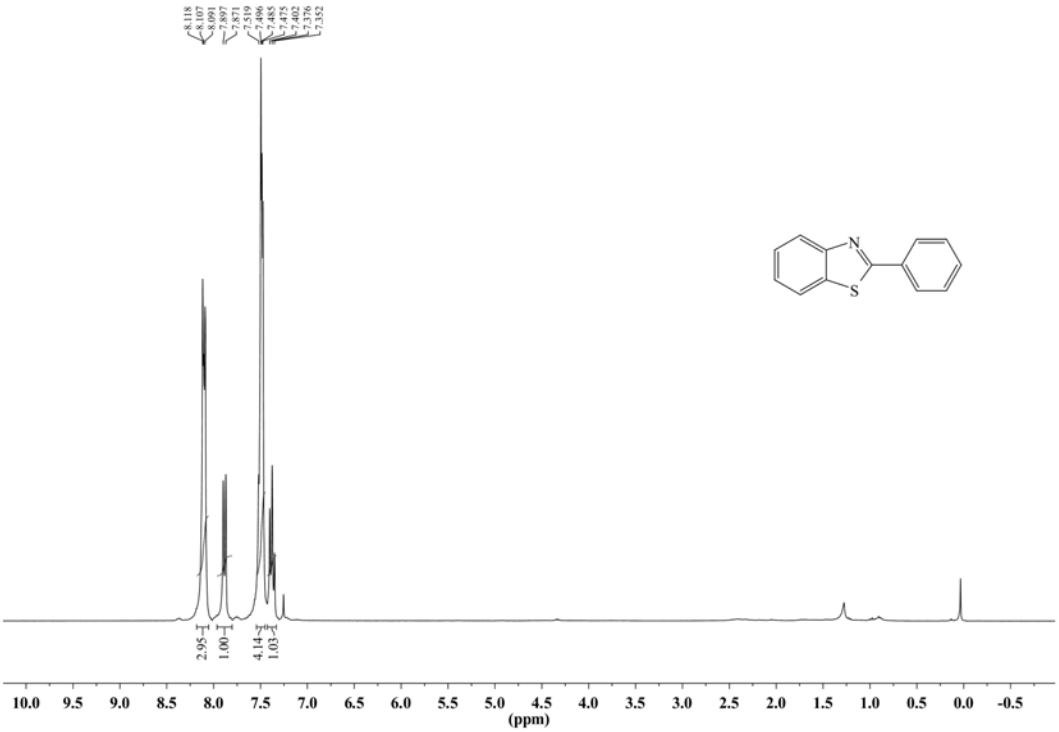

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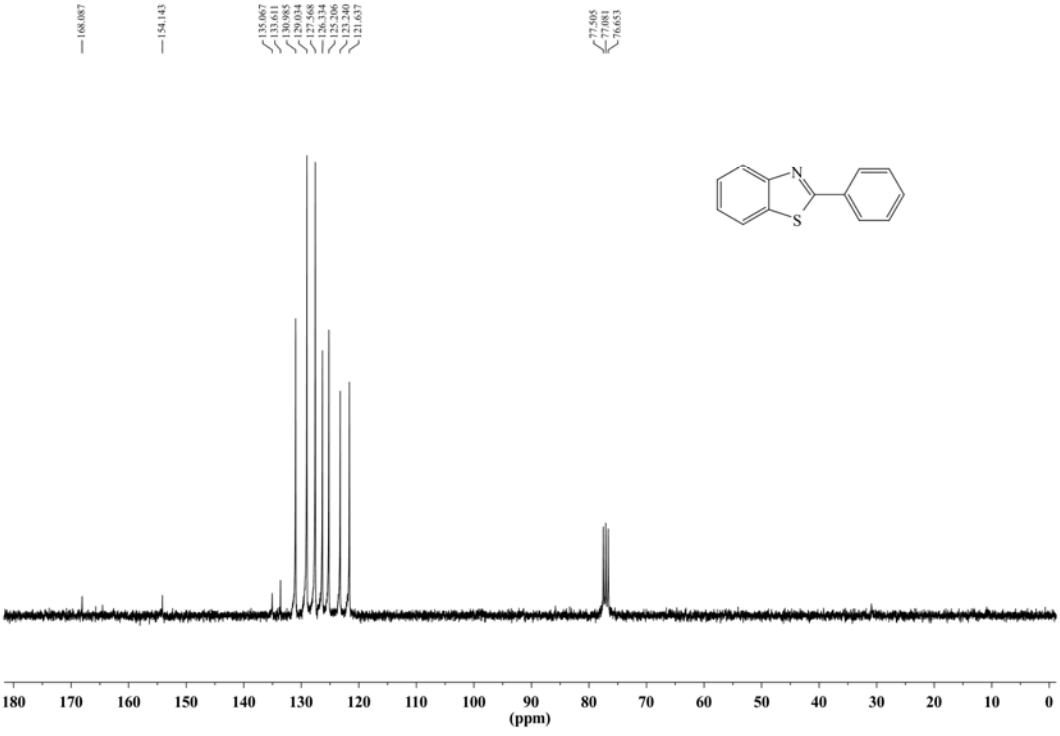
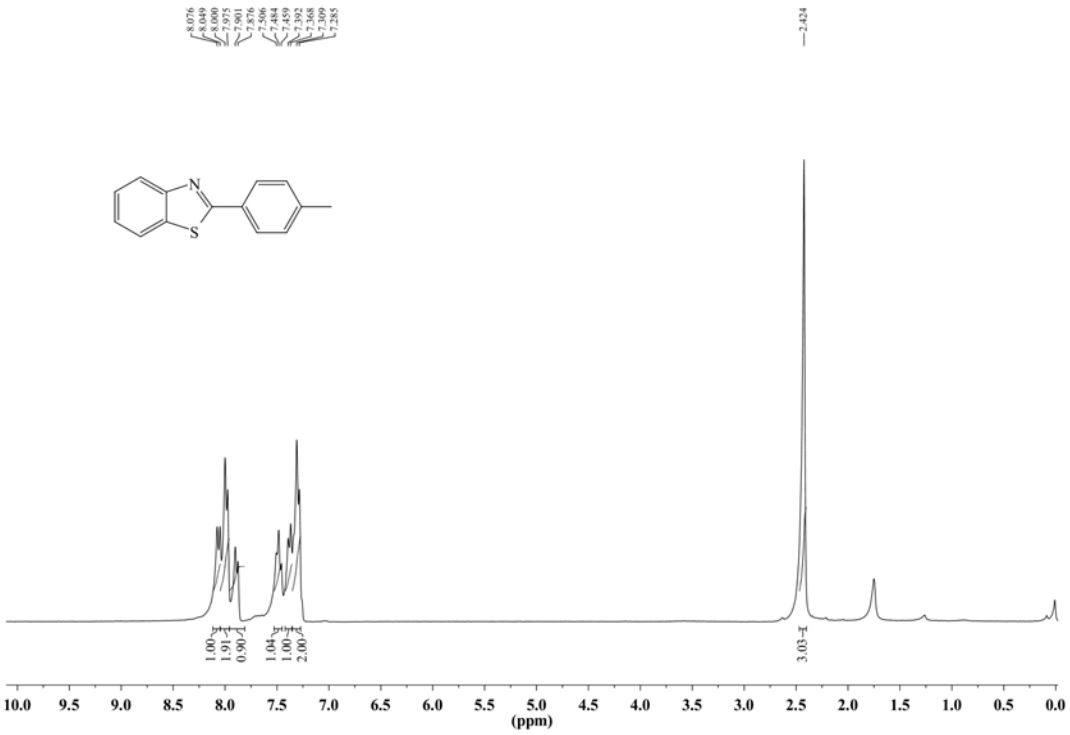
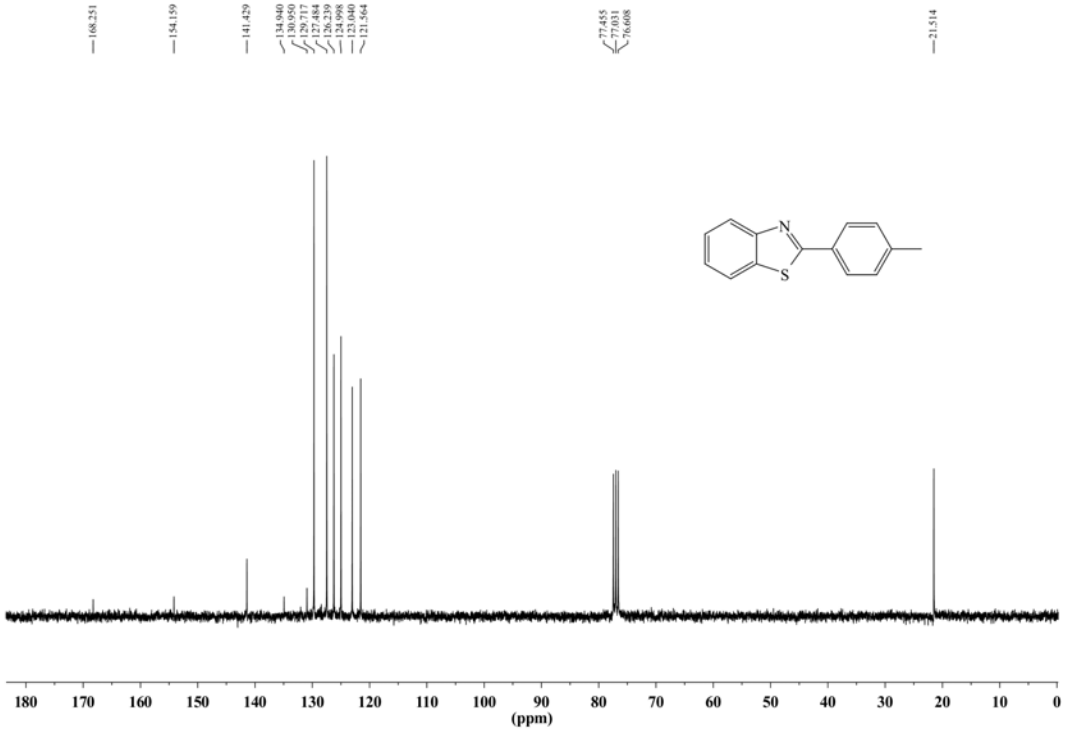


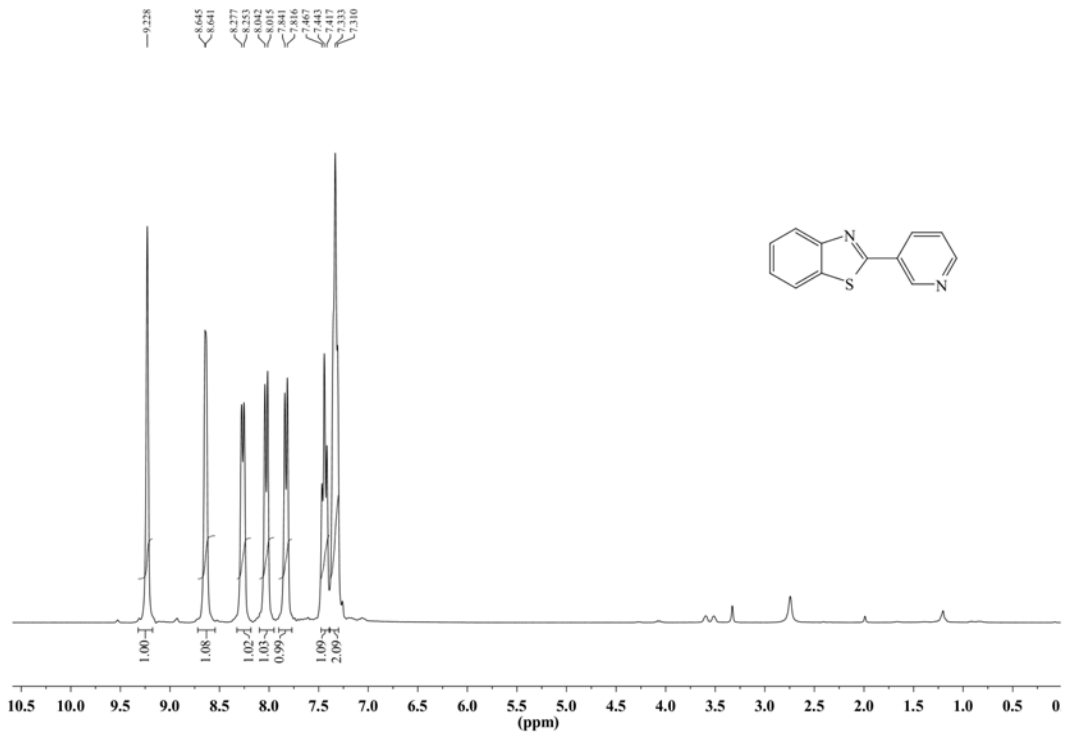
2-(p-Tolyl)benzo[d]thiazole (^{1}H NMR 300 MHz, $CDCl_3$)



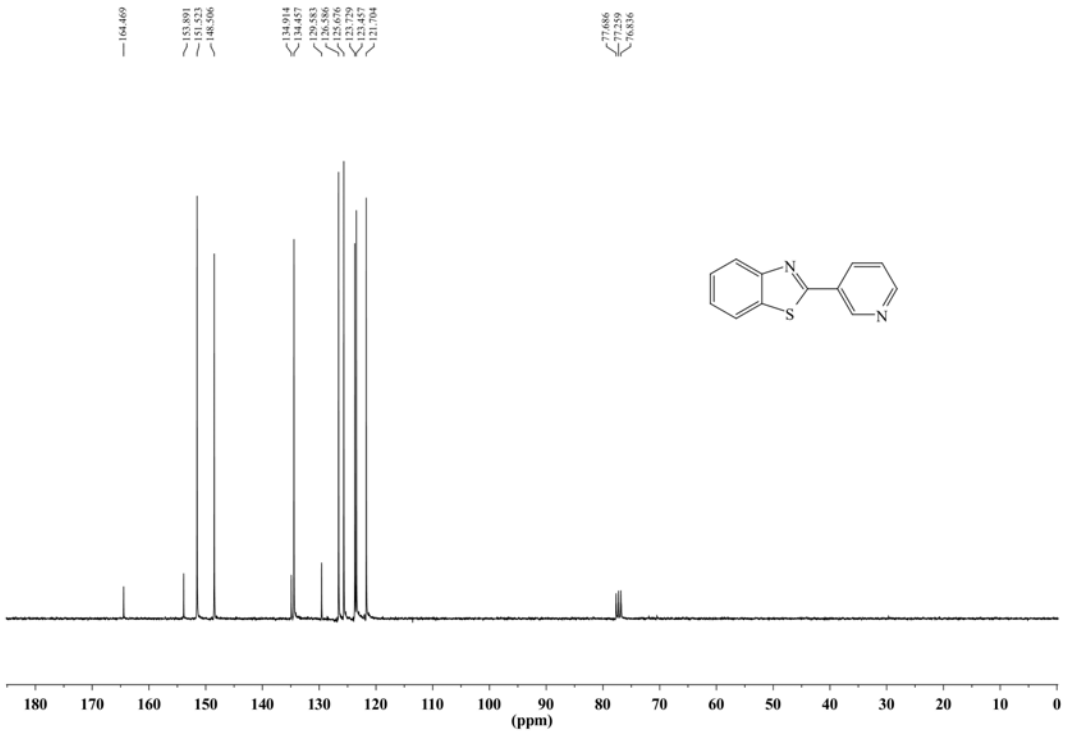
2-(p-Tolyl)benzo[d]thiazole (^{13}C NMR 75 MHz, $CDCl_3$)



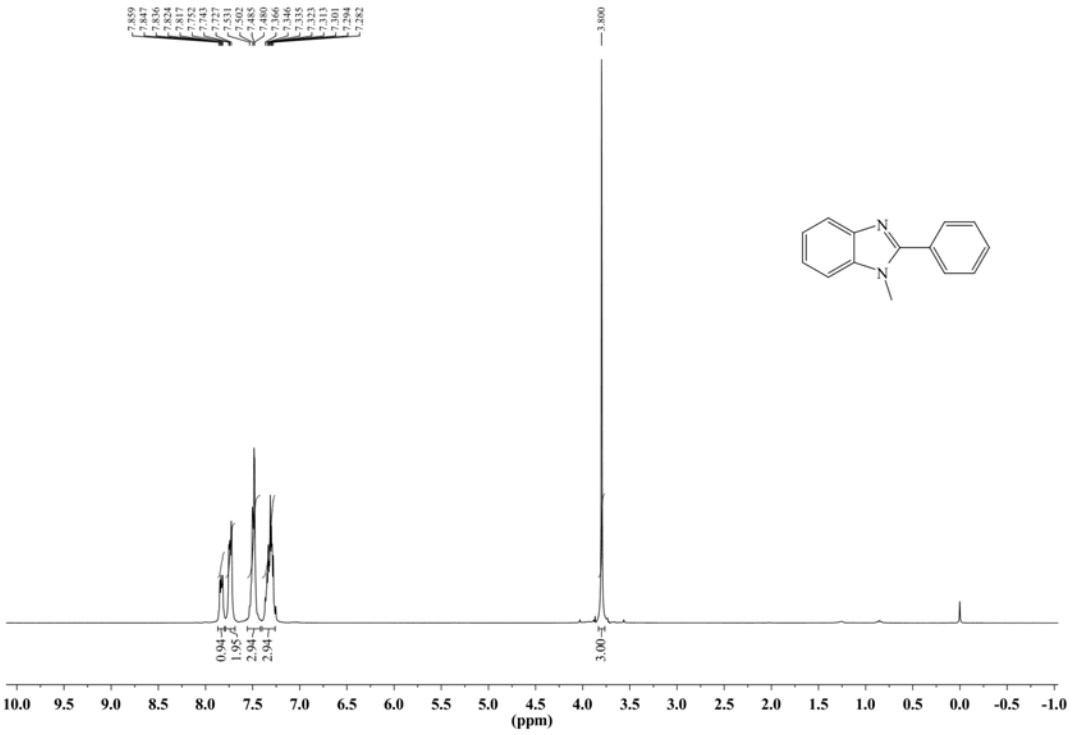
2-(pyridin-3-yl)benzo[d]thiazole (^{1}H NMR 300 MHz, $CDCl_3$)



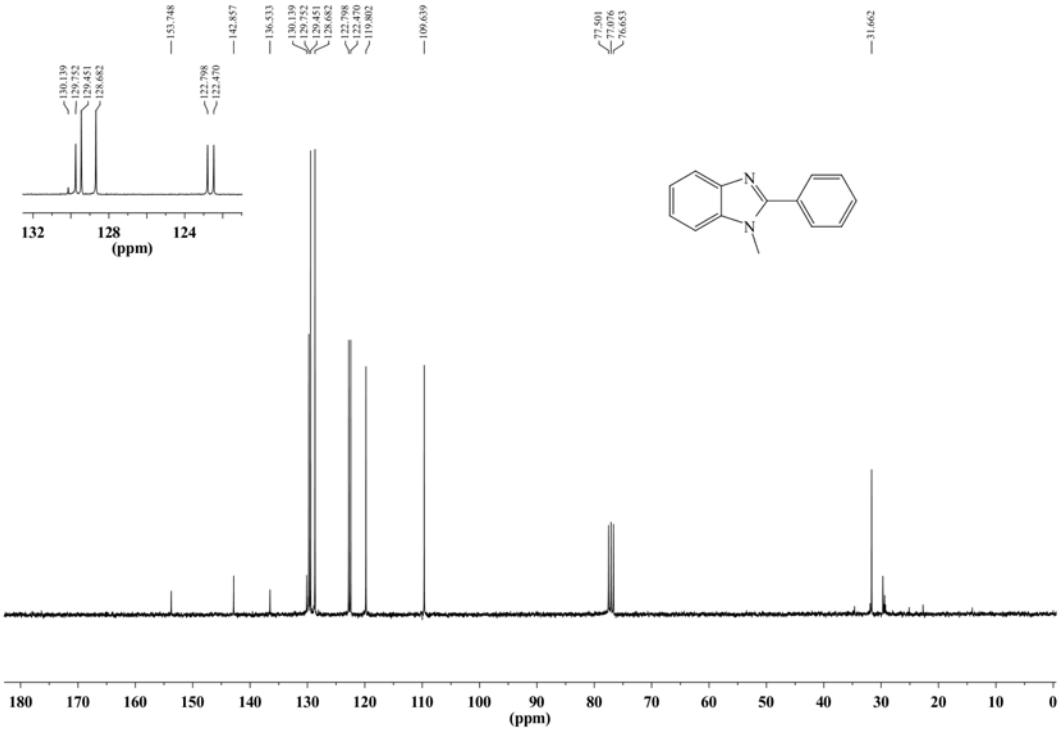
2-(pyridin-3-yl)benzo[d]thiazole (^{13}C NMR 75 MHz, $CDCl_3$)



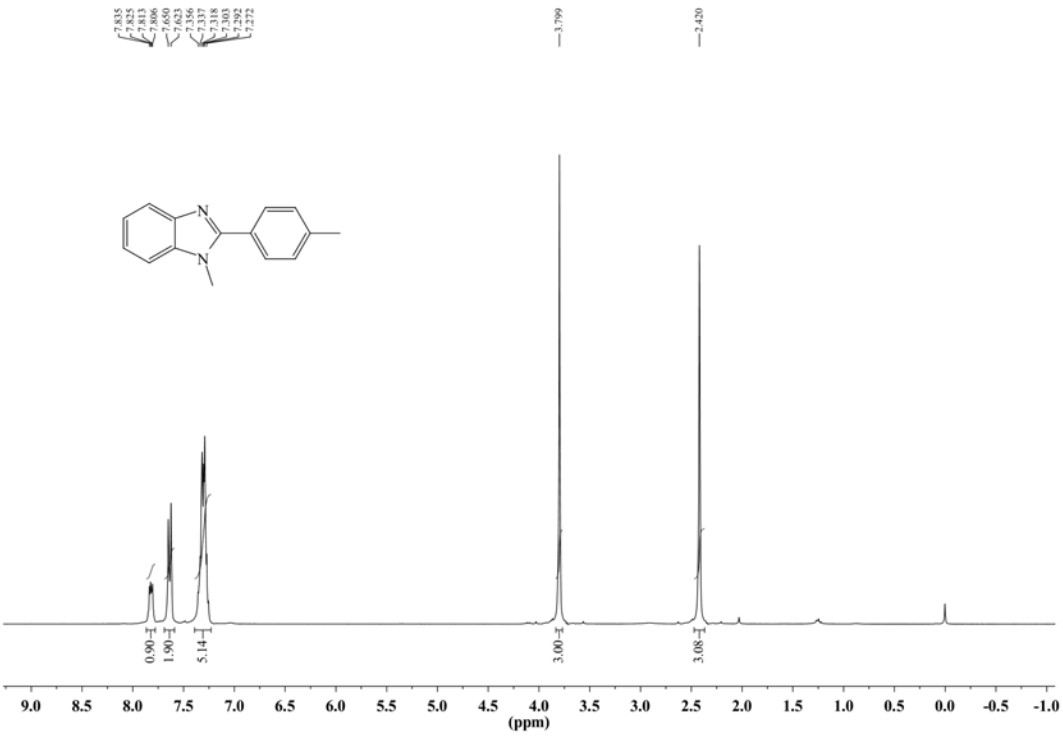
1-Methyl-2-phenyl-1H-benzo[d]imidazole (^{1}H NMR 300 MHz, $CDCl_3$)



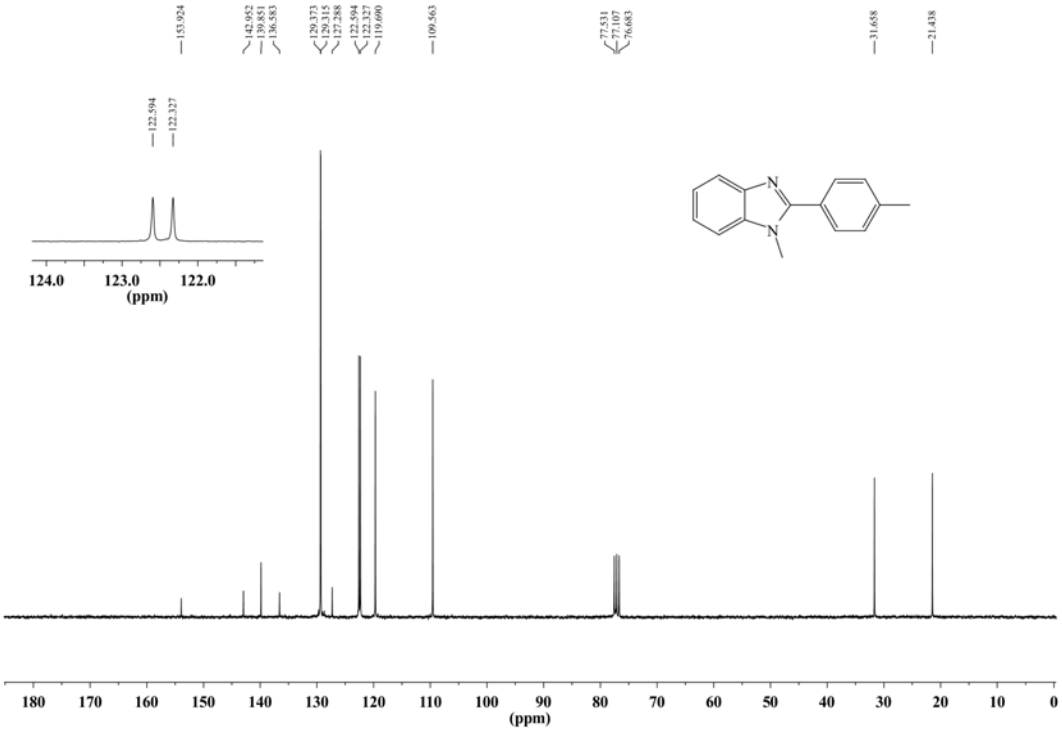
1-Methyl-2-phenyl-1H-benzo[d]imidazole (^{13}C NMR 75 MHz, $CDCl_3$)



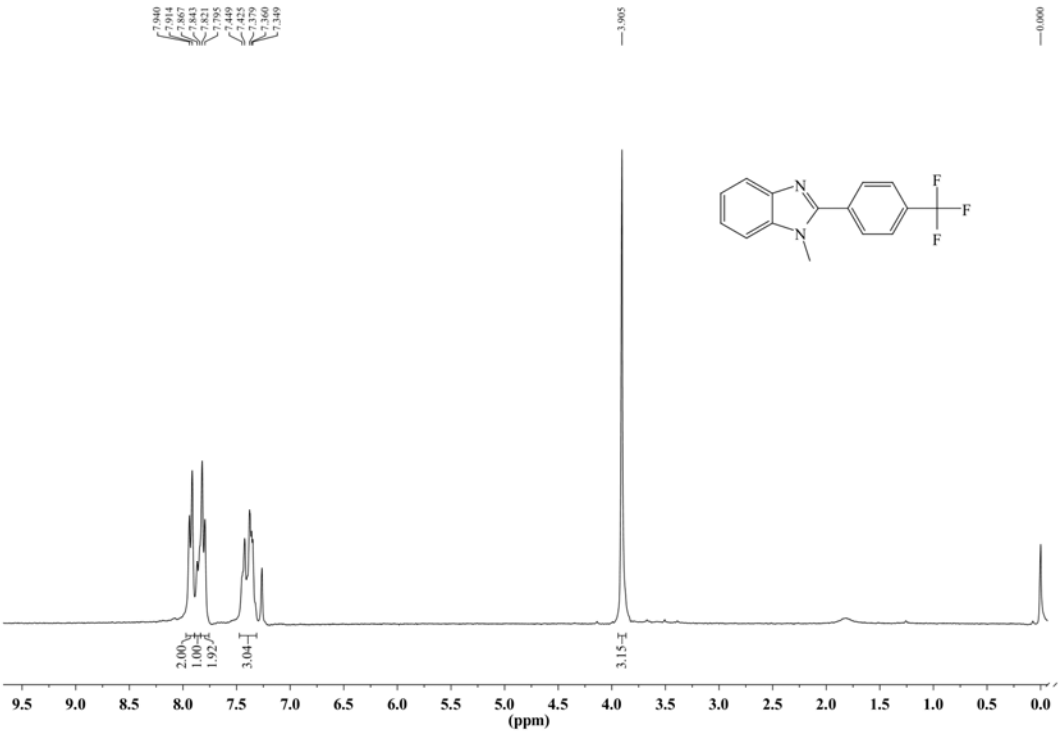
1-**Methyl-2-(p-tolyl)-1H-benzo[d]imidazole (**^{1}**H NMR 300 MHz, CDCl**$_3$**)**



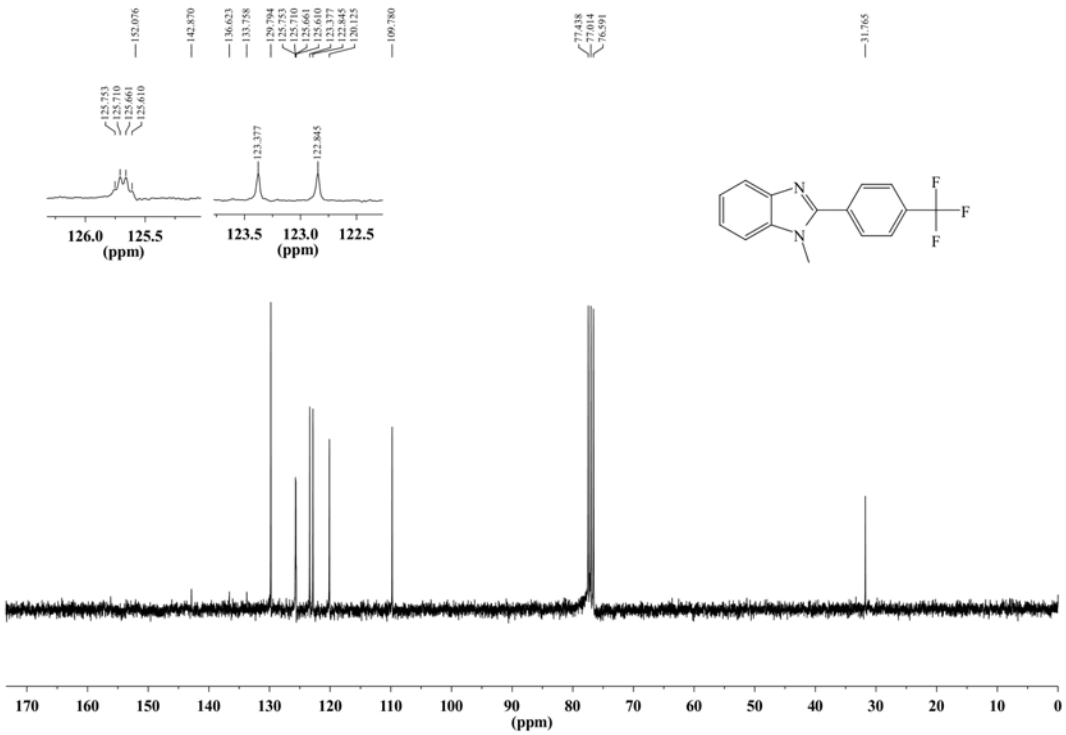
1-Methyl-2-(p-tolyl)-1H-benzo[d]imidazole (^{13}**C NMR 75 MHz, CDCl**$_3$**)**



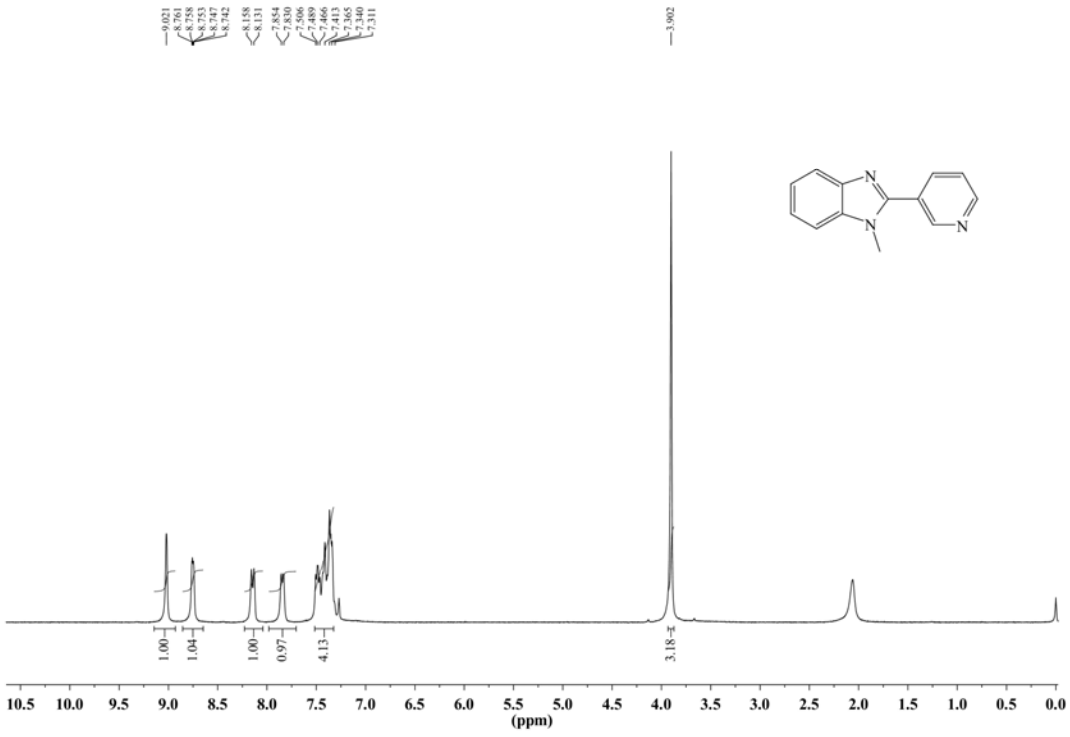
1-methyl-2-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazole (^{1}H NMR 300 MHz, $CDCl_3$)



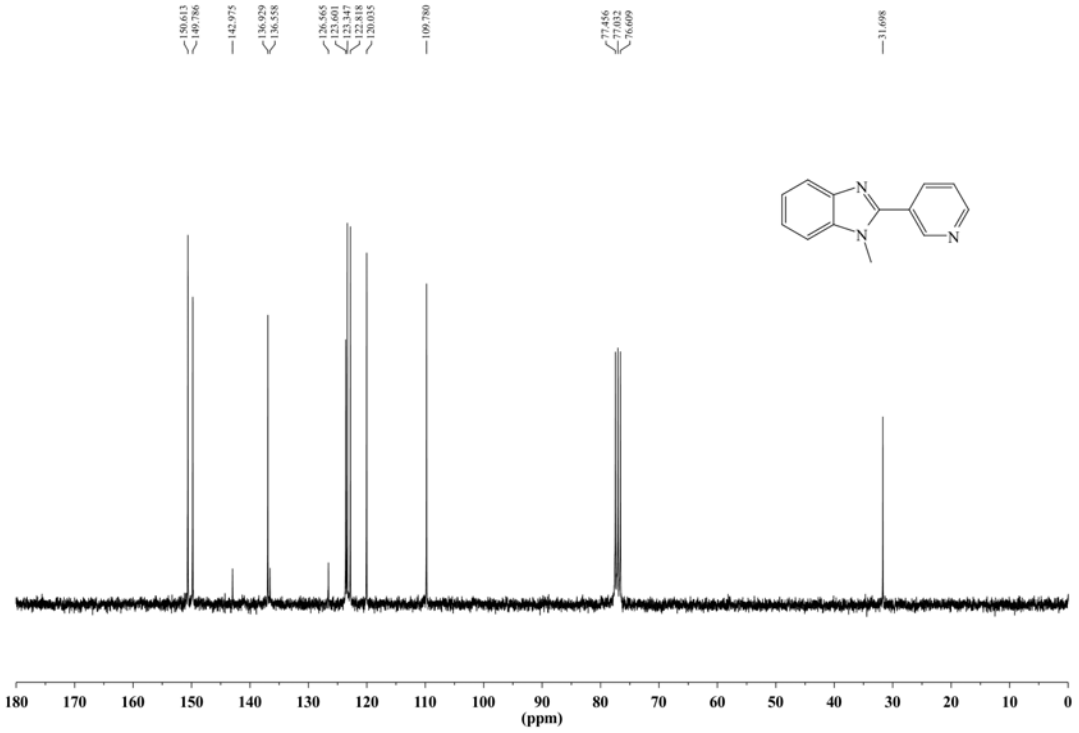
1-methyl-2-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazole (^{13}C NMR 75 MHz, $CDCl_3$)



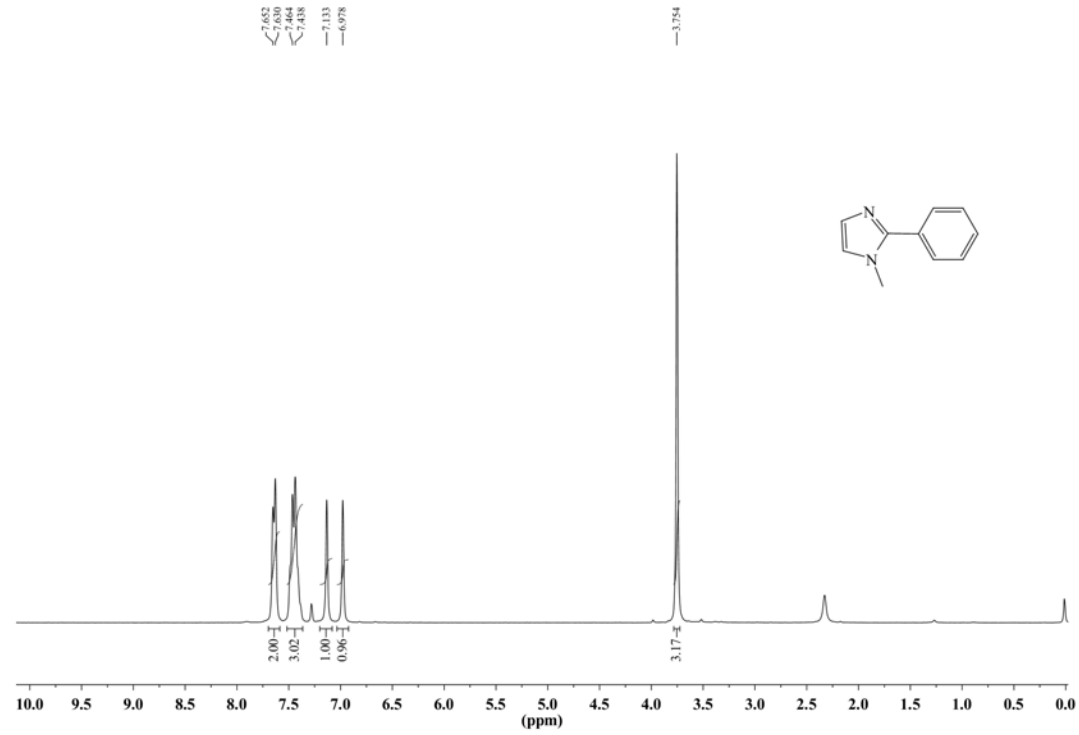
1-methyl-2-(pyridin-3-yl)-1H-benzo[d]imidazole (^{1}H NMR 300 MHz, $CDCl_3$)



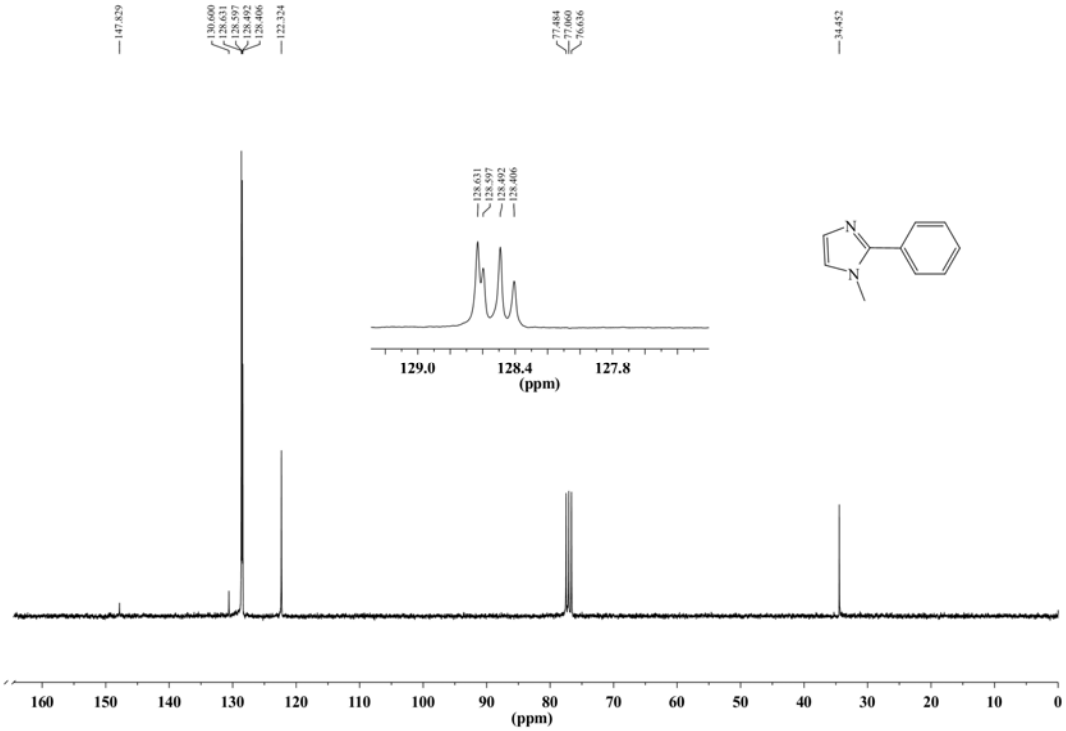
1-methyl-2-(pyridin-3-yl)-1H-benzo[d]imidazole (^{13}C NMR 75 MHz, $CDCl_3$)



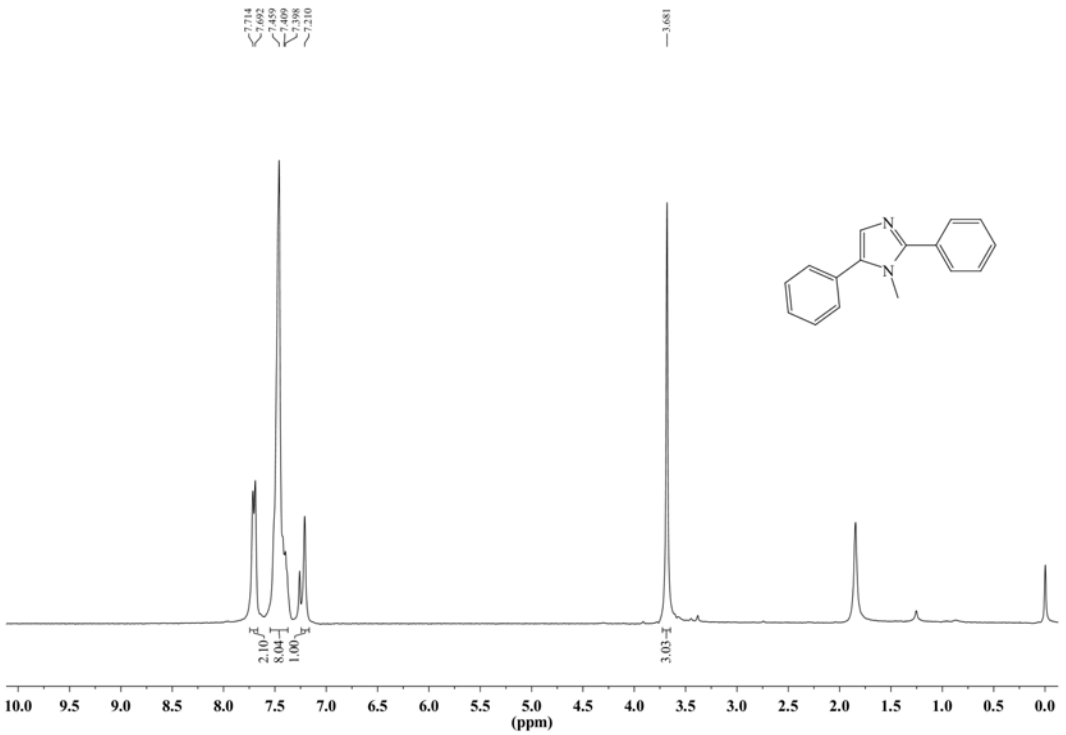
1-methyl-2-phenyl-1H-imidazole (^{1}H NMR 300 MHz, $CDCl_3$)



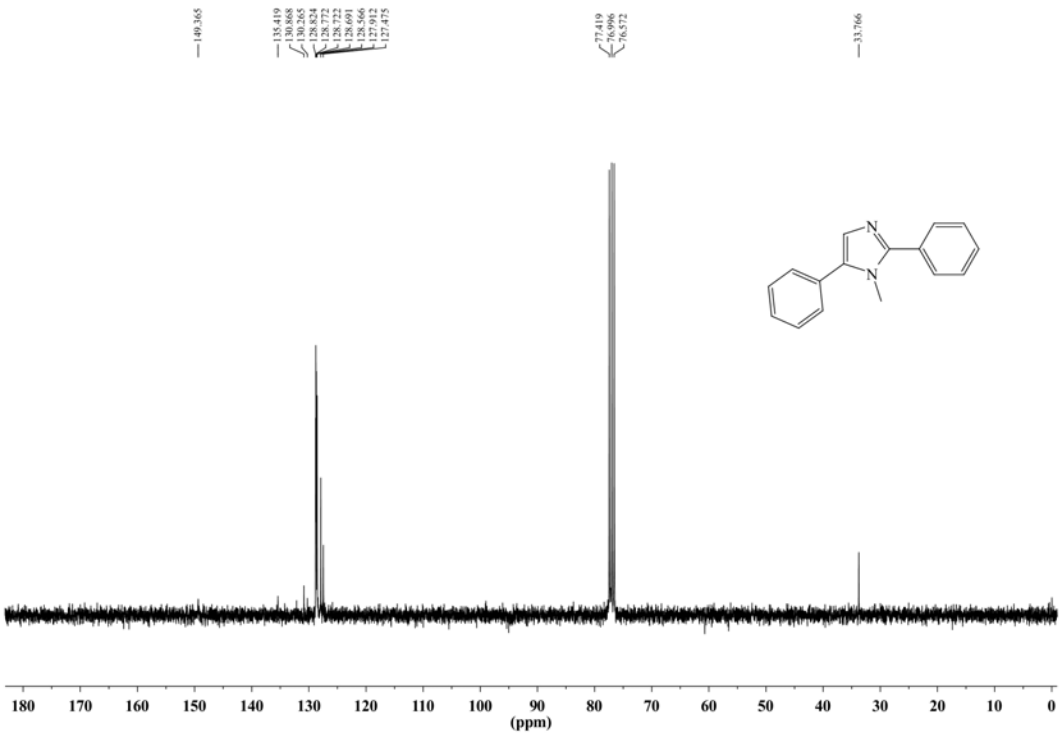
1-methyl-2-phenyl-1H-imidazole (^{13}C NMR 75 MHz, $CDCl_3$)



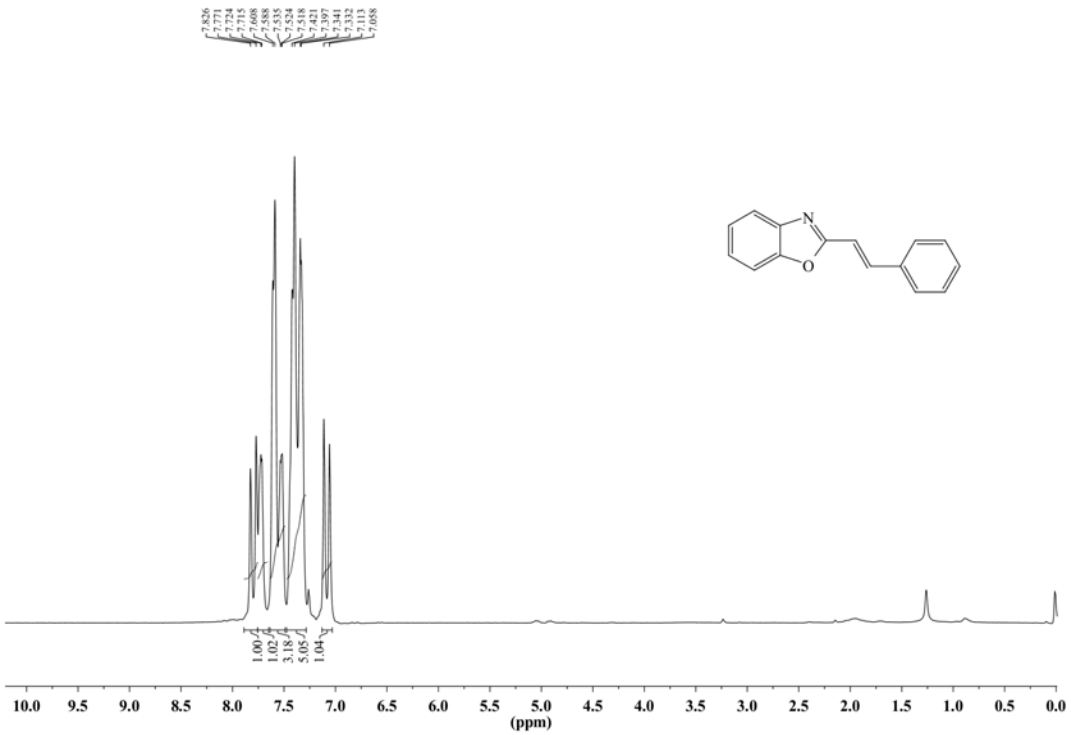
1-methyl-2,5-diphenyl-1H-imidazole (^{1}H NMR 300 MHz, $CDCl_3$)



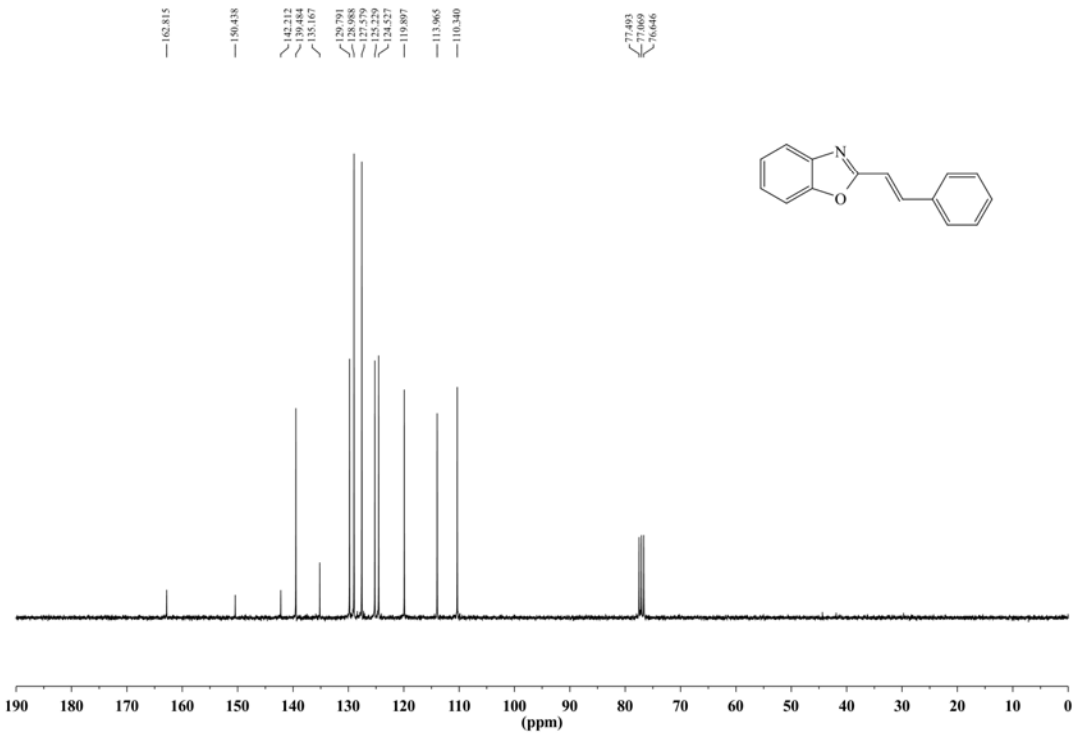
1-methyl-2,5-diphenyl-1H-imidazole (^{13}C NMR 75 MHz, $CDCl_3$)



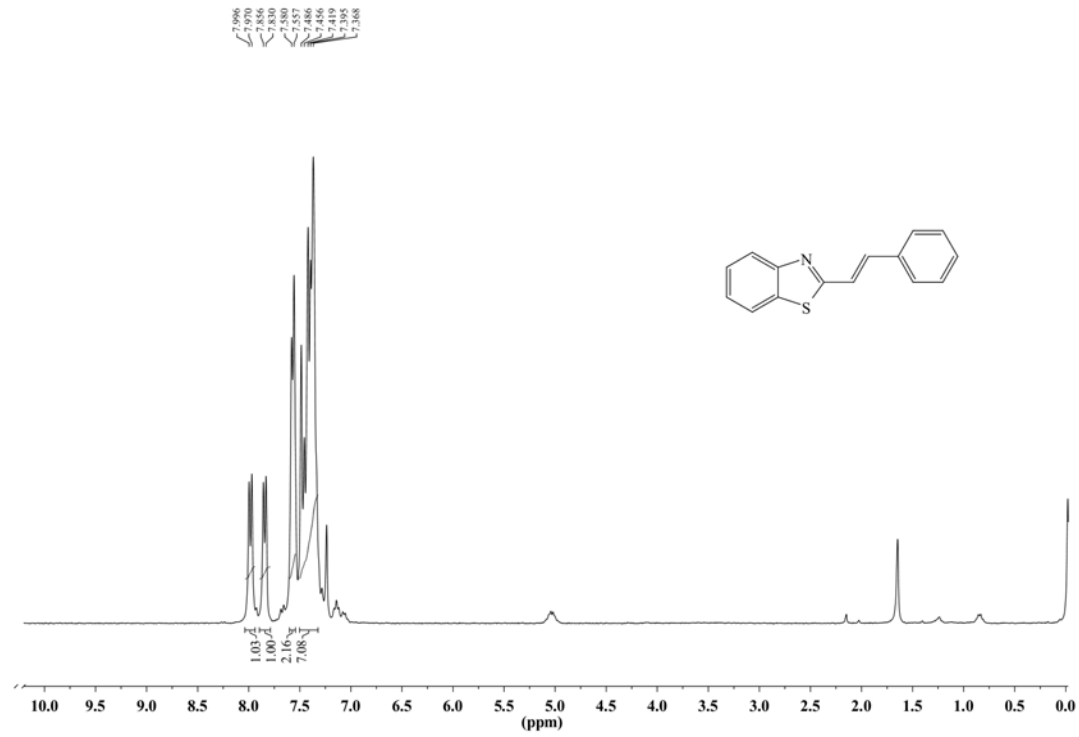
(E)-2-styrylbenzo[d]oxazole (1H NMR 300 MHz, CDCl3)



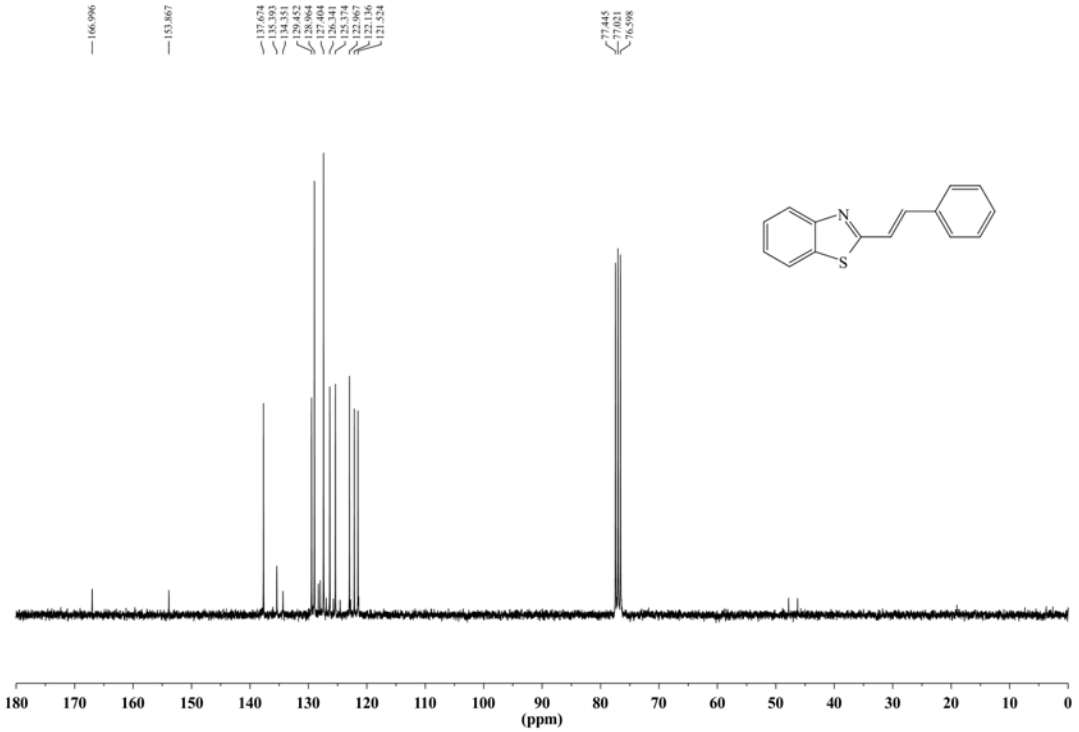
(E)-2-styrylbenzo[d]oxazole (13C NMR 75 MHz, CDCl3)



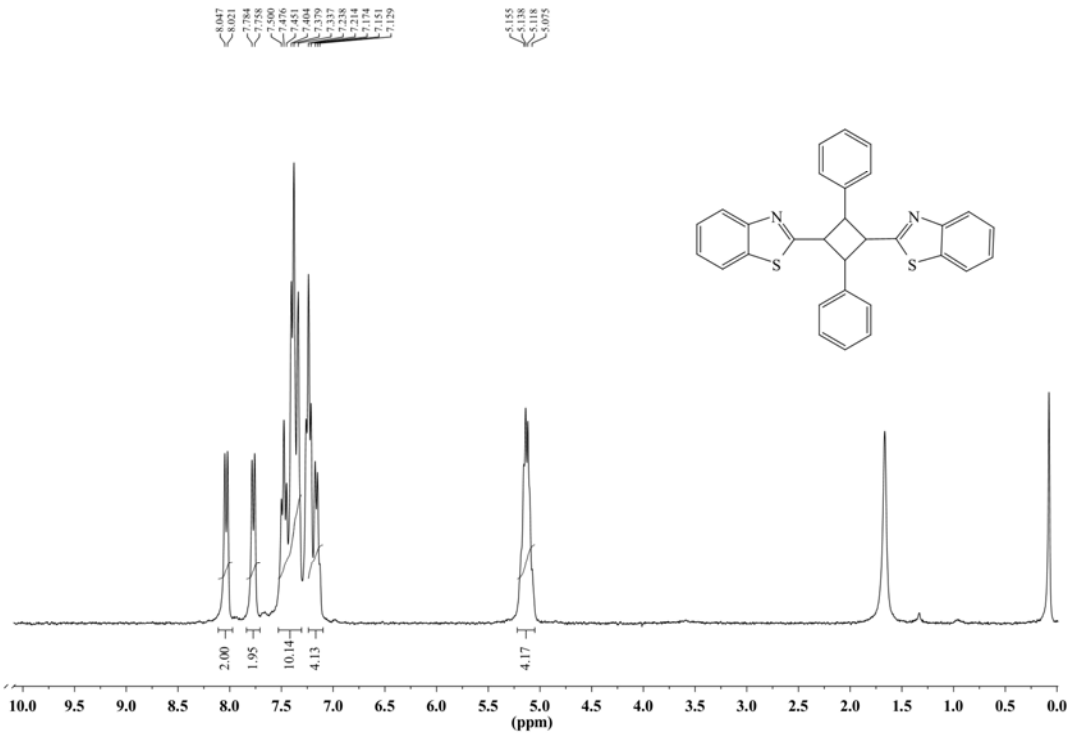
(E)-2-styrylbenzo[d]thiazole (^{1}H NMR 300 MHz, $CDCl_3$)



(E)-2-styrylbenzo[d]thiazole (^{13}C NMR 75 MHz, $CDCl_3$)

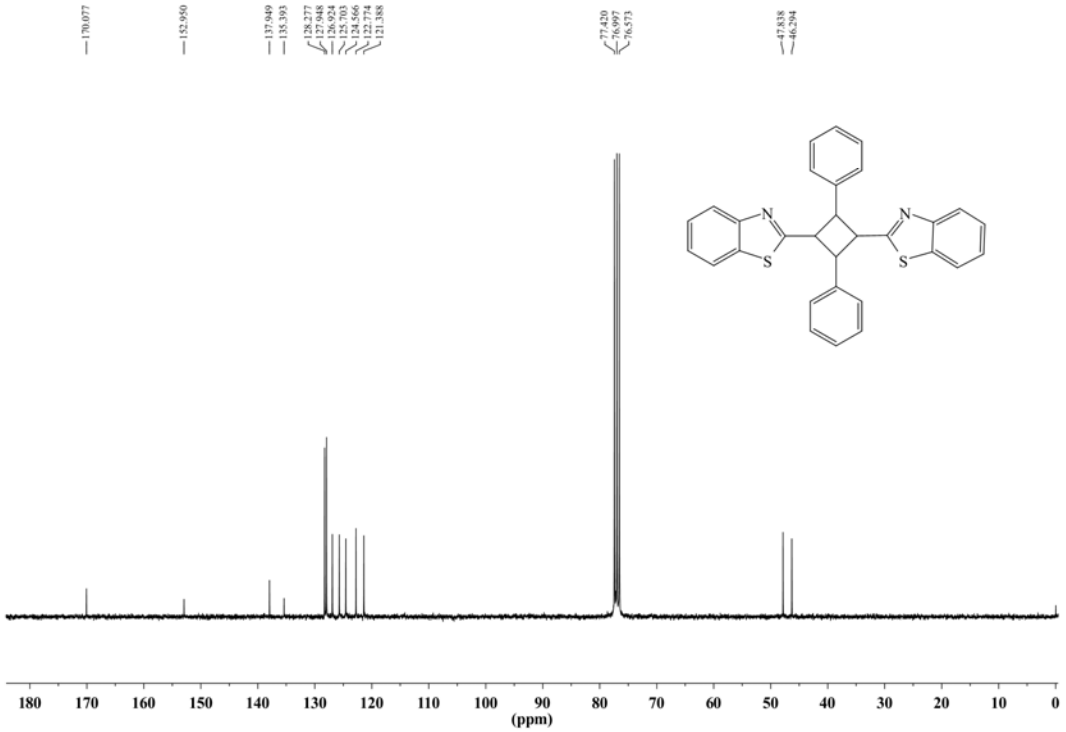


2,2'-(2,4-diphenylcyclobutane-1,3-diyl)bis(benzo[d]thiazole (^{1}H NMR 300 MHz, $CDCl_3$)

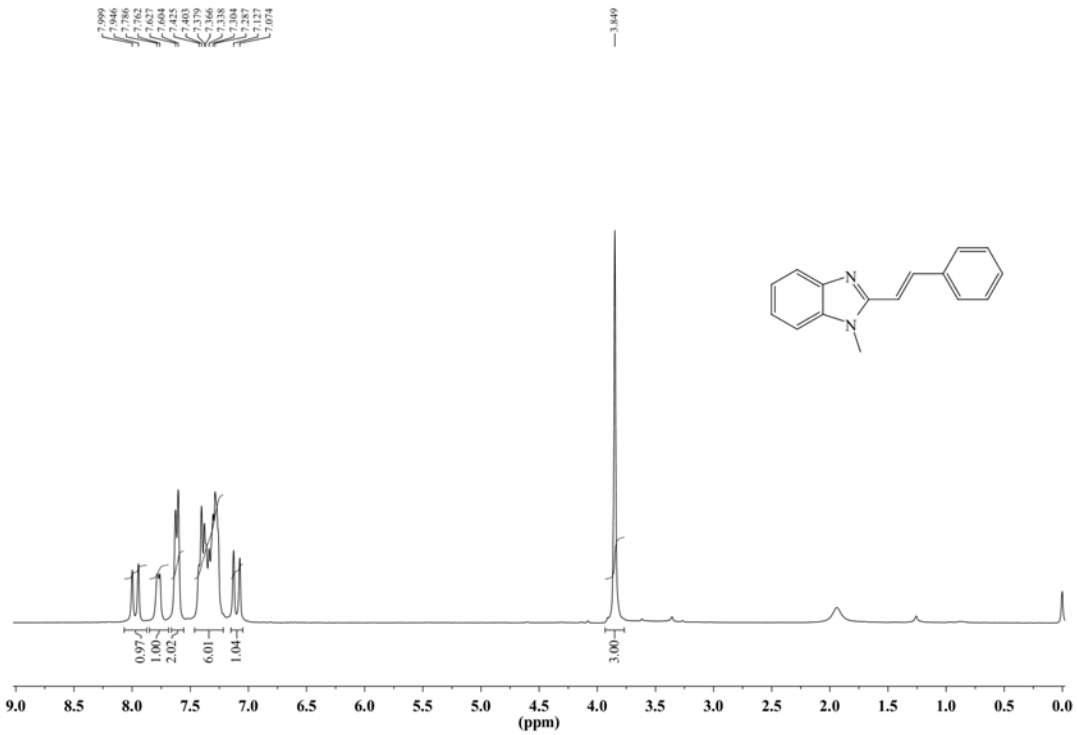


2,2'-(2,4-diphenylcyclobutane-1,3-diyl)bis(benzo[d]thiazole(^{13}C NMR 75 MHz,

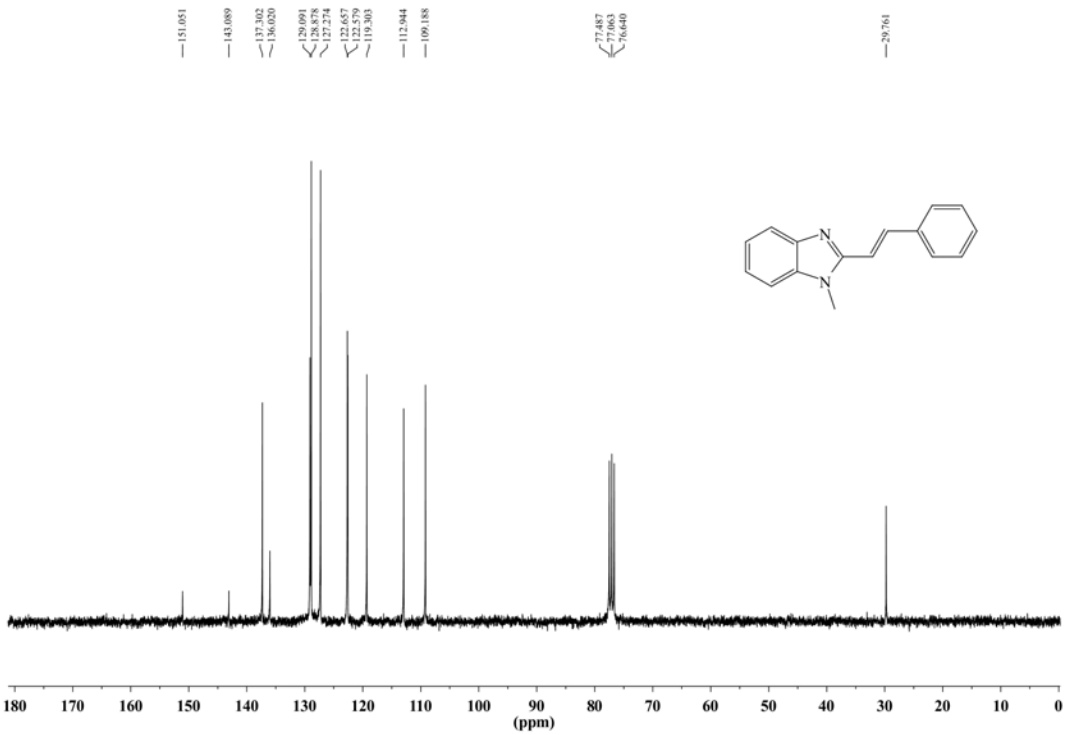
$CDCl_3$)



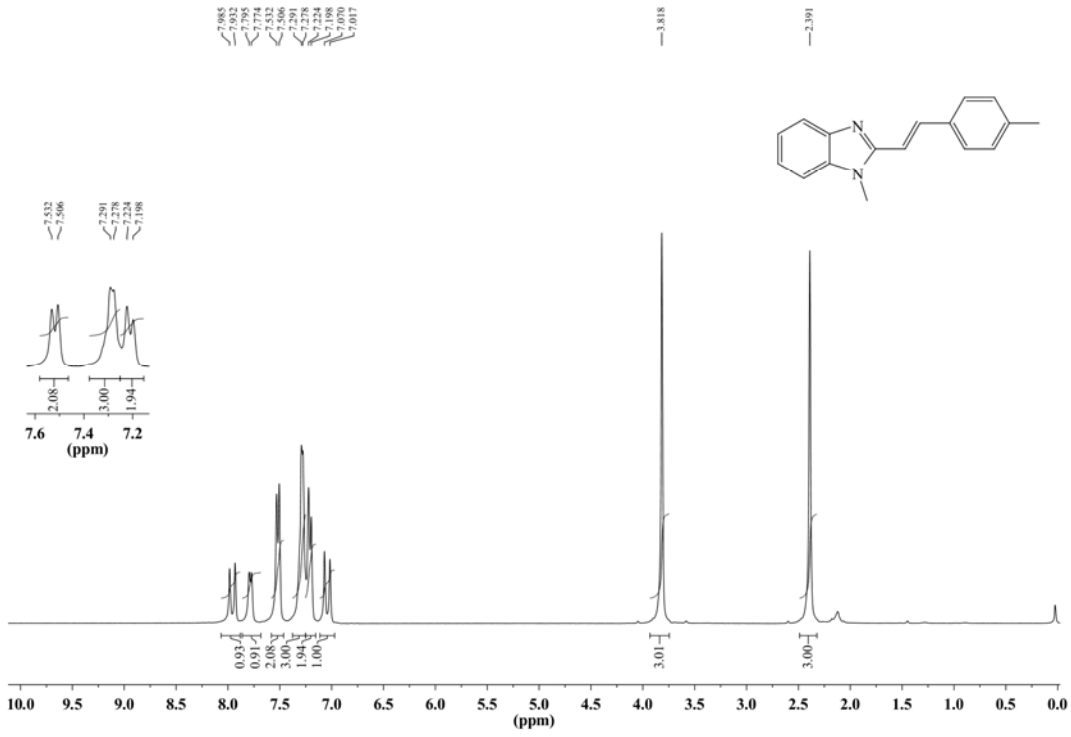
(E)-1-methyl-2-styryl-1H-benzo[d]imidazole (^{1}H NMR 300 MHz, $CDCl_3$)



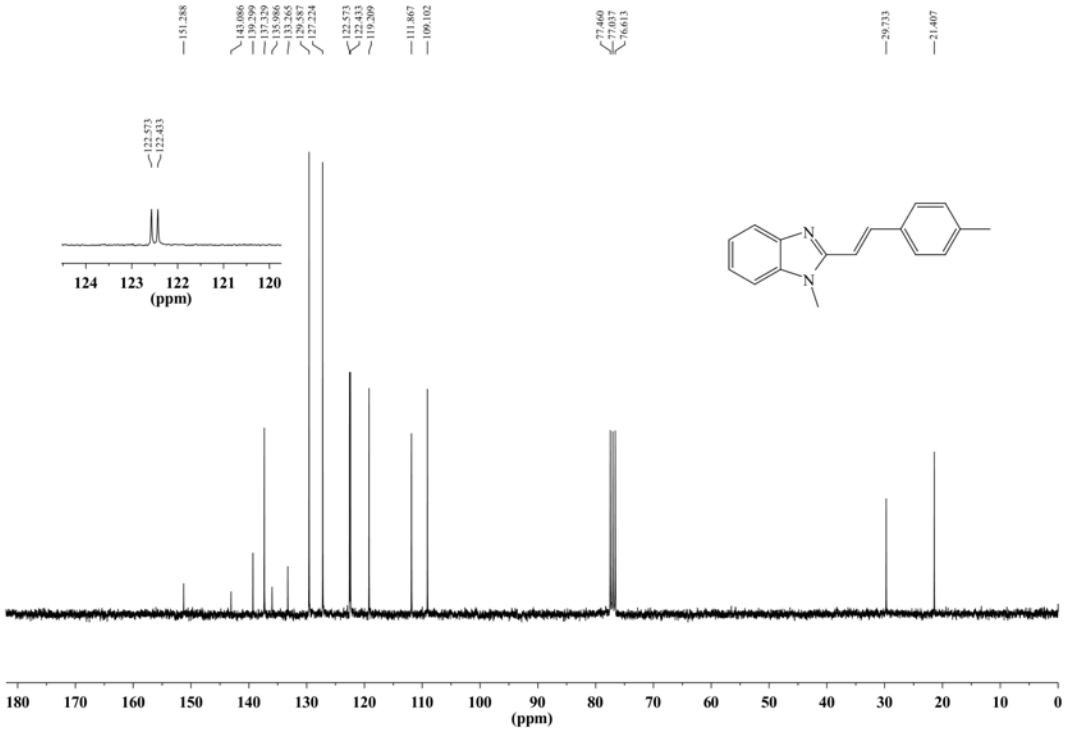
(E)-1-methyl-2-styryl-1H-benzo[d]imidazole (^{13}C NMR 75 MHz, $CDCl_3$)



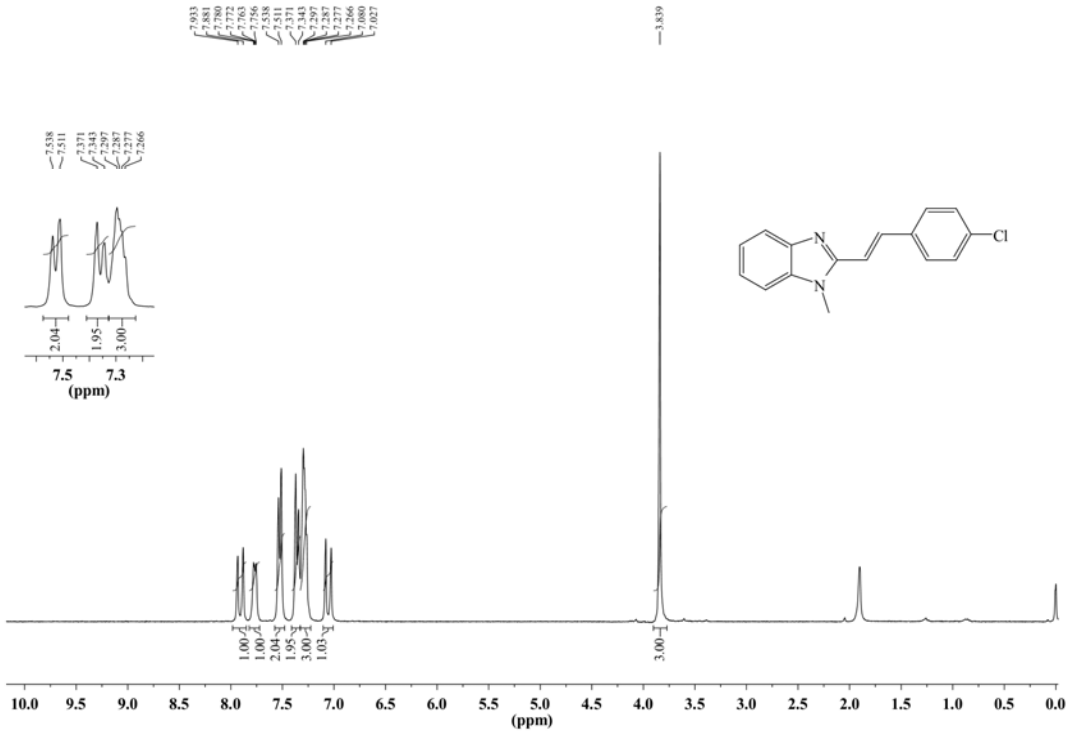
(E)-1-methyl-2-(4-methylstyryl)-1H-benzo[d]imidazole (^{1}H NMR 300 MHz, $CDCl_3$)



(E)-1-methyl-2-(4-methylstyryl)-1H-benzo[d]imidazole (^{13}C NMR 75 MHz, $CDCl_3$)



(E)-2-(4-chlorostyryl)-1-methyl-1H-benzo[d]imidazole (^{1}H NMR 300 MHz, $CDCl_3$)



(E)-2-(4-chlorostyryl)-1-methyl-1H-benzo[d]imidazole (^{13}C NMR 75 MHz,

$CDCl_3$)