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Copper Powder-catalyzed Cross Coupling Reaction of 1*H*-1,2,3-Triazoles with Aryl Boronic Acids

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Abstract The cross-coupling reaction between 1*H*-1,2,3-triazoles and aryl boronic acids catalyzed by copper powder is studied. N1-aryl and N2-aryl-1,2,3-trizaoles were obtained in the presence of cesium carbonate in acetonitrile under reflux temperature. The total yields were up to 87% with N1-arylation isomers as major products. This method shows good tolerance of various substituents attaching on benzene ring of benzotriazoles and aryl boronic acids.

Key words 1*H*-1,2,3-triazoles; aryl boronic acids; cross-coupling; copper powder; N-arylation

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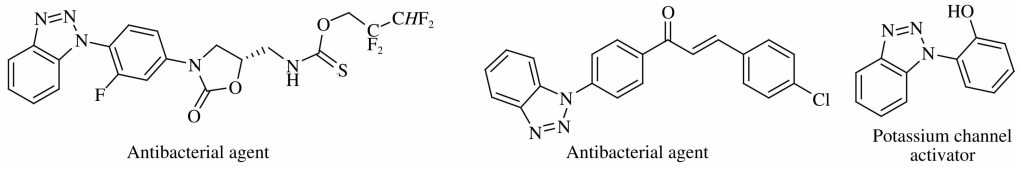
0 Introduction

Triazoles are one of the most important classes of heterocycles. They are also important building blocks and synthetic scarfs in organic chemistry, biological and medicinal sciences. For example, 1*H*-1,2,3-benzotriazoles (BTA) are structural motifs of many compounds that possess antibacterial, anticancer, antidepressant, antifungal, and antimalarial activities[1-4]. Some N-arylated BTA derivatives having biological activities are seen in Scheme 1. So many chemists have paid much attention to the investigation of synthetic methodology to enrich compound library of 1H-1,2,3-benzotriazoles.



Scheme 1 Examples of some biologically active 1-aryl-1*H*-1,2,3-benzotriazoles

With the increasing application of N-arylated triazole derivatives in all aspects such as biologicals[5,6], medicines[7-10] and materials[11], researchers did a lot of efficient efforts on the synthetic methodology. The synthesis of N-arylated BTA derivatives includes two ways: arylated click reaction and post-triazole arylation. In 2009, Moses and Zhang[12] reported a protocol for the synthesis of N1-arylated BTAs via benzyne click reaction. The Key to the procedure was in situ generation of reactive aryl azides and benzyne reaction partners. In 2014, Wróbel research group[13] developed a halogen-free three-step cascade reaction from nitroarenes and anilines to 1-aryl-1*H*-1,2,3-benzotriazoles. Cycloadditions of azides with arynes from photolysis of phthaloyl peroxide derivatives was also used to prepare 1-phenylbenzotriazole and 1-(4-methoxy) phenylbenzotriazole, but only 46% and 23% yield were obtained[14]. For the post triazoles arylation, previous research works were mainly focused on different arylation reagents and catalytic system. In most cases,

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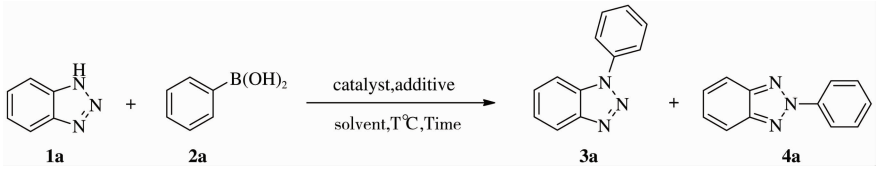
aryl halides were used as efficient arylation reagents[15,16]. In 2011, a highly N2-selective palladium-catalyzed arylation of 1,2,3-triazoles with aryl bromides, chlorides, and triflates as accessible arylation reagents was achieved in up to 99% yield by Buchwald and coworkers[17]. In 2013, Kamal and Swapna disclosed an improved iron oxide-catalyzed synthesis of N2-aryl substituted 1,2,3-triazoles via arylation reaction of in situ generated triazoles from chalcones and sodium azide in very good yields[18]. Aryl halides were utilized as efficient arylation reagents in this reaction. Shi group[19] developed an efficient synthetic method of N2-aryl-1,2,3-triazole via post-arylation of triazoles. Three different approaches, including SNAr, Cu(I) catalyzed aryl amidation and Cu(II) mediated boronic acid coupling, had been investigated in detail. This is the first example of the synthesis of N-aryl-1,2,3-triazoles with aryl boronic acids as arylation reagents. However, the scope of triazoles was limited to 4,5-disubstituted triazoles. Besides, few literatures were reported to synthesize N-aryl-1,2,3-benzotriazoles from benzotriazoles by using arylboric acids as arylation reagents.

Based on our previous investigations on the synthesis of BTA derivatives[20], herein, we describe a simple and cheap N-arylation reaction of benzotriazoles with aryl boronic acids catalyzed by copper powder and a series of N-aryl-benzotriazoles are synthesized under mild conditions.

1 Results and discussion

N-arylation reaction of BTA with phenylboronic acid was chosen as a model reaction to screen catalysts and to optimize reaction conditions. The results are listed in Table 1. Commercial copper powder as a catalyst and K_3PO_4 as a base were first used in this reaction. When the reaction was conducted in MeCN under reflux conditions for 24 h, 37% yield of N1-phenylation product **3a** and 24% yield of N2-phenylation product **4a** were obtained (Table 1, entry 1). Using K_2CO_3 instead of K_3PO_4 gave the similar results; but using Na_2CO_3 as a base, no reaction was occurred (entries 2 and 3). To our delight, using Cs_2CO_3 as a base led to the product isomers of **3a** and **4a** in total yield of 86% (entry 4). Subsequently, a series of bases, such as NaOH, KOH, $NaHCO_3$ and Et3N were further examined under the same conditions, inferior results were obtained even if the reaction was lasted for longer time (entries 5-8). These results reveal that bases play an important role for this N-arylation reaction. The effect of reaction solvents was also examined. When toluene was replaced by MeCN, **3a** was obtained in 37% yield and trace amount of **4a** was observed at 100 ℃ (entry 9). Unexpectedly, the use of NMP as a solvent at 120 ℃ did not get better yield (entry 10). Considering that all reactants and bases can be dissolved in water, the reaction was conducted in water under reflux temperature. However, trace of products was observed (entry 11). The cause may be due to the insolubility of copper powder in water. Reaction temperature and catalysts were also optimized. When the reaction was operated at room temperature for 48 hours, products were not detected (entry 12). However, when the reaction was carried out at 50 ℃ for 2 days, the total product yield was 78% (entry 13). Using CuI instead of Cu powder as a catalyst and the reaction was conducted at room temperature for 48 h, only trace of N-arylation product was obtained (entry 14). If the reaction was catalyzed by CuI in acetonitrile at 80 ℃ for 24 h, the total product yield was 73% (entry 15), which was close to the result catalyzed by Cu powder at 80 ℃ for 24 h. If no catalyst was added, the reaction did not occur (entry 16). Finally, the amount of Cu powder was examined. Reduced the amount of Cu powder from 20 mol% to 10 mol%, the total yield was greatly declined to 33% (entry 17). Increasing the dosage of this catalyst to 30 mol%, the total yield and the ratio of **3a**/**4a** had no manifest changes (entry 18). These results reveal that catalyst and temperature also played important role in the reaction.

Table 1　Optimization of the reaction conditions[a]



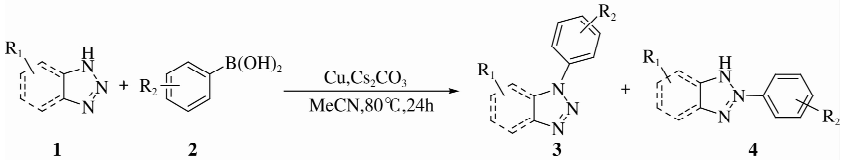
1a　**2a**　**3a**　**4a**

Entry	Catalyst	Base	Solvent	Temp/℃	Time /h	Yield /%	
						3a	**4a**
1	Cu	K_3PO_4	MeCN	80	24	37	24
2	Cu	K_2CO_3	MeCN	80	24	37	22
3	Cu	Na_2CO_3	MeCN	80	24	trace	
4	Cu	Cs_2CO_3	MeCN	80	24	60	26
5	Cu	NaOH	MeCN	80	24	39	23
6	Cu	KOH	MeCN	80	24	40	25
7	Cu	$NaHCO_3$	MeCN	80	48	20	18
8	Cu	Et3N	MeCN	80	36	34	16
9	Cu	Cs_2CO_3	Toluene	100	24	37	10
10	Cu	Cs_2CO_3	NMP	120	24	40	25
11	Cu	Cs_2CO_3	H_2O	reflux	24	trace	
12	Cu	Cs_2CO_3	MeCN	R. T.	48	NR	
13	Cu	Cs_2CO_3	MeCN	50	48	58	20
14	CuI	Cs_2CO_3	MeCN	R. T	48	trace	
15	CuI	Cs_2CO_3	MeCN	80	24	51	22
16	-	Cs_2CO_3	MeCN	80	48	NR	
18[b]	Cu	Cs_2CO_3	MeCN	80	48	25	8
19[c]	Cu	Cs_2CO_3	MeCN	80	24	59	23

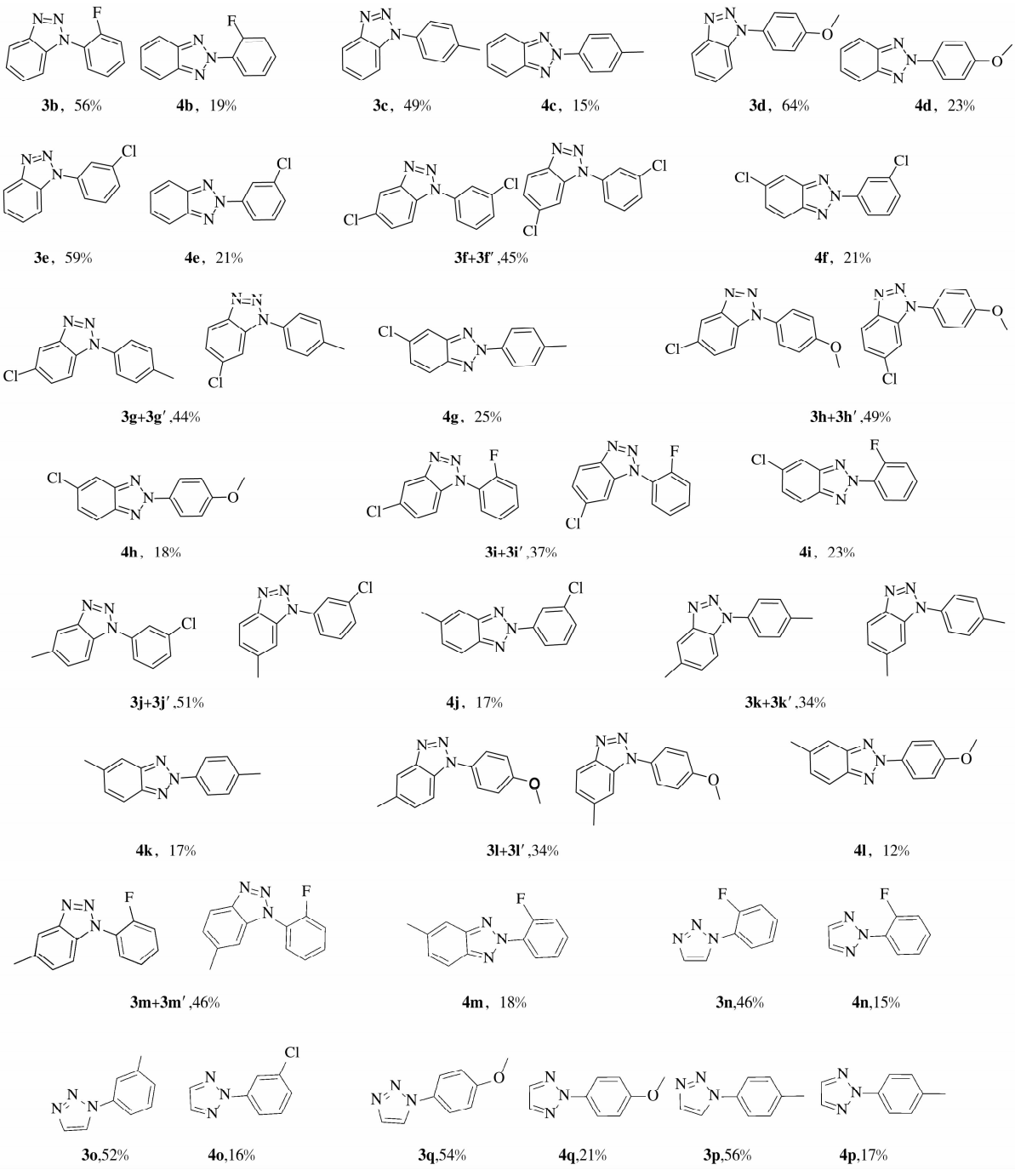
Notes: a: Reaction condition: **1a** (0.1 mmol), **2a** (0.15 mmol), catalyst (0.02 mmol), base (0.2 mmol), solvent (1.5 mL), Isolated yield after column chromatography, NR means no reaction; b: Catalyst (0.01 mmol); c: Catalyst (0.03 mmol).

Having optimized reaction conditions in hand, the scopes of the substrates were examined and the results are listed in Table 2. The reactions of various triazoles and substituted arylboronic acids delivered two product isomers, N1-and N2-arylation products, in good total yields up to 87%. N1-arylation compounds **3** were the major products and N2-arylation compounds **4** were the minor ones. The **3**/**4** molar ratio is between 2/1-5/1. Aryl boronic acids bearing both electron-donating (e. g., 4-CH_3 and 4-CH_3O) and electron-withdrawing groups (e. g., 2-F and 3-Cl) were all suitable for this transformation with BTA, giving desired products (**3b-3e** and **4b-4e**) in good yields. It is noteworthy that when there was a substituent (e. g., 5-Cl and 5-CH_3) attached on benzene ring of BTA, the major N1-arylation products were transformed into two regioisomers (**3f-3m** and **3f'-3m'**) which could not be separated by column chromatography, while the total yields and the ratios of **3**/**4** have not significant changes. The isomerization shows the formation of BTA N-anions in the presence of a base during the reaction. When 1*H*-1,2,3-triazole was treated with various aryl boronic acids under the optimized reaction conditions, N1-arylation products (**3n-3q**) in 42%-54% yield as well as N2-arylation products (**4n-4q**) in 13%-21% yield were obtained.

Table 2 N-Arylation of 1*H*-1,2,3-triazoles with various aryl boronic acids[a]



1 **2** **3** **4**



Notes: a: Reaction condition: **1a** (0.2 mmol), **2a** (0.4 mmol), Cu (0.04 mmol), Cs_2CO_3 (0.4 mmol), MeCN (3 mL). Isolated yield after column chromatography.

2 Conclusion

In summary, N-arylation reaction of triazoles using aryl boronic acids as arylation reagents is described. N1-and N2-arylation products were obtained in good total yields up to 87% with the former as ma-

jor products.

3 Experimental

To a 50 mL of round bottom flask was added 1,2,3-triazoles (0.2 mmol), aryl boronic acids (0.4 mmol), commercial copper powder (0.04 mmol), a base (0.4 mmol) and a solvent (3 mL), the mixture was stirred at indicated temperature for 24 h. The reaction was detected by TLC. After finished, the solvent was removed under vacuum and the residue was separated by silica gel column chromatography with ethyl acetate and petroleum ether (1:4 vol) as eluents to obtain the products.

1-Phenyl-1*H*-1,2,3-benzotriazole (3a). White solid, mp 86-88 ℃ (86-87 ℃).[21] ^{1}H NMR (400 MHz, $CDCl_3$) δ=8.08 (d, J=7.4 Hz, 1H), 7.70 (t, J=10.5 Hz, 3H), 7.54 (t, J=6.5 Hz, 2H), 7.50-7.42 (m, 2H), 7.37 (t, J=6.8 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=146.5, 137.0, 132.3, 129.8, 128.6, 128.2, 124.4, 122.8, 120.3, 110.3; (IR, KBr): 1726, 1593, 1496, 1276, 1087, 747, 694, 659 cm^{-1}.

2-Phenyl-2*H*-1,2,3-benzotriazole (4a). White solid, mp 106-108 ℃ (109-110 ℃).[19] ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.36-8.35 (m, 2H), 7.95-7.92 (m, 2H), 7.57-7.54 (m, 2H), 7.47-7.44 (m, 1H), 7.42 (dd, J=6.6 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=146.5, 137.0, 132.3, 129.8, 128.6, 128.2, 124.4, 122.8, 120.3, 110.3; (IR, KBr): 3440, 3137, 1631, 1400, 1121 cm^{-1}.

1-(2-Fluorophenyl)-1*H*-1,2,3-benzotriazole (3b). White solid, mp 74-76 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.08-8.01 (m, 1H), 7.60 (s, 1H), 7.49-7.42 (m, 2H), 7.41 (s, 1H), 7.34 (dd, J=6.0, Hz, 1H), 7.31-7.22 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=155.6 (d, J=253.8 Hz), 145.9, 133.5, 131.1 (d, J=7.7 Hz), 128.32, 127.7, 125.2 (d, J=3.9 Hz), 124.4, 120.1, 117.2 (d, J=19.2 Hz), 110.5(d, J=4.5 Hz); (IR, KBr): 3074, 1606, 1506, 1451, 1110, 1056, 934, 814, 744, 686, 573, 540, 505 cm^{-1}.

2-(2-Fluorophenyl)-2*H*-1,2,3-benzotriazole (4b).[22] White solid, mp 76-78 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ=7.97 (t, J=7.8 Hz, 1H), 7.91 (d, J=6.6 Hz, 2H), 7.42 (s, 1H), 7.39 (d, J=6.6 Hz, 2H), 7.31 (d, J=10.8 Hz, 1H), 7.28 (d, J=7.6 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=155.56 (d, J=253.8 Hz), 145.87(s), 133.5(m), 131.1 (d, J=7.7 Hz), 128.3, 127.7, 125.3, 125.2, 124.4, 120.1, 117.2 (d, J=19.2 Hz), 110.6; (IR, KBr): 1503, 1462, 1403, 1347, 1234, 956, 740 cm^{-1}.

1-(*p*-Tolyl)-1*H*-1,2,3-benzotriazole (3c). White solid, mp 92-94 ℃ (95-95.5 ℃)[12]; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.13 (d, J=8.4 Hz, 1H), 7.71 (d, J=8.4 Hz, 1H), 7.64 (d, J=7.2 Hz, 2H), 7.52 (t, J=7.2 Hz, 1H), 7.42 (d, J=7.8 Hz, 1H), 7.40 (d, J=7.2 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=146.5, 138.8, 134.6, 132.4, 130.4, 128.1, 124.3, 122.8, 120.2, 110.4, 21.2; (IR, KBr): 1903, 1606, 1514, 1452, 1188, 1066, 1004, 819, 736, 662 cm^{-1}.

2-(*p*-Tolyl)-2*H*-1,2,3-benzotriazole (4c). White solid, mp 118-120 ℃ (119-120 ℃)[23]; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.16 (d, J=7.8 Hz, 2H), 7.88-7.84 (m, 2H), 7.37-7.32 (m, 2H), 7.28 (d, J=7.9 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=144.9, 139.2, 138.2, 130.0, 127.0, 120.5, 118.3, 21.2; (IR, KBr): 1562, 1504, 1409, 1286, 1215, 960, 815, 503 cm^{-1}.

1-(4-Methoxyphenyl)-1*H*-1,2,3-benzotriazole (3d). White solid, mp 96-98 ℃ (98-99 ℃)[23]; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.01 (d, J=8.4 Hz, 1H), 7.55 (dd, J=6.6, 7.8 Hz, 3H), 7.40 (t, J=7.8 Hz, 1H), 7.30 (t, J=7.8 Hz, 1H), 6.99 (d, J=8.4 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.8, 146.2, 132.6, 129.9, 128.0, 124.5, 124.2, 120.1, 114.9, 110.2, 55.6; (IR, KBr): 2326, 1608, 1517, 1448, 1251, 1184, 1060, 829, 744 cm^{-1}.

2-(4-Methoxyphenyl)-2*H*-1,2,3-benzotriazole (4d). White solid, mp 111-113 ℃ (111-113 ℃)[24]; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.20 (d, J=9.0 Hz, 2H), 7.93-7.91 (m, 2H), 7.41-7.40 (m, 2H), 6.98 (d, J=8.4 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=160.1, 144.9, 134.0, 126.8, 122.0, 118.1, 114.5, 55.6; (IR, KBr): 2924, 1600, 1509, 1408, 1298, 1247, 1180, 1029, 966, 842, 785, 744, 631 cm^{-1}.

1-(3-**Chlorophenyl**)-1***H***-1,2,3-**benzotriazole** (**3e**). White solid, mp 105-107 ℃ (106 ℃)[25]; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.14 (d, J=8.4 Hz, 1H), 7.82 (s, 1H), 7.74 (d, J=8.4 Hz, 1H), 7.70 (d, J=7.8 Hz, 1H), 7.58-7.53 (m, 1H), 7.53 (d, J=7.8 Hz, 1H), 7.47 (d, J=9.0 Hz, 1H), 7.44 (d, J=7.8 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=146.6, 138.0, 135.6, 132.0, 130.9, 128.7, 128.6, 124.6, 122.9, 120.7, 120.5, 110.1; (IR, KBr): 3076, 1591, 1481, 1442, 1286, 1059, 741, 680 cm^{-1}.

2-(3-**Chlorophenyl**)-2***H***-1,2,3-**benzotriazole** (**4e**).[26] White solid, mp 140-142 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.34 (s, 1H), 8.20 (d, J=7.8 Hz, 1H), 7.93-7.92 (m, 2H), 7.42 (t, J=7.8 Hz, 1H), 7.36 (d, J=6.0 Hz, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=145.1, 141.1, 135.3, 130.5, 128.9, 127.6, 120.9, 118.6, 118.4; (IR, KBr): 1589, 1480, 1406, 1342, 1278, 1217, 963, 876, 742, 667, 443 cm^{-1}.

Mixture of 5-**Chloro**-1-(3-**Chlorophenyl**)-1***H***-1,2,3-**benzotriazole** (**3f**) **and** 6-**Chloro**-1-(3-**Chlorophenyl**)-1***H***-1,2,3-**benzotriazole** (**3f'**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09-8.05 (m, 1H), 7.81-7.77 (m, 1H), 7.69-7.64 (m, 2H), 7.58-7.53 (m, 2H), 7.52-7.49 (m, 1H)

5-**Chloro**-2-(3-**chlorophenyl**)-2***H***-1, 2, 3-**benzotriazole** (**4f**). White solid, mp 159-161 ℃ (157-159 ℃)[27]; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.31 (t, J=1.8 Hz, 1H), 8.19-8.15 (m, 1H), 7.87-7.83 (m, 1H), 7.80 (d, J=9.0 Hz, 1H), 7.42 (t, J=8.0 Hz, 1H), 7.39-7.36 (m, 1H), 7.32 (dd, J=7.8, 9.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=145.4, 143.6, 140.9, 135.4, 133.4, 130.5, 129.2, 129.2, 120.9, 119.6, 118.6, 117.4; (IR, KBr): 2924, 1728, 1591, 1481, 1276, 1109, 806, 671, 595 cm^{-1}.

Mixture of 5-**Chloro**-1-(***p*-**tolyl**)-1***H***-1,2,3-**benzotriazole** (**3g**) **and** 6-**Chloro**-1-(***p*-**tolyl**)-1***H***-1,2,3-**benzotriazole** (**3g'**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (s, 2H), 7.65 (d, J=8.4 Hz, 2H), 7.61 (d, J=7.2 Hz, 4H), 7.48 (d, J=8.0 Hz, 2H), 7.41 (d, J=7.8 Hz, 4H), 2.47 (s, 6H).

5-**Chloro**-2-(***p*-**tolyl**)-2***H***-1,2,3-**benzotriazole** (**4g**). White solid, mp 122-124 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.07 (s, 1H), 7.59 (d, J=8.4 Hz, 1H), 7.55 (d, J=6.6 Hz, 2H), 7.43 (d, J=8.8 Hz, 1H), 7.35 (d, J=7.2 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=145.2, 143.4, 139.5, 137.9, 132.7, 130.0, 128.5, 120.5, 119.4, 117.3, 21.2; (IR, KBr): 2923, 1732, 1504, 1399, 1105, 1045, 875, 821, 511 cm^{-1}.

Mixture of 5-**Chloro**-1-(4-**methoxyphenyl**)-1***H***-1,2,3-**benzotriazole** (**3h**) **and** 6-**Chloro**-1-(4-**meth-oxyphenyl**)-1***H***-1,2,3-**benzotriazole** (**3h'**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (s, 1H), 8.04 (d, J=9.0 Hz, 1H), 7.66 (s, 1H), 7.65-7.57 (m, 5H), 7.48 (d, J=8.4 Hz, 1H), 7.38 (d, J=9.0 Hz, 1H), 7.11 (dd, J=8.4 Hz, 4H), 3.91 (s, 6H).

5-**Chloro**-2-(4-**methoxyphenyl**)-2***H***-1, 2, 3-**benzotriazole** (**4h**). White solid, mp 139-141 ℃ (138-139)[24]; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.20-8.15 (m, 2H), 7.83 (d, J=1.2 Hz, 1H), 7.78 (d, J=9.0 Hz, 1H), 7.28 (dd, J=9.0, 1.8 Hz, 1H), 7.00-6.95 (m, 2H), 3.82 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=160.4, 145.1, 143.3, 133.7, 132.6, 128.3, 122.0, 119.3, 117.2, 114.5, 55.6; (IR, KBr): 1734, 1604, 1508, 1251, 1043, 830, 799 cm^{-1}.

Mixture of 5-**Chloro**-1-(2-**fluorophenyl**)-1***H***-1,2,3-**benzotriazole** (**3i**) **and** 6-**Chloro**-1-(2-**fluorophenyl**)-1***H***-1,2,3-**benzotriazole** (**3i'**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, J=8.4 Hz, 1H), 7.86 (s, 1H), 7.66 (dd, J=16.8 Hz, 2H), 7.49 (s, 2H), 7.35 (dd, J=16.2 Hz, 2H).

5-**Chloro**-2-(2-**fluorophenyl**)-2***H***-1,2,3-**benzotriazole** (**4i**). White solid, mp 118-120 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ=7.95 (t, J=7.2 Hz, 1H), 7.90 (d, J=1.2 Hz, 1H), 7.85 (d, J=9.0 Hz, 1H), 7.48-7.40 (m, 1H), 7.36-7.31 (m, 1H), 7.29 (t, J=8.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ=155.2 (d, J=256.7 Hz), 145.8, 144.1, 137.8, 130.8, 130.7, 130.6, 126.4, 124.9 (d, J=3.7 Hz), 118.1(s), 117.9 (d, J=20.2 Hz), 116.7; (IR, KBr): 1599, 1503, 1400, 1120, 805, 757 cm^{-1}.

Mixture of 1-(3-**Chlorophenyl**)-5-**methyl**-1***H***-1,2,3-**benzotriazole** (**3j**) **and** 1-(3-**Chlorophenyl**)-6-**methyl**-1***H***-1,2,3-**benzotriazole** (**3j'**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, J=8.4 Hz, 1H), 7.89 (s, 1H), 7.

82-7.80 (m,2H),7.70-7.67 (m,2H),7.62 (d,J=8.4 Hz,1H),7.55-7.49 (m,4H),7.47-7.44 (m,2H),7.39 (d,J=8.4 Hz,1H),7.27 (d,J=8.0 Hz,2H),2.55 (s,3H),2.54 (s,3H).

2-(3-**Chlorophenyl**)-5-**methyl**-2***H***-1,2,3-**benzotriazole** (**4j**). White solid, mp 121-123 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.31 (t,J=1.8 Hz,1H),8.17 (d,J=8.4 Hz,1H),7.73 (d,J=9.0 Hz,1H),7.58 (s,1H),7.40 (t,J=7.8 Hz,1H),7.34 (d,J=7.8 Hz,1H),7.20 (d,J=9.6 Hz,2H),2.45 (s,3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=145.6,143.9,141.2,137.8,135.2,130.6,130.4,128.6,120.7,118.4,117.8,116.5,22.2; (IR,KBr):2923,1732,1589,1479,1262,1101,1026,966,849,797,667,589 cm^{-1}.

Mixture of 5-**Methyl**-1-(***p*-tolyl**)-1***H***-1,2,3-**benzotriazole** (**3k**) **and** 6-**Methyl**-1-(***p*-tolyl**)-1***H***-1,2,3-**benzotriazole** (**3k'**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (d,J=8.4 Hz,3H),7.80 (d,J=9.0 Hz,2H),7.66 (s,2H),7.33 (d,J=8.4 Hz,4H),7.23-7.23 (m,3H),2.51 (s,3H),2.43 (s,3H).

5-**Methyl**-2-(***p*-tolyl**)-2***H***-1,2,3-**benzotriazole** (**4k**).[28] White solid, mp 120-122 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.13 (d,J=8.4 Hz,2H),7.73 (d,J=9.0 Hz,1H),7.59 (s,1H),7.27 (d,J=8.4 Hz,2H),7.18 (d,J=4.2 Hz,1H),2.44 (s,3H),2.37 (s,3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=145.4,143.6,138.8,138.2,137.1,129.9,129.9,120.3,117.7,116.4,22.2,21.1; (IR,KBr):1728,1560,1506,1400,1112,970,799,595 cm^{-1}.

Mixture of 1-(4-**Methoxyphenyl**)-5-**methyl**-1***H***-1,2,3-**benzotriazole** (**3l**) **and** 1-(4-**Methoxyphenyl**)-6-**methyl**-1***H***-1,2,3-**benzotriazole** (**3l'**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d,J=8.4 Hz,1H),7.87 (s,1H),7.64 (dd,J=9.0 Hz,4H),7.54 (d,J=8.4 Hz,1H),7.42 (s,1H),7.34 (d,J=8.4 Hz,1H),7.23 (d,J=8.4 Hz,1H),7.09 (dd,J=9.0 Hz,4H),3.89 (d,J=2.4 Hz,6H),2.52 (d,J=4.8 Hz,6H).

2-(4-**Methoxyphenyl**)-5-**methyl**-2***H***-1,2,3-**benzotriazole** (**4l**). White solid, mp 121-123 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.17 (d,J=9.0 Hz,2H),7.73 (d,J=9.0 Hz,1H),7.58 (s,1H),7.17 (t,J=8.4 Hz,1H),6.97 (d,J=9.0 Hz,2H),3.82 (s,3H),2.44 (s,3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=159.9,145.4,143.6,137.0,134.1,129.7,121.8,117.5,116.3,114.4,55.6,22.1; (IR,KBr):2917,1890,1602,1508,1249,1020,829,797,758,521 cm^{-1}.

Mixture of 1-(2-**Fluorophenyl**)-5-**methyl**-1***H***-1,2,3-**benzotriazole** (**3m**) **and** 1-(2-**Fluorophenyl**)-6-**methyl**-1***H***-1,2,3-**benzotriazole** (**3m'**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d,J=8.4 Hz,1H),7.86 (s,1H),7.66 (dd,J=16.2 Hz,2H),7.49 (s,2H),7.34 (t,J=7.8 Hz,6H),7.22 (d,J=10.2 Hz,2H),2.51 (s,3H),2.49 (s,3H).

2-(2-**Fluorophenyl**)-5-**methyl**-2***H***-1,2,3-**benzotriazole** (**4m**). White solid, mp 54-56 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ=7.94 (t,J=7.8 Hz,1H),7.78 (d,J=8.8 Hz,1H),7.63 (s,1H),7.44-7.35 (m,1H),7.32-7.24 (m,2H),7.23-7.16 (m,1H),2.45 (s,3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ=155.2 (d,J=256.7 Hz),145.8,144.1,137.8,130.8 (d,J=8.0 Hz),130.6,126.4,124.9,124.9,118.1,117.9 (d,J=20.2 Hz),116.7 (s),22.4; (IR,KBr):2918,1499,1273,1230,1201,1117,966,848,800,762 cm^{-1}.

1-(2-**Fluorophenyl**)-1***H***-1,2,3-**triazole** (**3n**).[29] White oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.06 (s,1H),7.92 (t,J=7.8 Hz,1H),7.82 (s,1H),7.38 (d,J=6.0 Hz,1H),7.30-7.26 (m,1H),7.24 (d,J=9.0 Hz,1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=153.4 (d,J=250.7 Hz),134.2,130.2,130.1,125.3,125.2,124.9,117.0 (d,J=19.9 Hz); (IR,KBr):3133,1629,1515,1400,1223,1110,1022,817,759,666 cm^{-1}.

2-(2-**Fluorophenyl**)-2***H***-1,2,3-**triazole** (**4n**).[30] White oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ=7.82 (s,1H),7.76 (t,J=7.6 Hz,1H),7.33 (dd,J=13.2,7.2 Hz,1H),7.25-7.20 (m,1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=154.6 (d,J=255.1 Hz),135.9 129.7,129.7,125.19 (s),124.5,124.5,117.5 (d,J=20.1 Hz); (IR,KBr):3135,1730,1631,1400,1271,1118,800 cm^{-1}.

1-(3-**Chlorophenyl**)-1***H***-1,2,3-**triazole** (**3o**). White solid, mp 90-92 ℃ (91-93 °C)[31]; ^{1}H NMR (600 MHz, $CDCl_3$) δ=8.01 (s,1H),7.88 (s,1H),7.82 (s,1H),7.68 (d,J=7.8 Hz,1H),7.50 (t,J=7.8, Hz,1H),7.45 (d,J=7.5 Hz,1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ=137.8,135.6,134.7,130.8,128.8,

121.7,120.9,118.6; (IR,KBr):3113,1589,1464,1323,1226,1083,1035,890,788,474 cm^{-1}.

2-(3-**Chlorophenyl**)-2***H***-1,2,3-**triazole** (**4o**). White oil;^{1}H NMR (600 MHz,$CDCl_3$) δ=8.04 (s,1H), 7.90 (dd,*J*=8.2,1H),7.73 (s,2H),7.32 (t,*J*=8.4 Hz,1H),7.26-7.22 (m,1H);^{13}C NMR (151 MHz, $CDCl_3$) δ=140.6,135.9,135.1,130.3,127.5,119.2,116.9; (IR,KBr):3126,1595,1485,1406,1261, 1106,956,823,779,666 cm^{-1}.

1-(***p*-Tolyl**)-1***H***-1,2,3-**triazole** (**3p**). White solid,mp 76-78 ℃ (78-80 ℃)[31];^{1}H NMR (600 MHz, $CDCl_3$) δ=7.88 (s,1H),7.77 (s,1H),7.55 (d,*J*=7.8 Hz,2H),7.26 (d,*J*=7.8 Hz,2H),2.36 (s, 3H);^{13}C NMR (151 MHz,$CDCl_3$) δ=139.0,134.7,134.3,130.3,121.8,120.6,21.1; (IR,KBr):3134, 1681,1598,1517,1401,1226,1116,813 cm^{-1}.

2-(***p*-Tolyl**)-2***H***-1,2,3-**triazole** (**4p**).[32] White oil;^{1}H NMR (600 MHz,$CDCl_3$) δ=7.88 (d,*J*=7.8 Hz,2H),7.72 (s,2H),7.21 (d,*J*=8.4 Hz,2H),2.34 (s,3H);^{13}C NMR (151 MHz,$CDCl_3$) δ=137.7, 137.5,135.2,129.8,118.9,21.0; (IR,KBr):3145,1631,1400,1262,1118,996,621 cm^{-1}.

1-(4-**Methoxyphenyl**)-1***H***-1,2,3-**triazole** (**3q**). White oil;^{1}H NMR (600 MHz,$CDCl_3$) δ=7.84 (s, 1H),7.76 (s,1H),7.57 (d,*J*=9.0 Hz,2H),6.96 (d,*J*=8.4 Hz,2H),3.80 (s,3H);^{13}C NMR (151 MHz,$CDCl_3$) δ=159.8,134.3,130.5,122.3,121.8,114.8,55.6; (IR,KBr):3138,1614,1521,1400,1257, 1114,524 cm^{-1}.

2-(4-**Methoxyphenyl**)-2***H***-1,2,3-**triazole** (**4q**). White oil;^{1}H NMR (600 MHz,$CDCl_3$) δ=7.92 (d,*J*= 9.0 Hz,2H),7.71 (s,2H),6.93 (d,*J*=9.0 Hz,2H),3.79 (s,3H);^{13}C NMR (151 MHz,$CDCl_3$) δ=159. 0,135.0,120.4,119.5,114.3,55.6; (IR,KBr):3139,1514,1408,1251,1031,953,831,621,527 cm^{-1}.

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铜粉催化三氮唑与芳硼酸的交叉偶联反应研究

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摘　要　三氮唑类化合物是一类重要的有机杂环化合物，也是很多农药、医药和有机合成中间体的合成砌块. 许多含有 1,2,3-三氮唑结构单元的化合物表现出良好的抗菌、消炎、抗癌等生物活性. 以市售铜粉作为催化剂，以芳硼酸作为芳基化试剂，研究了 1*H*-1,2,3-三氮唑与芳硼酸的交叉偶联反应. 结果表明，1*H*-1,2,3-三氮唑发生了 N-芳基化反应，生成了 N1-芳基和 N2-芳基三氮唑的异构化产物，总收率最高 87%，二者的比例约为(2-5):1. 当取代的 1*H*-1,2,3-苯并三氮唑作为反应底物时，N1-芳基化产物又出现了两种不易分离的位置异构体.

关键词　三氮唑；芳基硼酸；交叉偶联反应；铜粉；N-芳基化反应