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[Cu(OH)(TMEDA)]$_2$Cl$_2$-Catalyzed Regioselective 2-Arylation of 5-Substituted Tetrazoles with Boronic Acids under Mild Conditions

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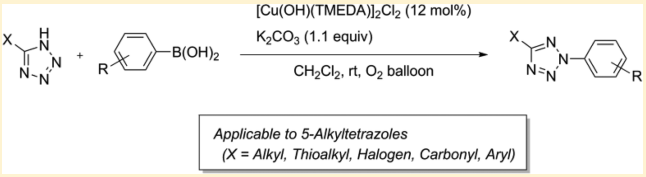
Supporting Information

ABSTRACT: A mild and regioselective 2-arylation of 5-substituted tetrazoles is described. The reaction proceeds regioselectively with a variety of arylboronic acids in the presence of [Cu(OH)(TMEDA)]$_2$Cl$_2$ to afford 2,5-disubstituted tetrazoles. This is the first report of highly regioselective arylation of 5-alkyltetrazoles.



Tetrazoles are versatile, N-containing heterocyclic compounds used in pharmaceuticals, agrochemicals, and materials science.[1] Moreover, 1-aryl-5-substituted tetrazoles are particularly useful as synthetic intermediates in biological research and medicinal chemistry,[2] with 1,3-dipolar cycloaddition reactions being the most common means of constructing 1,5-disubstituted tetrazoles. Such reactions include sodium azide with imidoylbenzotriazole[3] or sodium azide with nitriles.[4] Recently, the direct introduction of an aryl group into 1-substituted 5-bromotetrazole was achieved using a Suzuki–Miyaura coupling reaction.[5]

Historically, 2-aryl-5-substituted tetrazoles have been regarded as less important than 1-aryl-5-substituted tetrazoles. However, the former have recently exhibited remarkable biological properties such as hepatitis C serine protease inhibition,[6] metabotropic glutamate receptor antagonism,[7] inhibition of stearoyl-coenzyme A delta-9 desaturase,[8] and G-protein-coupled receptor agonism.[9] Despite these findings, however, reported methods for synthesizing 2-aryl-5-substituted tetrazoles are few. Kakehi's synthesis[10] is a representative method employing phenylsulfonylhydrazones and arenediazonium salts, both of which must also be synthesized. Several transition-metal-catalyzed direct 2-arylations of 5-substituted tetrazoles have been reported. A stoichiometric amount of Cu(OAc)$_2$ was found to mediate the cross-coupling of arylboronic acid and 5-phenyltetrazole,[11] and Ph$_2$ICl and 2-(tributylstannyl)tetrazole.[12] A catalytic version of Cu(OAc)$_2$ was achieved using Ph$_3$Bi(OAc)$_2$ and 5-phenyltetrazole.[13] Pd- and Cu-catalyzed 2-arylation has also been reported using Na salts of tetrazoles and Ar$_2$IBF$_4$ as substrates.[14] Although 2,5-disubstituted tetrazoles were selectively obtained, the process was complicated by the availability of substrates and wastes after the reaction. Han and co-workers[15] recently reported the synthesis of 2-aryl-5-substituted tetrazoles through the coupling of N–H-free 5-substituted tetrazoles with arylboronic acid in the presence of a catalytic amount of copper(II) oxide at 100 °C. Note, however, that tetrazoles are potentially explosive,[1,16] and avoiding high reaction temperatures is necessary. In addition, only 5-aryltetrazoles were used as substrates.

We report herein the catalytic and highly regioselective 2-arylation of 5-alkyl- and aryl-substituted tetrazoles under mild conditions. 5-Methyltetrazole was employed as a substrate, and the reaction was investigated using phenylboronic acid at room temperature in an O$_2$ atmosphere (Table 1). CuCl and CuCl$_2$ were initially selected as the catalytic copper salts, but no reaction occurred (entries 1 and 2). The use of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) as a coordinating ligand promoted the coupling reaction to afford 2-phenyl-5-methyltetrazole in a moderate yield (46%) and high regioselectivity (99:1) (entries 3 and 4). Under Han's conditions,[15] the coupling reaction of 5-methyltetrazole and phenylboronic acid afforded a mixture of 2-phenyl and 1-phenyl-5-methyltetrazoles.[17] The other coordinating ligands, *N*,*N*′-dimethylethylenediamine (DMEDA) and *N*,*N*,*N*′,*N*′-tetramethylpropylenediamine (TMPDA), appeared to be less effective than TMEDA (entries 5 and 6). A suitable steric environment around the ligand may be necessary for high regioselectivity. Other copper salts, such as CuBr, CuI, CuO, Cu$_2$O, CuOAc, and Cu(OAc)$_2$, gave poor results under the same conditions. The use of di-μ-hydroxobis[(*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) copper(II)] chloride[18] ([Cu(OH)(TMEDA)]$_2$Cl$_2$) as a catalyst led to a better result, although even less catalyst (6%) was used (entry 7). The best result was obtained using 12 mol % of catalyst (entry 8). Further exploration of the base and solvent systems showed that a combination of K$_2$CO$_3$ as the base and CH$_2$Cl$_2$ as the solvent was most effective. In addition, O$_2$ is required as an oxidant, and the reaction gave low yields in air or a N$_2$ atmosphere (entries 9 and 10).

The plausible mechanism is shown in Scheme 1, which is similar to that mentioned by Collman and co-workers.[18] First, copper(II) catalyst undergoes transmetalation with arylboronic acid, then tetrazole activated with the base could coordinate to

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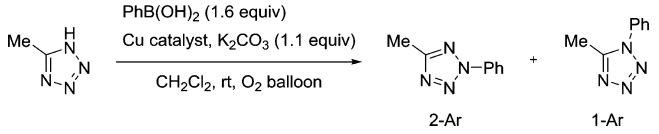
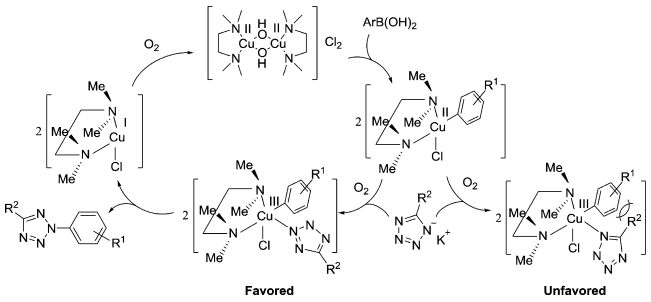
Table 1. Optimization of the Reaction Conditions



entry	Cu catalyst (mol %)	oxid.	time (h)	yield (%) (2-Ar/1-Ar)[a]
1	CuCl (12)	O_2	17	no reaction
2	$CuCl_2$ (12)	O_2	17	no reaction
3	CuCl (12)/TMEDA(12)	O_2	17	46 (99:1)
4	$CuCl_2$ (12)/TMEDA(12)	O_2	17	51 (99:1)
5	$CuCl_2$ (12)/DMEDA(12)	O_2	17	22 (94:6)
6	$CuCl_2$ (12)/TMPDA(12)	O_2	17	no reaction
7	$[Cu(OH)(TMEDA)]_2Cl_2$ (6)	O_2	17	57 (99:1)
8	$[Cu(OH)(TMEDA)]_2Cl_2$ (12)	O_2	14	69 (67)[b] (98:2)
9	$[Cu(OH)(TMEDA)]_2Cl_2$ (12)	air	14	23 (100:0)
10	$[Cu(OH)(TMEDA)]_2Cl_2$ (12)	none	14	10 (100:0)

[a]Yield and 2-Ar/1-Ar ratio were determined by HPLC. [b]Isolated yield is indicated in the parentheses.

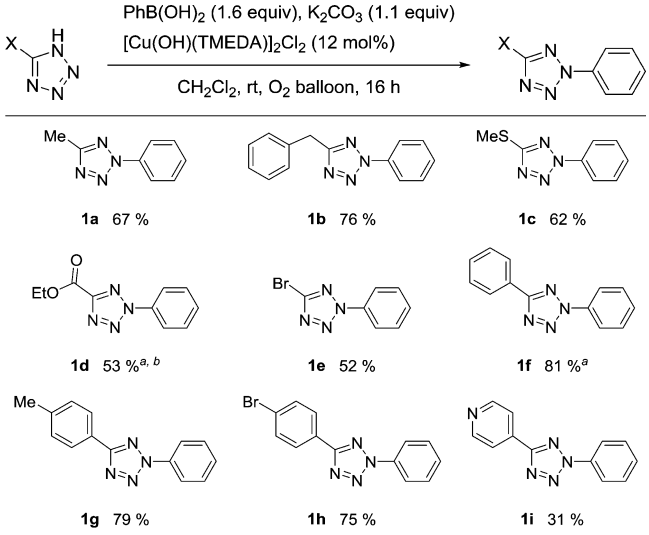
Scheme 1



copper in the presence of O_2 atomosphere to generate copper(III) species. Although Collman and co-workers used the same catalyst for coupling of imidazole, no reaction occurred with tetrazole under the same conditions. The addition of K_2CO_3 was essential for this reaction since the nucleophilicity of tetrazoles and imidazoles is different. In addition, at this point, two types of coordination of tetrazole could be considered and the coordination with the 2-position of tetrazole formed a more favorable transition state than that with 1-position of tetrazole because of steric repulsion between the substituent on the 5-position and the aryl group. Then, reductive elimination of the tetrazole and aryl group led to the coupling product and the regeneration of a copper(II) catalyst.

After optimizing the reaction conditions, the generalities of the reactions using various 5-substituted tetrazoles and phenylboronic acid were explored (Table 2). The reaction of 5-benzyltetrazole was regioselective and gave 2-phenyl-5-benzyltetrazole **1b** with a 76% yield. The presence of a sulfur atom had a negligible effect on the overall results, and the desired 2-phenyl-5-methylthiotetrazole **1c** was obtained with a 62% yield and high regioselectivity. Substrates bearing ester groups or a halogen atom (Br) also yielded coupling products (**1d** and **1e**) and would be useful synthons for modified tetrazoles. The coupling of 5-aryltetrazoles with phenylboronic acid proceeded smoothly, giving the corresponding 2,5-disubstituted products in good yields (**1f**–**1h**). The reaction of 5-(4-pyridyl)tetrazole selectively produced 2-phenyl-5-pyridyltetrazole **1i** with an acceptable yield. Note that, in these reactions, only the phenyl group was introduced at the 2-position and that 1-phenyltetrazole was not observed, even following reactions with compound **1i**.

Table 2. Reaction of Various Tetrazoles with Phenylboronic Acid



[a]LiCl (0.5 equiv) was added. [b]$PhB(OH)_2$ (3.0 equiv) was used. Reaction time 17 h.

Next, reactions with various arylboronic acids were used to explore the influence of the aryl substituent (Table 3). Phenylboronic acids bearing electron-donating groups such as methyl, methoxy, and benzyloxy groups reacted with 5-methyltetrazole with moderate yields (**2a**–**2c**). Reactions of various halo-substituted phenylboronic acids yielded products similar to those obtained with phenylboronic acid and afforded the desired 2,5-disubstituted tetrazoles **2d**–**h** with high regioselectivity. 2-Aryl-substituted tetrazoles were the major products in these cases, while 1-aryl-substituted tetrazoles were not detected.

In summary, a novel method for the regioselective synthesis of 2,5-disubstituted tetrazoles by direct coupling of 5-substituted tetrazoles with arylboronic acids in the presence of a catalytic amount of $[Cu(OH)(TMEDA)]_2Cl_2$ in an O_2 atmosphere was developed. The reaction can be conducted at room temperature and is applicable to both 5-aryltetrazoles and 5-alkyltetrazoles. The products were obtained as nearly pure single regioisomers. This is the first report of such high

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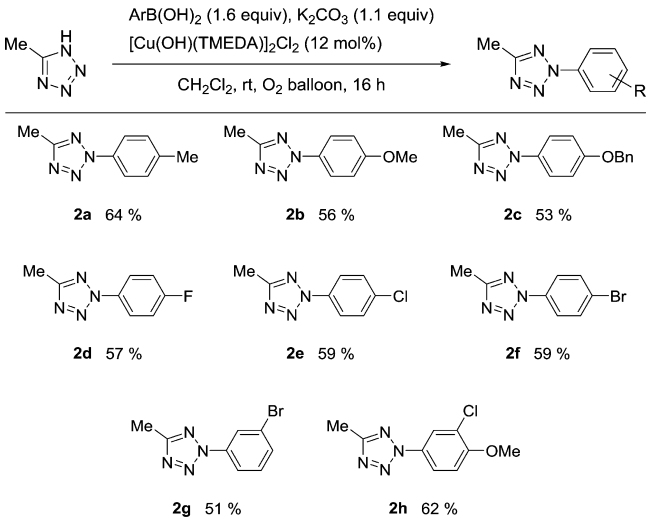
Table 3. Reaction of 5-Methyltetrazole with Various Arylboronic Acids



regioselectivity in coupling reactions of 5-alkyltetrazoles. This method therefore offers a facile and practical route to various 2,5-disubstituted tetrazoles.

EXPERIMENTAL SECTION

General Information. Melting points were uncorrected. ^{1}H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz with tetramethylsilane as an internal standard. IR spectra were recorded using an attenuated total reflectance measurement. High-resolution mass spectra were recorded on a time-of-flight instrument using electrospray ionization method. Column chromatography was performed with silica gel 60N (40−100 μm, spherical, neutral). Analytical high-performance liquid chromatography was performed using Imtakt Unison UK-C18 column.

Materials. Unless otherwise noted, materials and solvents were purchased and used without further purification. 5-Bromo-1*H*-tetrazole[19] and 1*H*-tetrazole-5-carboxylic acid ethyl ester[20] were prepared according to the reported procedure. Products **1b**,[21] **1d**,[22] **1f**,[23] **1g**,[24] **1h**,[12,14] and **1i**[23] are known in the literature.

General Procedure. K_2CO_3 (1.1 equiv), $[Cu(OH)(TMEDA)]_2Cl_2$ (12 mol %), and arylboronic acid (1.6−3.0 equiv) were added to a solution of a tetrazole in CH_2Cl_2 (0.1−0.2 M solution) at room temperature. After the mixture stirred at room temperature for 16 h under O_2, 10% aqueous NH_3 was added and extracted with CH_2Cl_2. The organic layer was washed with 10% aqueous NaCl, dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was purified by flash SiO_2 column chromatography to give the 2,5-disubstituted tetrazole.

5-Methyl-2-phenyl-2*H*-tetrazole (1a). 1a (108.8 mg, 67%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and phenylboronic acid (195.1 mg, 1.60 mmol): eluent, 1:2 hexane/CH_2Cl_2; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11−8.08 (2H, m), 7.57−7.45 (3H, m), 2.64 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 136.9, 129.6, 129.5, 119.7, 11.0; HRMS (ESI) calcd for $C_8H_9N_4$ $[M + H]^+$ 161.0827, found 161.0825.

5-Benzyl-2-phenyl-2*H*-tetrazole (1b).[21] 1b (181.2 mg, 76%) was obtained from 5-benzyl-1*H*-tetrazole (160.2 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and phenylboronic acid (195.1 mg, 1.60 mmol): eluent, 2:3 hexane/CH_2Cl_2; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11−8.08 (2H, m), 7.55−7.23 (8H, m), 4.34 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 136.9, 136.6, 129.6, 129.5, 128.9, 128.7, 127.0, 119.9, 31.9; HRMS (ESI) calcd for $C_{14}H_{13}N_4$ $[M + H]^+$ 237.1140, found 237.1135.

5-Methylthio-2-phenyl-2*H*-tetrazole (1c). 1c (120.5 mg, 62%) was obtained from 5-methylthio-1*H*-tetrazole (116.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and phenylboronic acid (195.1 mg, 1.60 mmol): eluent, 1:1 hexane/CH_2Cl_2; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10−8.07 (2H, m), 7.57−7.46 (3H, m), 2.76 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 136.7, 129.7, 119.6, 14.5; HRMS (ESI) calcd for $C_8H_9N_4S$ $[M + H]^+$ 193.0548, found 193.0546.

2-Phenyl-2*H*-tetrazole-5-carboxylic Acid Ethyl Ester (1d).[22] 1d (0.82 g, 53%) was obtained from 1*H*-tetrazole-5-carboxylic acid ethyl ester (1.00 g, 7.04 mmol), K_2CO_3 (1.07 g, 7.74 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (0.39 g, 0.84 mmol), LiCl (0.15 g, 3.52 mmol), and phenylboronic acid (2.58 g, 21.12 mmol): eluent, 15:1 hexane/AcOEt; white solid; mp 72−73 °C (EtOH); IR (ATR) cm^{-1} 1736; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22−8.20 (2H, m), 7.62−7.53 (3H, m), 4.59 (2H, q, J = 7.2 Hz), 1.50 (3H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 136.4, 130.7, 129.9, 120.4, 62.8, 14.2; HRMS (ESI) calcd for $C_{10}H_{11}N_4O_2$ $[M + H]^+$ 219.0882, found 219.0886.

5-Bromo-2-phenyl-2*H*-tetrazole (1e). 1e (118.6 mg, 52%) was obtained from 5-bromo-1*H*-tetrazole (149.0 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and phenylboronic acid (195.1 mg, 1.60 mmol): eluent, 3:2 hexane/CH_2Cl_2; white solid; mp 49−50 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.08 (2H, m), 7.60−7.51 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 136.4, 130.4, 129.8, 119.7; HRMS (ESI) calcd for $C_7H_6BrN_4$ $[M + H]^+$ 224.9776, found 224.9774.

2,5-Diphenyl-2*H*-tetrazole (1f).[23] 1f (180.4 mg, 81%) was obtained from 5-phenyl-1*H*-tetrazole (146.2 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), LiCl (21.2 mg, 0.50 mmol), and phenylboronic acid (195.1 mg, 1.60 mmol): eluent, 3:1 hexane/CH_2Cl_2; white solid; mp 102−103 °C (EtOH, lit.[10] 101−102 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28−8.19 (4H, m), 7.61−7.49 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 137.0, 130.6, 129.7, 129.6, 129.0, 127.2, 127.1, 119.9; HRMS (ESI) calcd for $C_{13}H_{11}N_4$ $[M + H]^+$ 223.0984, found 223.0984.

5-(4-Methylphenyl)-2-phenyl-2*H*-tetrazole (1g).[24] 1g (187.6 mg, 79%) was obtained from 5-(4-methylphenyl)-1*H*-tetrazole (160.2 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and phenylboronic acid (195.1 mg, 1.60 mmol): eluent, 1:1 hexane/CH_2Cl_2; white solid; mp 94−95 °C (EtOH, lit.[10] 94−95 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.13 (4H, m), 7.60−7.47 (3H, m), 7.33 (2H, d, J = 7.6 Hz), 2.44 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 140.8, 137.0, 129.7, 129.5, 127.0, 124.4, 119.9, 21.5; HRMS (ESI) calcd for $C_{14}H_{13}N_4$ $[M + H]^+$ 237.1140, found 237.1134.

5-(4-Bromophenyl)-2-phenyl-2*H*-tetrazole (1h). 1h (228.2 mg, 75%) was obtained from 5-(4-bromophenyl)-1*H*-tetrazole (225.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and phenylboronic acid (195.1 mg, 1.60 mmol): eluent, 1:1 hexane/CH_2Cl_2; white solid; mp 113−114 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.12 (4H, m), 7.68−7.49 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 136.8, 132.2, 129.8, 129.7, 128.6, 126.1, 125.0, 119.9; HRMS (ESI) calcd for $C_{13}H_{10}BrN_4$ $[M + H]^+$ 301.0089, found 301.0085.

4-(2-Phenyl-2*H*-tetrazol-5-yl)pyridine (1i).[23] 1i (69.9 mg, 31%) was obtained from 5-(4-pyridyl)-1*H*-tetrazole (147.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and phenylboronic acid (195.1 mg, 1.60 mmol): eluent, 5:1 CH_2Cl_2/AcOEt; white solid; mp 142−143 °C (EtOH, lit.[25] 141.5−142.5 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (2H, dd, J = 4.4, 1.6 Hz), 8.22−8.19 (2H, m), 8.13 (2H, dd, J = 4.4, 1.6 Hz), 7.63−7.53 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 150.8, 136.7, 134.5, 130.1, 129.8, 120.9, 120.0; HRMS (ESI) calcd for $C_{12}H_{10}N_5$ $[M + H]^+$ 224.0936, found 224.0925.

2-(4-Methylphenyl)-5-methyl-2*H*-tetrazole (2a). 2a (111.5 mg, 64%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and *p*-methylphenylboronic acid (217.5 mg, 1.60 mmol):

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eluent, 1:2 hexane/CH_2Cl_2; white solid; mp 69−70 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (2H, d, J = 8.8 Hz), 7.33 (2H, d, J = 8.4 Hz), 2.63 (3H, s), 2.43 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 139.7, 134.7, 130.1, 119.6, 21.2, 11.0; HRMS (ESI) calcd for $C_9H_{11}N_4$ $[M + H]^+$ 175.0984, found 175.0979.

2-(4-Methoxyphenyl)-5-methyl-2*H*-tetrazole (2b). 2b (106.5 mg, 56%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and *p*-methoxyphenylboronic acid (243.1 mg, 1.60 mmol): eluent, 1:6 hexane/CH_2Cl_2; white solid; mp 73−74 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (2H, d, J = 9.6 Hz), 7.03 (2H, d, J = 9.2 Hz), 3.88 (3H, s), 2.62 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 160.4, 130.5, 121.3, 114.6, 55.6, 11.0; HRMS (ESI) calcd for $C_9H_{11}N_4O$ $[M + H]^+$ 191.0933, found 191.0937.

2-(4-Benzyloxyphenyl)-5-methyl-2*H*-tetrazole (2c). 2c (142.7 mg, 53%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and 4-benzyloxyphenylboronic acid (364.9 mg, 1.60 mmol): eluent, 1:6 hexane/CH_2Cl_2; white solid; mp 113−114 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (2H, d, J = 8.8 Hz), 7.46−7.33 (5H, m), 7.10 (2H, d, J = 9.2 Hz), 5.14 (2H, s), 2.62 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 159.5, 136.3, 130.7, 128.7, 128.3, 127.5, 121.3, 115.6, 70.4, 11.0; HRMS (ESI) calcd for $C_{15}H_{15}N_4O$ $[M + H]^+$ 267.1246, found 267.1241.

2-(4-Fluorophenyl)-5-methyl-2*H*-tetrazole (2d). 2d (102.8 mg, 57%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and *p*-fluorophenylboronic acid (223.9 mg, 1.60 mmol): eluent, 1:2 hexane/CH_2Cl_2; white solid; mp 80−81 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.06 (2H, m), 7.27−7.21 (2H, m), 2.64 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 163.4, 161.6, 133.2, 121.7, 121.6, 116.8, 116.5, 11.0; HRMS (ESI) calcd for $C_8H_8FN_4$ $[M + H]^+$ 179.0733, found 179.0730.

2-(4-Chlorophenyl)-5-methyl-2*H*-tetrazole (2e). 2e (115.2 mg, 59%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and *p*-chlorophenylboronic acid (250.2 mg, 1.60 mmol): eluent, 1:2 hexane/CH_2Cl_2; white solid; mp 84−85 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (2H, d, J = 9.2 Hz), 7.52 (2H, d, J = 8.8 Hz), 2.64 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 135.3, 129.8, 120.9, 11.0; HRMS (ESI) calcd for $C_8H_8ClN_4$ $[M + H]^+$ 195.0437, found 195.0439.

2-(4-Bromophenyl)-5-methyl-2*H*-tetrazole (2f). 2f (142.4 mg, 59%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and *p*-bromophenylboronic acid (321.3 mg, 1.60 mmol): eluent, 1:2 hexane/CH_2Cl_2; white solid; mp 92−93 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (2H, d, J = 8.8 Hz), 7.68 (2H, d, J = 9.2 Hz), 2.64 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 135.8, 132.8, 123.3, 121.1, 11.0; HRMS (ESI) calcd for $C_8H_8BrN_4$ $[M + H]^+$ 238.9932, found 238.9933.

2-(3-Bromophenyl)-5-methyl-2*H*-tetrazole (2g). 2g (123.3 mg, 51%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and *m*-bromophenylboronic acid (321.3 mg, 1.60 mmol): eluent, 1:2 hexane/CH_2Cl_2; white solid; mp 65−66 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (1H, t, J = 2.0 Hz), 8.06 (1H, ddd, J = 8.0, 2.0, 1.2 Hz), 7.61 (1H, ddd, J = 8.0, 2.0, 1.2 Hz), 7.42 (1H, t, J = 8.0 Hz), 2.65 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 137.6, 132.5, 131.0, 123.2, 122.8, 118.2, 11.0; HRMS (ESI) calcd for $C_8H_8BrN_4$ $[M + H]^+$ 238.9932, found 238.9928.

2-(3-Chloro-4-methoxyphenyl)-5-methyl-2*H*-tetrazole (2h). 2h (139.8 mg, 62%) was obtained from 5-methyl-1*H*-tetrazole (84.1 mg, 1.00 mmol), K_2CO_3 (152.0 mg, 1.10 mmol), $[Cu(OH)(TMEDA)]_2Cl_2$ (55.7 mg, 0.12 mmol), and 3-chloro-4-methoxyphenylboronic acid (298.2 mg, 1.60 mmol): eluent, 1:6 hexane/CH_2Cl_2; white solid; mp 140−141 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (1H, d, J = 2.8 Hz), 7.97 (1H, dd, J = 8.8, 2.8 Hz), 7.06 (1H, d, J = 8.8 Hz), 3.98 (3H, s), 2.63 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 155.9, 130.4, 123.6, 122.0, 119.1, 112.2, 56.5, 11.0; HRMS (ESI) calcd for $C_9H_{10}ClN_4O$ $[M + H]^+$ 225.0543, found 225.0542.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of all compounds (**1a−1i, 2a−2h**). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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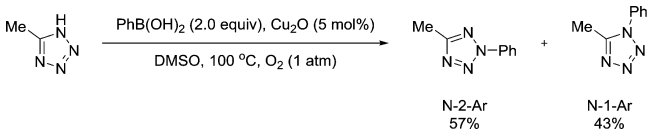

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