DOI: 10.1002/cjoc.201280012

Environmental Friendly Azide-Alkyne Cycloaddition Reaction of Azides, Alkynes, and Organic Halides or Epoxides in Water: Efficient "Click" Synthesis of 1,2,3-Triazole Derivatives by Cu Catalyst

Liu, Jianming(刘建明) Liu, Muwen(刘慕文) Yue, Yuanyuan(岳园园)
Yao, Meihuan(姚美焕) Zhuo, Kelei*(卓克垒)

Key Laboratory of Green Chemical Media and Reactions (*Ministry of Education*), *School of Chemistry and Environmental Science*, *Henan Normal University*, *Xinxiang*, *Henan 453007*, *China*

An efficient click synthesis of 1,2,3-triazole derivatives from benzyl halides or alkyl halides, epoxides, terminal alkynes, and sodium azides in the presence of copper salts and relative benzimidazole salts have been developed. This procedure eliminates the need to handle potentially organic azides, which are generated *in situ*. A broad spectrum of substrates can participate in the process effectively to produce the desired products in good yields.

Keywords copper catalyst, benzimidazole salts, 1,2,3-triazole derivatives, click chemistry, cycloaddition

Introduction

Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction has undergone a rapid development since its discovery in 2002.[1,2] Wide substrate scope, high synthetic efficiency and mild reaction condition have made it a fast and efficient approach to synthesize 1,4-disubstituted 1,2,3-triazoles, which is an important class of heterocyclic compounds due to its wide application in the preparation of dyes, photostabilizers, agrochemicals, biochemicals and organometallics.[3-5]

In this click reaction, many achievements have demonstrated that copper(I)[6-10] and copper(II) catalysts[11,12] are required for the reaction, respectively. However, using copper(I) and copper(II) salts combined with the same benzimidazolium salts as catalysts simultaneously has been rarely reported to the best of our knowledge. Furthermore, most of the aforementioned methods inherently suffer from harsh conditions such as organic azides, organic solvents and a large amount of strong base. Although organic azides are generally stable against most reaction conditions such as water and oxygen, the isolation or purification of lower concentration organic azides or polyazides can be difficult to handle. It is therefore desirable to develop a methodology that avoids the isolation of organic azides.[13]

Additionally, it is beneficial to develop an efficient catalyst system in water medium instead of organic solvents from the standpoint of green chemistry. As for the 1,3-dipolar cycloaddition, most of the reported copper catalytic systems have serious shortcoming in the broad tolerance of substrate and indispensability of additives such as reducing agents and bases. In this content, the developing of efficient catalysts, the broadening of the scope of substrates, and without adding any additives is desirable from the standpoint of green chemistry. In connection with the recent work in benzimidazole and related ligands and copper-catalyzed "click" chemistry,[14-16] we report herein an efficient catalyst system *in situ* prepared easily from Cu(I) and Cu(II) species in combination with benzimidazole salts. The catalyst system exhibits excellent catalytic performance for copper-catalyzed "click" chemistry for synthesis of 1,2,3-triazole framework.

Results and Discussion

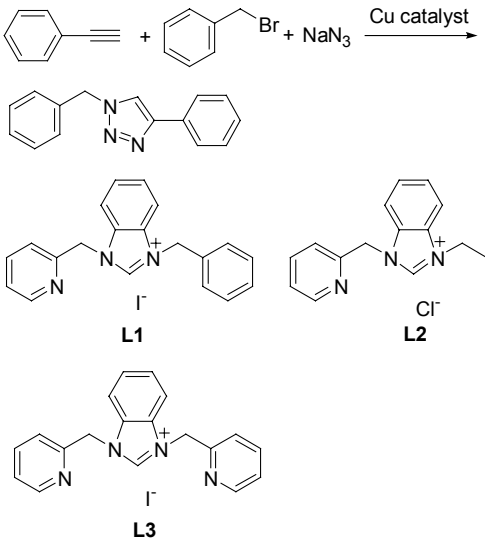
The cycloaddition of phenylacetylene, benzyl bromide and sodium azide was used as model reaction to establish the optimum conditions. Initially, catalytic activities of different ligands were examined with 1.0 mol% CuI as catalytic precursor in water at room temperature. Generally, all the used ligands **1**—**3** gave generally high yields, and up to 95% yield of the product 1,4-disubstituted 1,2,3-triazoles was achieved by using ligand **1** (Table 1, Entries 1—3). With this promising lead, a systematic screening of catalysts and solvents were carried out. The results were summarized in Table 1. It was found that the use of copper(I) catalytic precursor gave more than 90% yield of the products (Table

* E-mail: klzhuo@263.net; Fax: 00863733326336
Received May 20, 2011; accepted October 20, 2011.

CHINESE JOURNAL OF CHEMISTRY

1, Entries 1, and 4—6). In comparison, in the presence of copper(II) catalyst, the reaction yield was still very good, and the isolated yield was 88% (Table 1, Entries 7—12). During our optimization studies, screening different solvents (Table 1, Entries 13—14) revealed that the reaction was not dependent on the nature of the solvent.

Table 1 Screening of the different catalysts and conditions for azide-alkyne cycloaddition[a]

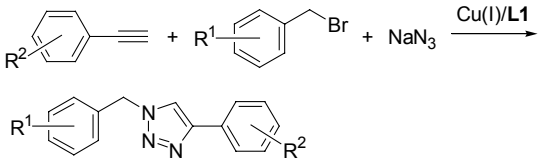


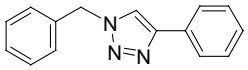
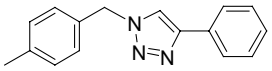
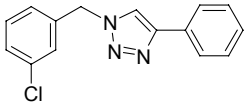
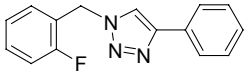
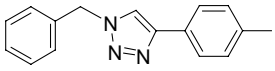
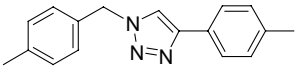
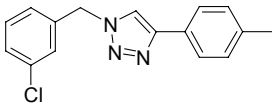
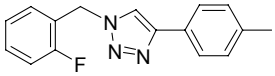
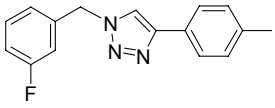
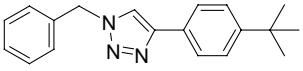
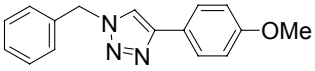
Entry	Cat.	Ligand	Solvent	Yield[b]/%
1	CuI	**L1**	H_2O	95
2	CuI	**L2**	H_2O	92
3	CuI	**L3**	H_2O	91
4	CuCl	**L1**	H_2O	91
5	CuBr	**L1**	H_2O	90
6	Cu_2O	**L1**	H_2O	90
7	$Cu(OAc)_2$	**L1**	H_2O	88
8	$CuSO_4$	**L1**	H_2O	87
9	$Cu(acac)_2$	**L1**	H_2O	84
10	$CuCl_2•2H_2O$	**L1**	H_2O	86
11	$Cu(NO_3)_2•3H_2O$	**L1**	H_2O	87
12	CuO	**L1**	H_2O	84
13[c]	CuI	**L1**	H_2O/CH_3CN	91
14[c]	CuI	**L1**	H_2O/THF	85

[a] Reaction conditions: copper catalyst (0.02 mmol), ligand (0.024 mmol), benzyl bromide (2.0 mmol), phenylacetylene (2.4 mmol), sodium azide (2.4 mmol), 24 h, solvent (5.0 mL), r.t. [b] Isolated yield. [c] A 1∶4 ratio of solvent.

Having established the effective catalytic system, we next examined the azide-alkyne cycloaddition reactions of a variety of benzyl bromides derivatives with alkynes to explore the reaction scope, and the results are summarized in Table 2. It was found that the reaction was applicable to various benzyl bromides with both electron-donating and electron-withdrawing substituents with alkynes bearing different alkyl groups in *para* position. In all cases, the cycloaddition reactions proceeded well, producing the desired products in high yields.

Table 2 One-pot synthesis of 1,2,3-triazoles from alkyl bromide, alkynes, and sodium azide[a]



Entry	R^1	R^2	Product	Yield[b]/%
1	H	H		95
2	*p*-Me	H		94
3	*m*-Cl	H		92
4	*o*-F	H		93
5	H	*p*-Me		94
6	*p*-Me	*p*-Me		93
7	*m*-Cl	*p*-Me		92
8	*o*-F	*p*-Me		85
9	*m*-F	*p*-Me		91
10	H	*p*-Bu		94
11	H	*p*-OMe		92

[a] Reaction conditions: CuI (0.02 mmol), **L1** (0.024 mmol), benzyl bromides (2.0 mmol), alkynes (2.4 mmol), sodium azide (2.4 mmol), H_2O (5.0 mL), 24 h, r.t. [b] Isolated yield.

In an attempt to broaden the scope of our methodology, the possibility of performing the reaction with alkyl halides and alkyl bromides instead of benzyl bromides derivatives was also investigated under N_2 atmosphere. In this way, the reaction between benzyl halides and phenylacetylene, *p*-methyl-phenylacetylene afforded the corresponding products in 86% and 89%

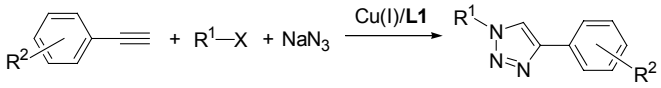
yields, respectively (Table 3, Entries 1, 3). This methodology could be extended to heterocyclic halides, such as 2-chloromethyl pyridine and 2-chloromethyl-1-methyl-benzimidazole, and the high yields of the targeted products were obtained (Table 3, Entries 4—6). The results indicated that the obtained products were useful bidentate ligands for complex formation and catalysis. Next, the reactions of alkyl bromides, phenylacetylene and sodium azide were also investigated, and the reactions afforded the corresponding products smoothly with moderate yields (Table 3, Entries 7—10).

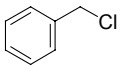
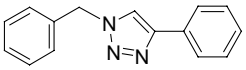
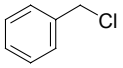
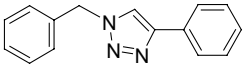
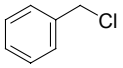
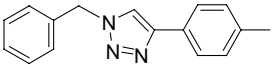
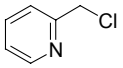
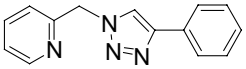
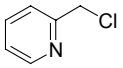
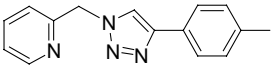
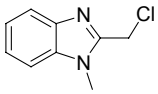
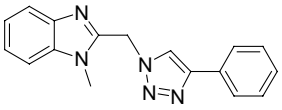
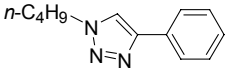
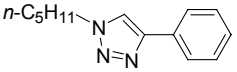
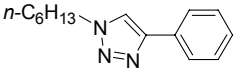
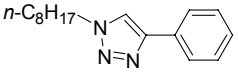
To probe the reaction scope and performance of copper(II) catalyst, we also examined other alkyl halides and epoxy compound under the optimized reaction condition. In comparison to copper(I) catalyst system, no significant difference was observed by using benzyl bromide, benzyl chloride and 2-chloromethyl pyridine (Table 4, Entries 1—3). However, phenylacetylene, sodium azides, and *n*-butyl bromide exhibited much lower reactivities (Table 4, Entry 4). Under the above optimized condition, the $Cu(OAc)_2$/**L1** was applied to the reactions of terminal alkynes and epoxides to produce regioselectively *β*-hydroxy-1,4-disubstituted 1,2,3-triazoles up to 91% yields (Table 4, Entries 5—8).

Conclusions

In conclusion, we have developed an efficient procedure for the copper-catalyzed azide-alkyne cycloaddition reaction of alkyl halides or epoxides, alkynes and sodium azide, which employed low loading of copper species in combination with benzimidazole salts as catalyst. The simple methodology avoided isolation and handling of potentially unstable organic azides and provided many corresponding 1,2,3-triazole derivatives in water medium. The studies here exhibit broad applicability to understand reactivities of different functional groups, such as benzyl bromides, benzyl halides, alkyl bromides, heterocyclic halides, and epoxies.

Table 3 CuI combined with **L1** catalyzed azide-alkyne cycloaddition to synthesize 1,2,3-triazoles[a]

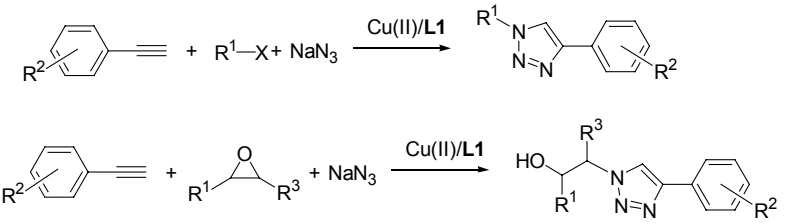


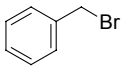
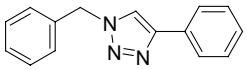
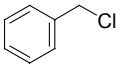
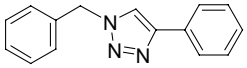
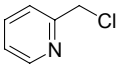
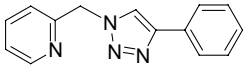
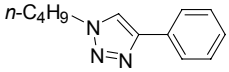
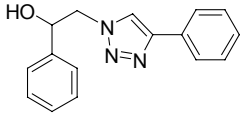
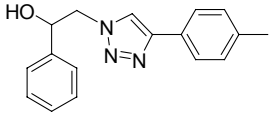
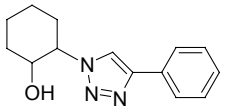
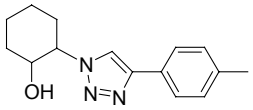
Entry	R^1-X	R^2	Time/h	Product	Yield[b]/%
1		H	48		86
2		H	24		50
3		*p*-Me	48		89
4[c]		H	24		84
5[c]		*p*-Me	24		88
6[c]		H	24		90
7[d]	*n*-C_4H_9Br	H	48		48
8[d]	*n*-$C_5H_{11}Br$	H	48		71
9[d]	*n*-$C_6H_{13}Br$	H	48		72
10[d]	*n*-$C_8H_{19}Br$	H	48		57

[a] Reaction conditions: CuI (0.04 mmol), **L1** (0.048 mmol), alkyl halides (2.0 mmol), alkynes (2.4 mmol), sodium azide (2.4 mmol), H_2O (5.0 mL), 48 h, N_2 atmosphere, r.t. [b] Isolated yield. [c] CuI (0.02 mmol), **L1** (0.024 mmol). [d] A 1∶4 ratio of H_2O/CH_3CN.

CHINESE JOURNAL OF CHEMISTRY

Table 4 Azide-alkyne cycloaddition catalyzed by copper(II) catalyst[a]



Entry	R^1-X	R^2	Product	Yield[b]/%
1		H		88
2		H		88
3		H		86
4[c]	*n*-C_4H_9Br	H		28
5		H		86
6		*p*-Me		91
7		H		90
8		*p*-Me		90

[a] Reaction conditions: $Cu(OAc)_2 \cdot H_2O$ (0.02 mmol), **L1** (0.024 mmol), alkyl halides (2.0 mmol), alkynes (2.4 mmol), sodium azide (2.4 mmol), H_2O (5.0 mL), 24 h, r.t. [b] Isolated yield. [c] A 1∶4 ratio of H_2O/CH_3CN, N_2 atmosphere.

Experimental

Synthesis of benzimidazole and related ligands

Synthesis of 1-benzyl-3-picolylbenzimidazole iodide (L1) To a solution of picolyl chloride, prepared by basifying of picolyl chloride hydrochloride (9.26 g, 56.4 mmol) in 100 mL acetone were added 1-benzyl-1*H*-benzo[*d*]imidazole (2.63 g, 12.6 mmol) and NaI (9.26 g, 61.8 mmol). After the mixture was stirred for 48 h, volatiles were removed *in vacuo*. The solid was dissolved in dichloromethane (50 mL), and the solution filtered through Celite. Addition of diethyl ether (200 mL) caused a solid to precipitate. The residual mixture was chromatographed on silica gel to give the desired product.

1-Benzyl-3-picolylbenzimidazole iodide (L1) ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 11.24 (s, 1H), 8.47 (d, J= 4.8 Hz, 1H), 7.88 (J=4.8, 2.0 Hz, 2H), 7.72—7.76 (m, 1H), 7.58 (dd, J=6.8, 1.6 Hz, 5H), 7.48—7.55 (m, 3H), 7.23—7.39 (m, 1H), 6.02 (s, 2H), 5.83 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 151.84, 149.70, 142.37, 137.68, 132.21, 131.82, 131.01, 129.41, 129.34, 128.36, 127.24, 127.21, 123.98, 123.77, 114.40, 113.52, 52.41, 51.62. HRMS calcd for $C_{20}H_{18}N_3$ ($M-I^-$) 300.1495, found 300.1494 ($M-I^-$).

Synthesis of 1-picolyl-3-picolylbenzimidazole iodide (L2) To a solution of picolyl chloride, prepared by basifying of picolyl chloride hydrochloride (9.26 g, 56.4 mmol) in 100 mL of acetone were added 1-picolyl-1*H*-benzo[*d*]imidazole (2.64 g, 12.6 mmol) and NaI (9.26 g, 61.8 mmol). After the mixture was stirred for 48 h, volatiles were removed *in vacuo*. The solid was dissolved in dichloromethane (50 mL), and the solution filtered through Celite. Addition of diethyl ether (200 mL) caused a solid to precipitate. The residual mixture was chromatographed on silica gel to give the desired product.

1-Picolyl-3-picolylbenzimidazole iodide (L2) ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 11.19 (s, 1H), 8.48 (d, J=4.8 Hz, 2H), 7.84 —7.87 (m, 4H), 7.71—7.75 (m, 2H), 7.51 (dd, J=6.4, 2.8 Hz, 2H), 7.23—7.26 (m, 2H), 5.98 (s, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 151.87, 149.75, 142.52, 137.70, 131.49, 127.20, 124.00, 123.75, 114.13, 52.58. HRMS calcd for $C_{19}H_{17}N_4$ ($M-I^-$) 301.1448, found 301.1448 ($M-I^-$).

Synthesis of 1-benzyl-3-picolylbenzimidazole chloride (L3) To a solution of 1-picolyl-1*H*-benzo[*d*]-imidazole (4.67 g, 22.2 mmol) in toluene (20 mL) was added benzyl chloride (7.5 mL, 65.4 mmol). After reflux for 12 h, the solvent was removed *in vacuo*. The product was obtained by recrystallization in ethyl alcohol.

1-Benzyl-3-picolylbenzimidazole chloride (L3) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.40 (s, 1H), 8.48 (d, J=4.8 Hz, 1H), 7.90—8.00 (m, 3H), 7.69 (d, J=7.6 Hz, 1H), 7.61—7.63 (m, 2H), 7.52 (d, J=6.8 Hz, 2H), 7.36—7.45 (m, 4H), 5.98 (s, 2H), 5.88 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 153.42, 150.00, 144.04, 137.97, 134.57, 131.92, 131.21, 129.43, 129.13, 128.65, 127.23, 127.10, 124.13, 123.24, 114.47, 51.30, 50.26. HRMS calcd for $C_{20}H_{18}N_3$ ($M-Cl^-$) 300.1495, found 300.1494 ($M-Cl^-$).

General procedure

General procedure for azide-alkyne cycloaddition reaction of benzyl bromides derivatives and alkynes and sodium azide in the presence of Cu(I), Cu(II) and L1 Benzyl bromides derivatives (2.0 mmol), alkynes (2.4 mmol) and sodium azide (2.4 mmol) were added and stirred in water (5.0 mL) in the presence of copper salts (0.02 mmol) and **L1** (0.024 mmol) at room temperature in a schlenk. After completion of the reaction, the water was removed *in vacuo*. The residual mixture was chromatographed on silica gel to give the desired product.

General procedure for azide-alkyne cycloaddition reaction from alkyl halides, alkyl bromides, alkynes, and sodium azide in the presence of CuI and L1 Alkyl bromides derivatives (2.0 mmol), alkynes (2.4 mmol) and sodium azide (2.4 mmol) were added and stirred in solvents (5.0 mL) in the presence of CuI (0.02 mmol) and **L1** (0.024 mmol) at room temperature in a schlenk under N_2 atmosphere. After completion of the reaction, the water was removed *in vacuo*. The residual mixture was chromatographed on silica gel to give the desired product.

Characterization of products

1-Benzyl-4-phenyl-1*H*-1,2,3-triazole[9b] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.82 (d, J=7.6 Hz, 2H), 7.72 (s, 1H), 7.32—7.44 (m, 4H), 7.00—7.10 (m, 4H), 5.58 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 148.34, 137.05, 130.75, 130.31, 128.83, 128.28, 125.70, 123.51, 119.60, 115.87, 115.66, 115.05, 114.85, 53.52. EI-MS *m*/*z*: 235 (M^+).

1-(4-Methylbenzyl)-4-phenyl-1*H*-1,2,3-triazole[12b] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.80 (dd, J=1.2, 7.2 Hz, 2H), 7.66 (s, 1H), 7.19—7.42 (m, 7H), 5.54 (s, 2H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 148.09, 138.71, 131.60, 130.53, 129.78, 128.76, 128.11, 125.66, 119.40, 54.02, 21.15. EI-MS *m*/*z*: 249 (M^+).

1-(3-Chlorobenzyl)-4-phenyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.82 (dd, J=1.2, 7.2 Hz, 2H), 7.72 (s, 1H), 7.18—7.44 (m, 7H), 5.56 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 148.38, 136.61, 135.00, 130.44, 130.30, 128.97, 128.83, 128.28, 128.04, 126.04, 125.70, 115.96, 53.47. HRMS calcd for $C_{15}H_{13}ClN_3$ ($M+H^+$) 270.0793, found 290.0782 ($M+H^+$).

1-(2-Fluorobenzyl)-4-phenyl-1*H*-1,2,3-triazole[15a] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.82 (d, J=7.2 Hz, 2H), 7.79 (s, 1H), 7.13—7.46 (m, 7H), 5.65 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.73, 159.27, 148.17, 130.95, 130.87, 130.57, 130.53, 130.37, 128.79, 128.20, 125.70, 124.89, 124.85, 122.01, 121.86, 119.70, 115.92, 115.71, 47.73, 47.69. EI-MS *m*/*z*: 253 (M^+).

1-Benzyl-4-*p*-tolyl-1*H*-1,2,3-triazole[9c] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.70 (d, J=8.0 Hz, 2H), 7.65 (s, 1H), 7.21—7.43 (m, 7H), 5.58 (s, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 137.99, 134.72, 129.47, 129.11, 128.72, 128.04, 127.67, 125.57, 54.18, 21.26. EI-MS *m*/*z*: 249 (M^+).

1-(4-Methylbenzyl)-4-*p*-tolyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.69 (d, J=8.0 Hz, 2H), 7.61 (s, 1H), 7.19—7.22 (m, 6H), 5.53 (s, 2H), 2.37 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 148.16, 138.65, 137.92, 131.69, 129.76, 129.44, 128.10, 127.74, 125.56, 119.07, 53.96, 21.25, 21.15. HRMS calcd for $C_{17}H_{18}N_3$ ($M+H^+$) 264.1495, found 264.1499 ($M+H^+$).

1-(3-Chlorobenzyl)-4-*p*-tolyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.70 (d, J=8.0 Hz, 2H), 7.69 (s, 1H), 7.17—7.33 (m, 6H), 5.53 (s, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 148.40, 138.18, 136.65, 134.97, 130.42, 129.51, 128.93, 128.04, 127.42, 126.05, 125.61, 119.26, 53.45, 21.27. HRMS calcd for $C_{16}H_{15}ClN_3$ ($M+H^+$) 284.0949, found 284.0943 ($M+H^+$).

1-(2-Fluorobenzyl)-4-*p*-tolyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.72 (d, J=6.8 Hz, 2H), 7.70 (s, 1H), 7.12—7.38 (m, 6H), 5.63 (s, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.72, 159.25, 148.27, 138.03, 130.89, 130.81, 130.55, 130.52, 129.46, 127.58, 125.60, 124.86, 124.83, 122.08, 121.93, 119.32, 115.90, 115.69, 47.67, 47.62, 21.25. HRMS calcd for $C_{16}H_{15}FN_3$ ($M+H^+$) 268.1245, found 268.1244 ($M+H^+$).

1-(3-Fluorobenzyl)-4-*p*-tolyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.70 (d, J=8 Hz, 2H), 7.68 (s, 1H), 7.22—7.24 (m, 6H), 5.57 (s, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 164.21, 161.75, 148.42, 138.14, 137.14, 137.07, 130.80, 130.72, 129.50, 127.48, 125.60, 123.51, 123.48, 119.24, 115.83, 115.62, 115.06, 114.84, 53.48, 21.26. HRMS calcd for $C_{16}H_{15}FN_3$ ($M+H^+$) 268.1245, found 268.1247 ($M+$

H^+).

1-Benzyl-4-(4-*tert*-butylphenyl)-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.74 (d, J=8.4 Hz, 2H), 7.66 (s, 1H), 7.30—7.45 (m, 7H), 5.59 (s, 2H), 1.35 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 151.27, 148.20, 134.76, 129.10, 128.70, 127.97, 127.64, 125.70, 125.41, 119.29, 54.15, 34.63, 31.26. HRMS calcd for $C_{19}H_{22}N_3$ ($M+H^+$) 292.1808, found 292.1803 ($M+H^+$).

1-Benzyl-4-(4-methoxyphenyl)-1*H*-1,2,3-triazole[9b] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.73 (d, J=8.8 Hz, 2H), 7.59 (s, 1H), 7.33—7.38 (m, 5H), 6.93 (d, J=8.8 Hz, 2H), 5.57 (s, 2H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.56, 148.05, 134.75, 129.10, 128.71, 128.01, 126.97, 123.23, 118.71, 114.17, 55.28, 54.15. EI-MS m/z: 275 (M^+).

2-((4-Phenyl-1*H*-1,2,3-triazol-1-yl)methyl)pyridine[15a] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.60 (d, J=4.0 Hz, 1H), 7.95 (s, 1H), 7.2 (d, J=7.2 Hz, 2H), 7.67—7.72 (m, 1H), 7.39 (dd, J=7.2, 1.2 Hz, 2H), 7.23—7.34 (m, 3H), 5.71 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 154.43, 149.68, 148.19, 137.44, 130.48, 128.78, 128.15, 125.68, 123.45, 122.46, 120.21, 55.63. EI-MS m/z: 237 (M^+).

2-((4-*p*-Tolyl-1*H*-1,2,3-triazol-1-yl)methyl)pyridine ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.60 (d, J=4.4 Hz, 1H), 7.90 (s, 1H), 7.66—7.73 (m, 3H), 7.20—7.26 (m, 4H), 5.69 (s, 2H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 154.50, 149.63, 148.26, 137.98, 137.44, 129.46, 127.66, 125.59, 123.42, 122.44, 119.87, 55.59, 21.25. HRMS calcd for $C_{15}H_{15}N_4$ ($M+H^+$) 251.1291, found 251.1286 ($M+H^+$).

1-Methyl-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-1H-benzo[*d*]imidazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.96 (s, 1H), 7.77 (t, J=8.0 Hz, 3H), 7.32—7.42 (m, 6H), 5.93 (s, 2H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 148.59, 142.00, 136.05, 130.04, 128.81, 128.36, 125.65, 123.84, 122.88, 120.09, 119.81, 109.86, 46.78, 30.33. HRMS calcd for $C_{13}H_{18}N_3$ ($M+H^+$) 216.1495, found 216.1498 ($M+H^+$). HRMS calcd for $C_{17}H_{16}N_5$ ($M+H^+$) 290.1400, found 290.1401 ($M+H^+$).

1-Butyl-4-phenyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.84 (dd, J=7.2, 1.2 Hz, 2H), 7.762 (s, 1H), 7.34—7.45 (m, 3H), 4.39 (t, J=7.6 Hz, 2H), 1.92—1.96 (m, 2H), 1.37—1.43 (m, 2H), 0.96 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 147.66, 130.67, 128.79, 128.04, 125.65, 119.41, 50.11, 32.28, 19.68, 13.44. HRMS calcd for $C_{12}H_{16}N_3$ ($M+H^+$) 202.1339, found 202.1347 ($M+H^+$).

1-Pentyl-4-phenyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.84 (d, J=7.6 Hz, 2H), 7.77 (s, 1H), 7.32—7.45 (m, 3H), 4.38 (t, J=7.2 Hz, 2H), 1.93—2.00 (m, 2H), 1.31—1.41 (m, 4H), 0.87—1.27 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 147.64, 132.44, 130.72, 128.78, 128.43, 128.02, 125.63, 119.49, 50.37, 30.00, 28.55, 22.07, 13.82. HRMS calcd for $C_{13}H_{18}N_3$ ($M+H^+$) 216.1495, found 216.1498 ($M+H^+$).

1-Hexyl-4-phenyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.84 (d, J=7.6 Hz, 2H), 7.77 (s, 1H), 7.32—7.45 (m, 3H), 4.39 (t, J=7.2 Hz, 2H), 1.92—1.99 (m, 2H), 1.27—1.34 (m, 6H), 0.88 (t, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 147.60, 130.64, 128.80, 128.06, 125.65, 119.45, 50.43, 31.13, 30.28, 26.13, 22.39, 13.92. HRMS calcd for $C_{14}H_{20}N_3$ ($M+H^+$) 230.1652, found 230.1642 ($M+H^+$).

1-Octyl-4-phenyl-1*H*-1,2,3-triazole ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.84 (d, J=7.6 Hz, 2H), 7.76 (s, 1H), 7.32—7.46 (m, 3H), 4.39 (t, J=6.8 Hz, 2H), 1.92—1.97 (m, 2H), 1.28—1.36 (m, 12H), 0.87 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 147.32, 130.69, 128.79, 128.03, 125.64, 50.41, 31.67, 30.32, 29.02, 28.94, 26.46, 22.57, 14.04. HRMS calcd for $C_{16}H_{24}N_3$ ($M+H^+$) 258.1965, found 258.1962 ($M+H^+$).

1-Phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethanol[12c] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.82 (s, 1H), 7.86 (d, J=7.6 Hz, 2H), 7.31—7.47 (m, 9H), 5.82—5.85 (m, 1H), 4.30—4.36 (t, J=10 Hz, 1H), 4.02—4.06 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 146.63, 137.75, 131.26, 129.32, 129.14, 128.71, 128.25, 127.56, 125.53, 121.34, 66.87, 63.59. EI-MS m/z: 265 (M^+).

1-Phenyl-2-(4-*p*-tolyl-1*H*-1,2,3-triazol-1-yl)ethanol ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.76 (s, 1H), 7.74 (d, J=8.0 Hz, 2H), 7.24—7.41 (m, 7H), 5.80—5.84 (m, 1H), 5.35 (t, J=5.2 Hz, 1H), 4.29—4.36 (m, 1H), 4.01—4.06 (m, 1H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 146.69, 137.79, 137.51, 129.86, 129.12, 128.69, 128.51, 127.56, 125.48, 120.89, 66.83, 63.59, 21.26. HRMS calcd for $C_{17}H_{18}N_3O$ ($M+H^+$) 280.1444, found 280.1438 ($M+H^+$).

2-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)cyclohexanol[12c] ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.58 (s, 1H), 7.83 (d, J=7.6 Hz, 2H), 7.42 (t, J=7.6 Hz, 2H), 7.32 (t, J=7.6 Hz, 1H), 4.99 (d, J=5.6 Hz, 1H), 4.20—4.26 (m, 1H), 3.76—3.80 (m, 1H), 3.34 (s, 1H), 1.36—2.01 (m, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 146.08, 131.58, 129.29, 128.03, 125.41, 120.95, 71.77, 66.45, 35.18, 32.40, 24.87, 24.31. EI-MS m/z: 243 (M^+).

2-(4-*p*-Tolyl-1*H*-1,2,3-triazol-1-yl)cyclohexanol ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.51 (s, 1H), 7.71 (d, J=7.6 Hz, 2H), 7.24 (d, J=7.6 Hz, 2H), 4.99 (d, J=5.6 Hz, 1H), 4.20 (t, J=8.4 Hz, 1H), 3.78 (s, 1H), 2.32 (s, 3H), 1.36—2.00 (m, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 146.14, 137.25, 129.83, 128.83, 125.37, 120.51, 71.77, 66.41, 35.20, 32.42, 24.88, 24.32, 21.25. HRMS calcd for $C_{15}H_{20}N_3O$ ($M+2H^+$) 258.1601, found 258.1604 ($M+2H^+$).

Acknowledgement

This work was supported by the National Natural Science Foundation of China (Nos. 20973055, 21103044).

References

[1] Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.

[2] Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596.

[3] (a) Wang, Q.; Chan, T. R.; Hilgraf, R.; Fokin, V. V.; Sharpless, K. B.; Finn, M. G. *J. Am. Chem. Soc.* **2003**, *125*, 3192; (b) Speers, A. E.; Adam, G. C.; Cravatt, B. F. *J. Am. Chem. Soc.* **2003**, *125*, 4686.

[4] (1) Anderson, J. C.; Schultz, P. G. *J. Am. Chem. Soc.* **2003**, *125*, 11782; (2) Link, A. J.; Tirrell, D. A. *J. Am. Chem. Soc.* **2003**, *125*, 11164.

[5] (a) Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Frechet, J. M. J.; Sharpless, K. B.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2004**, *43*, 3928; (b) Collman, J. P.; Devaraj, N. K.; Chidsey, C. E. D. *Langmuir* **2004**, *20*, 1051.

[6] (a) Rodionov, V. O.; Presolski, S. I.; Gardinier, S.; Lim, Y. H.; Finn, M. G. *J. Am. Chem. Soc.* **2007**, *129*, 12696; (b) Rodionov, V. O.; Presolski, S. I.; Dìaz, D. D.; Fokin, V. V.; Finn, M. G. *J. Am. Chem. Soc.* **2007**, *129*, 12705.

[7] (a) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302; (b) Kappe, C. O.; Eycken, E. V. *Chem. Soc. Rev.* **2010**, *39*, 1280.

[8] (a) Chan, T. R.; Hilgraf, R.; Sharpless, K. B.; Fokin, V. V. *Org. Lett.* **2004**, *6*, 2853; (b) Girard, C.; Önen, E.; Aufort, M.; Beauvière, S.; Samson, E.; Herscovici, J. *Org. Lett.* **2006**, *8*, 1689; (c) Chassaing, S.; Kumarraja, M.; Sido, A. S. S.; Pale, P.; Sommer, J. *Org. Lett.* **2007**, *9*, 883; (d) Oezcubukcu, S.; Ozkal, E.; Jimeno, C.; Pericas, M. A. *Org. Lett.* **2009**, *11*, 4680.

[9] (a) Díez-González, S.; Correa, A.; Cavallo, L.; Nolan, S. P. *Chem. Eur. J.* **2006**, *12*, 7558; (b) Teyssot, M. L.; Chevry, A.; Traïkia, M.; El-Ghozzi, M.; Avignant, D.; Gautier, A. *Chem. Eur. J.* **2009**, *15*, 6322; (c) Yamaguchi, K.; Oishi, T.; Katayama, T.; Mizuno, N. *Chem. Eur. J.* **2009**, *15*, 10464; (d) Zhao, Y. B.; Yan, Z. Y.; Liang, Y. M. *Tetrahedron Lett.* **2006**, *47*, 1545; (e) Yan, Z. Y.; Zhao, Y. B.; Fan, M. J.; Liu, W. M.; Liang, Y. M. *Tetrahedron* **2005**, *61*, 9331; (f) Hu, Y. Y.; Hu, J.; Wang, X. C.; Guo, L. N.; Shu, X. Z.; Niu, Y. N.; Liang, Y. M. *Tetrahedron* **2010**, *66*, 80; (g) Saha, B.; Sharma, S.; Sawant, D.; Kundu, B. *Synlett* **2007**, *10*, 1591; (h) Lu, P.; Wang, Y. G. *Synlett* **2010**, *2*, 165.

[10] (a) Zhou, Y. H.; Lecourt, T.; Micouin, L. *Angew. Chem., Int. Ed.* **2010**, *122*, 2661; (b) Chattopadhyay, B.; Vera, C. R.; Chuprakov, S.; Gevorgyan, V. *Org. Lett.* **2010**, *12*, 2166; (c) Buckley, B. R.; Dann, S. E.; Heaney, H. *Chem. Eur. J.* **2010**, *16*, 6278; (d) Wu, Y. M.; Deng, J.; Fang, X.; Chen, Q. Y. *J. Fluorine Chem.* **2004**, *125*, 1415.

[11] (a) Candelon, N.; Lastécouères, D.; Diallo, A. K.; Aranzaes, J. R.; Astruc, D.; Vincent, J.-M. *Chem. Commun.* **2008**, 741; (b) Yousuf, S. K.; Mukherjee, D.; Singh, B.; Maityc, S.; Taneja, S. C. *Green Chem.* **2010**, *10*, 1568; (c) Jin, S.; Choudhary, G.; Cheng, Y. F.; Dai, C. F.; Li, M. Y.; Wang, B. H. *Chem. Commun.* **2009**, 5251; (d) Campbell-Verduyn, L. S.; Szymański, W.; Postema, C. P.; Dierckx, R. A.; Elsinga, P. H.; Janssen, D. B.; Fering, B. L. *Chem. Commun.* **2010**, 898.

[12] (a) Pachón, L. D.; Van Maarseveen, J. H.; Rothenberg, G. *Adv. Synth. Catal.* **2005**, *347*, 811; (b) Sharghi, H.; Khalifeh, R.; Doroodmanda, M. M. *Adv. Synth. Catal.* **2009**, *351*, 207; (c) Sharghi, H.; Beyzavi, M. H.; Safavi, A.; Doroodmanda, M. M.; Khalifeh, R. *Adv. Synth. Catal.* **2009**, *351*, 2391; (d) Lee, C. T.; Huang, S. L.; Lipshutz, B. H. *Adv. Synth. Catal.* **2009**, *351*, 3139.

[13] Scriven, E. F. V.; Turnbull, K. *Chem. Rev.*, **1988**, *2*, 351.

[14] (a) Feldman, A. K.; Colasson, B.; Fokin, V. V. *Org. Lett.* **2004**, *6*, 3897; (b) Appukkuttan, P.; Dehaen, W.; Fokin, V. V.; Van der Eycken, E. *Org. Lett.* **2004**, *6*, 4223; (c) Ackermann, L.; Potukuchi, H. K.; Landsberg, D.; Vicente, R. *Org. Lett.* **2008**, *10*, 3081; (d) Namitharan, K.; Kumarraja, M.; Pitchumani, K. *Chem. Eur. J.* **2009**, *15*, 2755.

[15] (a) Li, F. W.; Hor, T. S. A. *Chem. Eur. J.* **2009**, *15*, 10585; (b) Li, F. W.; Bai, S. Q.; Hor, T. S. A. *Organometallics* **2008**, *27*, 672; (c) McGuinness, D.; Cavell, K. J. *Organometallics* **2000**, *19*, 741; (d) Wang, X.; Liu, S.; Jin, G. X. *Organometallics* **2004**, *23*, 6002.

[16] Lin, I. J. B.; Vasam, C. S. *Coord. Chem. Rev.* **2007**, *254*, 642.

(E1105201 Zhao, X.; Lu, Z.)

