# **Regioselective Synthesis of 1,2,3-Triazoles by Use of a Silica-Supported Copper(I) Catalyst**

Tao Miao,<sup>a</sup> Lei Wang\*<sup>a,b</sup>

<sup>a</sup> Department of Chemistry, Huaibei Coal Teachers College, Huaibei, Anhui 235000, P. R. of China

<sup>b</sup> State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P. R. of China

Fax +86(561)3090518; E-mail: leiwang@hbcnc.edu.cn

Received 12 September 2007; revised 8 November 2007

**Abstract:** A 1,3-dipolar cycloaddition reaction catalyzed by copper(I) immobilized on organic–inorganic hybrid materials was developed. Terminal alkynes reacted with benzyl- or alkyl halides and sodium azide in the presence of a copper(I) catalyst immobilized on 3-aminopropyl- or 3-[(2-aminoethyl)amino]propyl-functionalized silica gel in ethanol. The reactions exclusively generated the corresponding regiospecific 1,4-disubstituted 1,2,3-triazoles in good to excellent yields. The azide intermediates do not need to be isolated during this procedure, and this should prove to be useful especially when unstable low-molecular-weight and polyvalent azides are used. Furthermore, the silica-supported copper could be recovered and recycled by simple filtration of the reaction solution and reused for ten consecutive trials without decrease in activity.

**Key words:** 1,2,3-triazoles, supported catalysis, organic–inorganic hybrid material, copper(I) catalyst, 1,3-dipolar cycloaddition

Huisgen 1,3-dipolar cycloaddition of azides and alkynes<sup>1</sup> to afford 1,2,3-triazole rings has been widely used in industrial applications and synthetic intermediates.<sup>2</sup> The high tolerance of other functionalities and the almost quantitative transformation under mild conditions make this reaction an ideal prototype to demonstrate the concept of click chemistry developed by Sharpless and co-workers.<sup>3</sup> However, the regioselectivity of this cycloaddition reaction is generally low and the reaction usually leads to a mixture of 1,4- and 1,5-regioisomers. In 2002, K. B. Sharpless<sup>4a</sup> and M. Meldal<sup>4b</sup> showed that the rate of this coupling is dramatically accelerated (up to 10<sup>7</sup> times) under copper(I) catalysis, and that only one specific regioisomer of 1,4-disubstituted 1,2,3-triazole could be obtained. The required copper(I) catalysts are usually prepared by in situ reduction of copper(II) salts with ascorbate,<sup>5</sup> or by comproportionation of copper(0) and copper(II).<sup>6</sup> The catalysts might be copper(0) nanosize clusters,<sup>7</sup> or appropriate copper(I) salts (CuI or CuBr) with triphenylphosphine,<sup>8</sup> iminopyridine,<sup>9</sup> or mono-<sup>4</sup> or polydentate<sup>10,11</sup> nitrogen ligands. However, the use of transition metals (copper powder, copper salts, or ruthenium salts<sup>12</sup>) and ligands has led to the problem of waste disposal.

The high costs of transition-metal catalysts coupled with the toxic effects associated with many transition metals have led to an increased interest in immobilizing catalysts onto a support. The classic supported reagents can facilitate both the isolation and recycling of the catalyst by filthus providing environmentally tration, cleaner processes.<sup>13</sup> Recent examples include the use of polystyrene-supported palladium as a catalyst for Suzuki coupling and the Sonogashira reaction.<sup>14</sup> The development of organic reagents grafted onto silica gels has attracted more and more attention in recent years, because the industry seeks more environmentally friendly chemical manufacturing processes.<sup>15</sup> Very recently, we reported a silica-supported palladium-catalyzed Sonogashira coupling reaction and a silica-supported copper(II)-catalyzed Ullmann diaryl etherification.<sup>16</sup>

Although organic azides are generally safe compounds, those of low molecular weight can be unstable and, therefore, difficult to handle.<sup>17</sup> This is especially true for small molecules with several azide functionalities that would be of much interest for the generation of polyvalent structures. Thus, a method that avoids isolation of organic azides is desirable. In situ generation of organic azides from suitable precursors followed by addition of alkyne in one pot to form the corresponding 1,2,3-triazoles would avoid the difficulties associated with the explosive nature of the azides. Maksikova described an in situ formation of 1,2,3-triazoles from alkyl halides, alkynes, and sodium azide.<sup>18</sup> This method requires the reagents to be heated at high temperatures for extended periods of time, resulting in a mixture of regioisomers and giving low yields. Recently, Fokin demonstrated a very effective one-pot preparation of 1,4-disubstituted 1,2,3-triazoles from a variety of readily available aromatic and aliphatic halides catalyzed by a combination of copper(I) and L-proline without isolation of potentially unstable organic azide intermediates.<sup>19,20</sup> At the same time, Eycken also found that microwave irradiation could accelerate the one-pot reaction, and a series of 1,4-disubstituted 1,2,3-triazoles were generated from the corresponding alkyl halides, sodium azide, and alkynes in the presence of copper(0) and copper(II) sulfate.<sup>20</sup> Kacprzak recently developed an efficient one-pot method for the synthesis of 1,4-disubstituted 1,2,3-triazoles from benzyl or alkyl halides, sodium azide, and alkynes in the presence of copper(I) in N,N-dimethylformamide.21

SYNTHESIS 2008, No. 3, pp 0363–0368 Advanced online publication: 10.01.2008 DOI: 10.1055/s-2008-1032037; Art ID: F16507SS © Georg Thieme Verlag Stuttgart · New York

Here we wish to report an efficient, safe, and green onepot synthesis of 1,4-disubstituted 1,2,3-triazoles from benzyl and alkyl halides, sodium azide, and alkynes in ethanol catalyzed by silica-supported copper(I) without any additives. The reactions proceeded smoothly to generate the corresponding 1,4-disubstituted 1,2,3-triazole derivatives in high yields. It is important to note that the silica-supported copper catalyst could be recovered and recycled by a simple filtration of the reaction solution. It could be reused for ten consecutive trials without significant loss of activity.

The copper catalysts immobilized on organic–inorganic hybrid materials were readily prepared in two-step procedures (Scheme 1). The silica gel (100–200 mesh, Aldrich) was treated with (3-aminopropyl)triethoxysilane or {3-[(2-aminoethyl)amino]propyl}triethoxysilane in dry toluene at 120 °C for 24 hours to afford 3-aminopropyl- or 3-[(2-aminoethyl)amino]propyl-functionalized silica gel (Silica-APTS or Silica-AAPTS, respectively; Scheme 1). The organic–inorganic hybrid materials were then treated with copper(I) iodide in *N*,*N*-dimethylformamide at room temperature for four hours to generate the silica-supported copper(I) catalysts **1** and **2** (Scheme 1).

The infrared absorption bands of 3-aminopropyl-functionalized silica gel (Silica-APTS) and 3-[(2-aminoethyl)amino]propyl-functionalized silica gel (Silica-AAPTS) were compared with those of their respective copper complexes, namely copper(I) catalysts 1 and 2 (Table 1). The wave number at which  $v_{Si-O}$  appears in the spectra of copper(I) catalysts 1 and 2 was lower than that in the spectra of the corresponding Silica-APTS and Silica-AAPTS, respectively. This is probably the coordination effect of copper(I) with the monodentate and bidentate ligands 3aminopropyl and 3-[(2-aminoethyl)amino]propyl. The elemental analysis data given in Table 1 shows that for Silica-APTS and Silica-AAPTS the loading could be readily quantified by CHN microanalysis, and was found on the basis of the nitrogen percentage to be 0.935 mmol/g of 3aminopropyl and 0.918 mmol/g of 3-[(2-aminoethyl)amino]propyl. The copper content of copper(I) catalysts 1 and

 
 Table 1
 IR and Microanalysis of Functionalized Silica and Functionalized-Silica-Immobilized Copper Catalysts

Sample	FT-IR (KBr, cm <sup>-1</sup> )		Microanalysis (wt%)		
	$\nu_{Si\!-\!O}$	$\nu_{C\!-\!H}$	C <sup>a</sup>	$\mathbf{N}^{\mathrm{a}}$	Cu <sup>b</sup>
Silica-APTS	1074	2926	3.85	1.31	_
Cu(I) cat. 1	1049	2918	3.43	1.18	2.76
Silica-AAPTS	1088	2941	6.56	2.57	-
Cu(I) cat. 2	1053	2937	6.05	2.32	5.28

<sup>a</sup> CHN microanalysis results.

<sup>b</sup> AAS analysis results.

**2** was found to be 2.76 and 5.28 wt%, respectively, on the basis of atomic absorption spectroscopy analysis.

For our initial screening experiments, the 1,3-dipolar cycloaddition reactions between benzyl chloride, sodium azide, and phenylacetylene was chosen as the model reaction (Table 2). We observed that when the reaction of the alkyne, alkyl halide, and sodium azide, in a 1:1:1 molar ratio, was catalyzed by the copper(I) catalyst 2 (5 mol%)in ethanol, stirring at 78 °C for 24 hours, the corresponding 1,4-disubstituted 1,2,3-triazole was obtained in 82% yield (Table 2, entry 3). Encouraged by this result, we continued our research to improve the yield of the product by the optimization of the reaction conditions. We examined the effect of the copper source on the one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles (Table 2, entries 1– 5). Copper(I) catalyst 1 prepared from copper(I) iodide was found to be the most effective one (Table 2, entry 2). This may be due the effect of the anion in silica-supported copper(I) catalysts on the catalytic activity. As a result, copper(I) catalyst 1 was used in the subsequent investigations because of its high efficiency, easy separation, and recyclability.

Then we turned our attention to investigating the effect of the solvent on the coupling reaction (Table 3). When the reactions were conducted in dimethyl sulfoxide and ethanol, the products were isolated in good to excellent yields



# Scheme 1



<sup>a</sup> Reagents and conditions: BnCl (0.50 mmol), PhC=CH (0.50 mmol), NaN<sub>3</sub> (0.50 mmol), Cu cat. (0.025 mmol Cu, 5 mol%), EtOH (2 mL), 78 °C, 24 h.

<sup>b</sup> Isolated yield.

<sup>c</sup> The silica-supported Cu(II) catalyst was prepared from Silica-APTS and Cu(OAc)<sub>2</sub>.

 
 Table 3
 Effect of Solvent on the One-Pot Synthesis of 1-Benzyl-4phenyl-1*H*-1,2,3-Triazole<sup>a</sup>

BnCl + NaN <sub>3</sub> +	PhC=CH (5 mol%) solvent	r I → Ph
Entry	Solvent/temperature (°C)	Yield <sup>b</sup> (%)
1	DMSO/100	80
2	EtOH/78	91
3	MeCN/81	58
4	dioxane/101	30
5	toluene/110	24

<sup>a</sup> Reagents and conditions: BnCl (0.50 mmol), PhC≡CH (0.50 mmol), NaN<sub>3</sub> (0.50 mmol), **1** (57.5 mg, 0.025 mmol Cu), EtOH (2 mL), 78 °C, 24 h.

<sup>b</sup> Isolated yield.

(80 and 91%, respectively; Table 3, entries 1 and 2). The use of acetonitrile, dioxane, and toluene as solvents led to slower reactions (Table 3, entries 3–5).

During the course of further optimization of the reaction conditions, it was found that when a 5 mol% loading of copper(I) catalyst **1** was used, the reactions were generally completed in a matter of hours, but the time, as expected, was inversely proportional to the temperature. A reaction temperature of 78 °C was found to be optimal. Thus, the optimal conditions for this reaction consist of the use of copper(I) catalyst **1** (5 mol%) in ethanol at 78 °C for 24 hours.

We investigated the reaction, using a variety of benzyland alkyl halides and alkynes as the substrates under the same conditions, and the results are summarized in Table 4. The corresponding 1,4-disubstituted 1,2,3-triazoles were isolated as regiospecific products in excellent yields under the present reaction conditions from the reactions of benzyl halides (BnBr, BnCl) with various terminal arylalkynes or aliphatic alkynes, including acetylenes with substituents containing functional groups, such as phenylacetylene, p-tolylacetylene, (p-chlorophenyl)acetylene, (p-bromophenyl)acetylene, dec-1-yne, oct-1-yne, or propargyl alcohol (Table 4, entries 1-8). Apart from benzyl halide derivatives, primary aliphatic bromides such as *n*-butyl bromide, *n*-hexyl bromide, *n*-octyl bromide, n-decyl bromide, and n-hexadecyl bromide also reacted with phenylacetylene and sodium azide under the standard reaction conditions to afford the corresponding 1,4-disubstituted 1,2,3-triazoles in good yields (Table 4, entries 9–13). As is evident from Table 4, electron-donating group (such as Me) or electron-withdrawing groups (such as  $NO_2$ ) and their location on the aromatic ring in substituted benzyl chlorides had little effect on the reaction (Table 4, entries 14 and 15). However, the reaction of aryl iodide, phenylacetylene, and sodium azide under the present reaction conditions gave the product in poor yield (Table 4, entry 16). Unfortunately, disubstituted acetylenes, such as diphenylacetylene, did not react with sodi-

**Table 4**One-Pot Synthesis of 1,4-Disubstituted 1,2,3-Triazolesfrom Alkyl Halides, Sodium Azide, and Alkynes<sup>a</sup>

R <sup>1</sup> X +	NaN₃ + R²C≡CH	1 (5 mol%) EtOH		<sup>2</sup>
Entry	$\mathbb{R}^1$	Х	R <sup>2</sup>	Yield <sup>b</sup> (%)
1	Bn	Cl	Ph	91
2	Bn	Br	Ph	92
3	Bn	Cl	Tol	85
4	Bn	Cl	p-ClC <sub>6</sub> H <sub>4</sub>	95
5	Bn	Cl	p-BrC <sub>6</sub> H <sub>4</sub>	90
6	Bn	Cl	$n - C_8 H_{17}$	90
7	Bn	Cl	<i>n</i> -C <sub>6</sub> H <sub>13</sub>	84
8	Bn	Br	CH <sub>2</sub> OH	77
9	<i>n</i> -Bu	Br	Ph	95
10	<i>n</i> -C <sub>6</sub> H <sub>13</sub>	Br	Ph	93
11	$n-C_8H_{17}$	Br	Ph	82
12	$n-C_{10}H_{21}$	Br	Ph	84
13	<i>n</i> -C <sub>16</sub> H <sub>33</sub>	Br	Ph	88
14	CH <sub>2</sub> Tol	Cl	Ph	89
15	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub>	Cl	Ph	90
16	Ph	Ι	Ph	42

 $^a$  Reagents and conditions:  $R^1X$  (0.50 mmol),  $R^2C\equiv CH$  (0.50 mmol),  $NaN_3$  (0.50 mmol), 1 (57.5 mg, 0.025 mmol Cu), EtOH (2 mL), 78 °C, 24 h.

<sup>b</sup> Isolated yield.

The recyclability of the silica-supported copper(I) catalyst 1 was also surveyed (Table 5). After a reaction, the solution was vacuum-filtered through a sintered glass funnel and washed successively with dichloromethane (1 mL), diethyl ether (1 mL), ethanol (1 mL), and hexane (1 mL). After being dried, the catalyst can be reused directly without further purification. Copper(I) catalyst 1 can be recovered, recycled, and reused for 10 consecutive trials without loss of activity (Table 5). Moreover, copper leaching in copper(I) catalyst 1 was also determined, and inductively coupled plasma analysis of the clear filtrates indicated that the copper content was <0.21 ppm.

 
 Table 5
 Use of Recovered Copper(I) Catalyst 1 in Successive
 **Trials**<sup>a</sup>

-N

BnCl + NaN <sub>3</sub> + PhC $\equiv$ CH $\xrightarrow{1 (5 \text{ mol}\%)}_{\text{EtOH}} \xrightarrow{N = N}_{N}$ Ph						
Entry <sup>b</sup>	Yield <sup>c</sup> (%)	Entry <sup>b</sup>	Yield <sup>c</sup> (%)			
1	91	6	93			
2	87	7	90			
3	94	8	87			
4	81	9	81			
5	86	10	84			

<sup>a</sup> Reagents and conditions: BnCl (0.50 mmol), PhC=CH (0.50 mmol), NaN<sub>3</sub> (0.50 mmol), 1 (57.5 mg, 0.025 mmol Cu), EtOH (2 mL), 78 °C, 24 h.

<sup>b</sup> The entry number corresponds to the trial number.

<sup>c</sup> Isolated yield.

In conclusion, a safe and efficient three-component reaction for the regioselective generation of 1,4-disubstituted 1,2,3-triazoles has been developed. The method avoids isolation and handling of potentially unstable small organic azides and provides triazole products in pure form. Furthermore, copper(I) catalyst 1 can be recovered and recycled by simple filtration of the reaction solution and reused for ten consecutive trials without decrease in activity.

Melting points were recorded on a WRS-2B melting point apparatus and are uncorrected. All <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a 300-MHz Bruker T-NMR spectrometer. Chemical shifts  $\delta$  are reported relative to TMS as internal standard. IR spectra were obtained on a Nicolet NEXUS 470 spectrophotometer. The CHN analysis was performed on a Vario El III elementary analyzer. Products were purified by flash chromatography (silica gel, 230-400 mesh). The chemicals were purchased from commercial suppliers (Aldrich, USA and Shanghai Chemical Company, China) and used without further purification.

## Copper(I) Catalyst 1

Activation of silica gel: Silica gel (100–200 mesh, Aldrich; 10.00 g) was introduced into a round-bottomed flask equipped with a reflux condenser. Concd H<sub>2</sub>SO<sub>4</sub> (80 mL) and HNO<sub>3</sub> (15 mL) were added and the mixture was heated in an oil bath at 140 °C for 24 h. The soln was filtered and the white powder was washed with distilled H<sub>2</sub>O until a neutral pH was attained. The solid was again washed consecutively with acetone (30 mL), MeOH (30 mL), and CH<sub>2</sub>Cl<sub>2</sub> (30 mL), and dried under vacuum at 150 °C for 48 h.

Preparation of Silica-APTS: Anhyd toluene (20 mL), the activated silica obtained from the above procedure (3.00 g), and (3-aminopropyl)triethoxysilane (APTS) (10 mL) were introduced successively into a 50-mL round-bottomed flask. The mixture was refluxed for 24 h, and then filtered. The solid was washed consecutively with acetone (10 mL) and CH<sub>2</sub>Cl<sub>2</sub> (10 mL), and dried under reduced pressure at 60 °C; yield (Silica-APTS): 3.26 g.

Loading with Cu(I): In a small Schlenk tube, Silica-APTS [1.00 g,  $0.935 \text{ mmol} (CH_2)_3 NH_2/g]$  was mixed with CuI (0.096 g, 0.5 mmol) in DMF (5 mL). The mixture was stirred for 4 h under a N<sub>2</sub> atmosphere at r.t. The soln was filtered and the solid was washed consecutively with acetone (5 mL) and MeOH (5 mL), and the solid was dried under reduced pressure at r.t. for 16 h; this gave copper(I) catalyst 1 as a pale blue powder; yield:1.03 g.

# Copper(I) Catalyst 2

In a 50-mL round-bottomed flask were introduced successively anhyd toluene (20 mL), activated silica (3.00 g) and {3-[(2-aminoethyl)amino]propyl}triethoxysilane (AAPTS) (10 mL). The soln was refluxed for 24 h. The soln was filtered and the solid was washed consecutively with acetone (10 mL) and CH<sub>2</sub>Cl<sub>2</sub> (10 mL), and dried under reduced pressure at 60 °C; yield (Silica-APPTS): 3.38 g.

In a small Schlenk tube, the Silica-AAPTS [1.00 g, 0.918 mmol (CH<sub>2</sub>)<sub>3</sub>NH(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub>/g] was mixed with CuI (0.191 g, 1.0 mmol) in DMF (5 mL). The mixture was stirred under a N<sub>2</sub> atmosphere at r.t. for 4 h. The soln was filtered and the solid was washed consecutively with acetone (5 mL) and MeOH (5 mL), and the solid was dried under reduced pressure at r.t. for 16 h; this gave 2 as a pale blue powder; yield: 1.06 g.

## One-Pot Synthesis of 1,2,3-Triazoles; General Procedure

Under an atmosphere of N2, a two-necked round-bottomed flask containing a stirrer bar was charged with organic halide R<sup>1</sup>X (1.0 mmol), NaN<sub>3</sub> (1.0 mmol), terminal alkyne R<sup>2</sup>C=CH (1.0 mmol), copper(I) catalyst 1 (115 mg, 0.05 mmol), and EtOH (3.0 mL). The mixture was heated and stirred at 78 °C for 24 h. After cooling to r.t., the reaction mixture was vacuum-filtered through a sinteredglass funnel and washed with CH2Cl2 (5 mL). The combined organic layers were dried (MgSO<sub>4</sub>) and evaporated under reduced pressure. The residue was finally purified by flash chromatography (silica gel) to give the desired product.

## **Recycling of the Silica-Supported Copper Catalyst**

After the reaction had been carried out, the mixture (containing ca. 1 g catalyst 1) was vacuum-filtered onto a sintered-glass funnel, and the residue was consecutively washed with CH<sub>2</sub>Cl<sub>2</sub> (5 mL), Et<sub>2</sub>O (5 mL), EtOH (5 mL), and hexane (5 mL). After the catalyst had been dried in an oven at 60 °C for 4 h, it could be reused directly without further purification.

# 1-Benzyl-4-phenyl-1H-1,2,3-triazole<sup>20</sup>

IR (KBr): 1494, 1469, 1450, 1361, 1224, 1140, 1076, 1046, 972, 807, 769, 731 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 5.58 (s, 2 H), 7.42–7.75 (m, 8 H), 7.67 (s, 1 H), 7.82 (d, J = 7.1 Hz, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 53.66, 119.10, 124.74, 125.47, 126.08, 129.97, 134.17, 147.64.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.35 (s, 3 H), 5.55 (s, 2 H), 7.18–7.21 (m, 2 H), 7.26–7.38 (m, 5 H), 7.64 (s, 1 H), 7.70 (d, *J* = 7.8 Hz, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 21.20, 54.16, 119.20, 125.55, 126.04, 127.50, 128.67, 129.42, 134.62, 137.99, 148.15.

Anal. Calcd for  $C_{16}H_{15}N_3$ : C, 77.08; H, 6.06; N, 16.85. Found: C, 76.90; H, 5.93; N, 17.17.

## 1-Benzyl-4-(4-chlorophenyl)-1H-1,2,3-triazole

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 5.55 (s, 2 H), 7.28–7.33 (m, 2 H), 7.35–7.38 (m, 5 H), 7.67 (s, 1 H), 7.72 (d, *J* = 9.0 Hz, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 54.24, 119.62, 126.87, 128.03, 128.92, 129.11, 133.84, 134.37, 146.95.

Anal. Calcd for  $C_{15}H_{12}N_3Cl: C, 66.79; H, 4.48; N, 15.58$ . Found: C, 66.68; H, 4.42; N, 15.72.

### 1-Benzyl-4-(4-bromophenyl)-1H-1,2,3-triazole

<sup>1</sup>H NMR (300 MHz,  $CDCl_3$ ):  $\delta = 5.58$  (s, 2 H), 7.26 (s, 1 H), 7.31–7.33 (m, 2 H), 7.40–7.41 (m, 2 H), 7.51–7.54 (m, 2 H), 7.66–7.69 (m, 3 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 54.20, 119.42, 126.07, 128.17, 128.97, 129.41, 133.95, 134.85, 147.11.

Anal. Calcd for  $C_{15}H_{21}N_3Br: C, 57.34; H, 3.85; N, 13.37$ . Found: C, 57.42; H, 3.73; N, 13.25.

## 1-Benzyl-4-octyl-1H-1,2,3-triazole

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.85$  (t, J = 6.5 Hz, 3 H), 1.23–1.27 (m, 10 H), 1.59–1.63 (m, 2 H), 2.66 (t, J = 7.7 Hz, 2 H), 5.46 (s, 2 H), 7.18–7.34 (m, 6 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 14.00, 22.55, 25.61, 29.09, 31.72, 53.86, 120.45, 127.83, 128.92, 134.91, 148.83.

Anal. Calcd for  $C_{10}H_{11}N_3O$ : C, 75.23; H, 9.28; N, 15.48. Found: C, 75.11; H, 9.11; N, 15.78.

## 1-Benzyl-4-hexyl-1H-1,2,3-triazole

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.86$  (t, J = 6.6 Hz, 3 H), 1.28–1.32 (m, 6 H), 1.58–1.68 (m, 2 H), 2.68 (t, J = 7.7 Hz, 2 H), 5.46 (s, 2 H), 7.18–7.37 (m, 6 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 14.00, 22.49, 25.67, 28.86, 31.48, 53.91, 120.42, 127.88, 128.98, 134.95, 148.92.

Anal. Calcd for  $C_{15}H_{21}N_3$ : C, 74.03; H, 8.70; N, 17.27. Found: C, 73.90; H, 8.62; N, 17.48.

# (1-Benzyl-1H-1,2,3-triazol-4-yl)methanol

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.10 (br s, 1 H), 4.71 (s, 2 H), 5.46 (s, 2 H), 7.20–7.39 (m, 6 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 52.21, 55.09, 122.15, 127.31, 128.84, 129.58, 135.67, 146.39.

Anal. Calcd for  $C_{10}H_{11}N_3O$ : C, 63.48; H, 5.86; N, 22.21. Found: C, 63.32; H, 5.78; N, 22.38.

### 1-Butyl-4-phenyl-1*H*-1,2,3-triazole

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.99$  (t, J = 7.4 Hz, 3 H), 1.34– 1.41 (m, 2 H), 1.87–1.96 (m, 2 H), 4.40 (t, J = 6.5 Hz, 2 H), 7.26– 7.34 (m, 1 H), 7.39–7.44 (m, 2 H), 7.75 (s, 1 H), 7.82 (d, J = 3.6 Hz, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 13.39, 19.24, 31.80, 49.78, 119.08, 125.56, 127.97, 128.59, 128.72, 130.63, 147.59.

Anal. Calcd for C<sub>12</sub>H<sub>15</sub>N<sub>3</sub>: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.80; H, 7.39; N, 20.81.

## 1-Hexyl-4-phenyl-1H-1,2,3-triazole

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.86$  (t, J = 6.8 Hz, 3 H), 1.25–1.37 (m, 6 H), 1.88–1.98 (m, 2 H), 4.38 (t, J = 7.2 Hz, 2 H), 7.26–7.35 (m, 1 H), 7.39–7.44 (m, 2 H), 7.75 (s, 1 H), 7.84 (t, J = 3.6 Hz, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 13.85, 22.32, 26.07, 30.22, 31.06, 50.44, 119.49, 125.61, 128.00, 130.54, 147.62.

Anal. Calcd for  $C_{14}H_{19}N_3$ : C, 73.33; H, 8.35; N, 18.32. Found: C, 73.15; H, 8.51; N, 18.34.

## 1-Octyl-4-phenyl-1H-1,2,3-triazole<sup>21</sup>

IR (KBr): 2954, 2918, 2847, 1465, 1216, 1079, 762, 696 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.86$  (t, J = 6.8 Hz, 3 H), 1.25– 1.33 (m, 10 H), 1.88–1.97 (m, 2 H), 4.37 (t, J = 7.2 Hz, 2 H), 7.26– 7.34 (m, 1 H), 7.38–7.44 (m, 2 H), 7.74 (s, 1 H), 7.83 (t, J = 4.4 Hz, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 14.00, 22.52, 26.42, 28.90, 30.28, 31.63, 50.39, 119.39, 125.62, 128.02, 130.60, 147.58.

## 1-Decyl-4-phenyl-1H-1,2,3-triazole

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.86 (t, *J* = 6.8 Hz, 3 H), 1.24– 1.32 (m, 14 H), 1.87–1.94 (m, 2 H), 4.36 (t, *J* = 7.2 Hz, 2 H), 7.26– 7.34 (m, 1 H), 7.38–7.43 (m, 2 H), 7.76 (s, 1 H), 7.80–7.84 (m, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 14.18, 22.71, 26.61, 28.99, 30.58, 31.70, 50.51, 119.42, 125.60, 128.72, 130.66, 147.64.

Anal. Calcd for  $C_{18}H_{27}N_3$ : C, 75.74; H, 9.53; N, 14.72. Found: C, 75.89; H, 9.38; N, 14.73.

## 1-(4-Methylbenzyl)-4-phenyl-1H-1,2,3-triazole

<sup>1</sup>H NMR (300 MHz,  $CDCl_3$ ):  $\delta = 2.35$  (s, 3 H,), 5.50 (s, 2 H), 7.18–721 (m, 4 H), 7.30–741 (m, 3 H), 7.66 (s, 1 H), 7.79–781 (m, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 21.06, 53.86, 119.36, 125.53, 127.98, 128.66, 129.66, 131.54, 138.55, 147.96.

Anal. Calcd for  $C_{16}H_{15}N_3$ : C, 77.08; H, 6.06; N, 16.85. Found: C, 76.87; H, 6.12; N, 17.01.

# 1-(4-Nitrobenzyl)-4-phenyl-1H-1,2,3-triazole<sup>20</sup>

IR (KBr): 1608, 1601, 1581, 1518, 1465, 1442, 1426, 1351, 1223, 1111, 1079, 1046, 1016, 862, 802, 764 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 5.62 (s, 2 H), 7.18–7.38 (m, 5 H), 7.67–7.75 (m, 3 H), 8.15–8.18 (m, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 53.61, 119.89, 123.92, 124.37, 125.67, 128.59, 128.71, 130.09, 141.64, 142.59, 148.02.

### 1,4-Diphenyl-1,2,3-triazole<sup>22</sup>

IR (KBr): 3123, 3059, 2374, 1596, 1504, 1481 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.26–7.32 (m, 1 H), 7.38–7.40 (m, 3 H), 7.47 (t, *J* = 5.8 Hz, 2 H), 7.74 (d, *J* = 6.2 Hz, 2 H), 7.91 (d, *J* = 6.0 Hz, 2 H), 8.12 (s, 1 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 117.8, 120.1, 125.2, 128.9, 127.9, 128.4, 129.7, 130.9, 137.5, 148.7.

## Acknowledgments

We gratefully acknowledge financial support from the National Natural Science Foundation of China.

# References

- (a) Huisgen, R.; Szeimies, G.; Moebius, L. Chem. Ber. 1967, 100, 2494. (b) Huisgen, R. In 1,3-Dipolar Cycloaddition Chemistry; Padwa, A., Ed.; Wiley: New York, 1984, 1–176.
   (c) Huisgen, R. Pure Appl. Chem. 1989, 61, 613. (d) Gil, M. V.; Arevalo, M. J.; Lopez, O. Synthesis 2007, 1589.
- (2) For reviews, see: (a) Fan, W. Q.; Katritzky, A. R. In Comprehensive Heterocyclic Chemistry II, Vol. 4; Katritzky, A. R.; Rees, C. W.; Scriven, C. W. V., Eds.; Elsevier: Oxford, 1996, 1–126. (b) Dehne, H. In Houben– Weyl, Vol. E8d; Schaumann, E., Ed.; Thieme: Stuttgart, 1994, 305–405. (c) Abu-Orabi, S. T.; Alfah, M. A.; Jibril, I.; Marii, F. M.; Ali, A. A. S. J. Heterocycl. Chem. 1989, 26, 1461.
- (3) (a) Lewis, W. G.; Green, L. G.; Grynszpan, F.; Radic, Z.; Carlier, P. R.; Taylor, P.; Finn, M. G.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 1053. (b) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2001**, *40*, 2004.
- (4) (a) Rostovtsev, V. V.; Green, L. G.; Folkin, V. V.; Sharpless,
  K. B. Angew. Chem. Int. Ed. 2002, 41, 2596. (b) Tornoe, C.
  W.; Christensen, C.; Meldal, M. J. Org. Chem. 2002, 67, 3057.
- (5) For a review of reactions of ascorbic acid with transition metals, see: (a) Davies, M. B. *Polyhedron* **1992**, *11*, 285; and references cited therein . The redox properties of ascorbic acid are summarized in: (b) Creutz, C. *Inorg. Chem.* **1981**, *20*, 4449.
- (6) (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) Himo, F.; Lovell, T.; Hilgraf, R.; Rostovtsev, V. V.; Noodleman, L.; Sharpless, K. B.; Fokin, V. V. J. Am. Chem. Soc. 2005, 127, 210.
- (7) (a) Pachón, L. D.; Maarseveen, J. H.; Rothenberg, G. Adv. Synth. Catal. 2005, 347, 811. (b) Orgueira, H. A.; Fokas, D.; Isome, Y.; Chan, P. C. M.; Baldino, C. M. Tetrahedron Lett. 2005, 46, 2911.
- (8) (a) Wu, P.; Alina, K. F.; Anne, K. N.; Craig, J. H.; Scheel, A.; Voit, B.; Pyun, J.; Jean, M. J. F.; Sharpless, K. B.; Fokin, V. V. Angew. Chem. Int. Ed. 2004, 43, 3928. (b) Binder, W. H.; Kluger, C. Macromolecules 2004, 37, 9321.
- (9) Mantovani, G.; Ladmiral, V.; Tao, L.; Haddleton, D. M. Chem. Commun. 2005, 2089.
- (10) Speers, A. E.; Cravatt, B. F. Chem. Biol. 2004, 11, 535.

- (11) (a) Link, A. J.; Tirrell, D. A. J. Am. Chem. Soc. 2003, 125, 11164. (b) Chan, T. R.; Hilgraf, R.; Sharpless, K. B.; Fokin, V. V. Org. Lett. 2004, 6, 2853.
- (12) Zhang, L.; Chen, X.; Xue, P.; Sun, H. H. Y.; Williams, I. D.; Sharpless, K. B.; Fokin, V. V.; Jia, G. J. Am. Chem. Soc. 2005, 127, 15998.
- (13) (a) Kirschnig, A.; Monenschein, H.; Wittenberg, R. Angew. Chem. Int. Ed. 2001, 40, 650. (b) Clapham, B.; Reger, T. S.; Janda, K. D. Tetrahedron 2001, 57, 4637.
- (14) (a) Uozumi, Y.; Nakai, Y. *Org. Lett.* 2002, *4*, 2997.
  (b) Gonthier, E.; Breinbauer, R. *Synlett* 2003, 1049.
  (c) Tyrrell, E.; Al-Saardi, A.; Millet, J. *Synlett* 2005, 487.
- (15) (a) Clark, J. H. Chemistry of Waste Minimisation; Chapman and Hall: Glasgow, 1995. (b) Clark, J. H.; Macquarrie, D. J. Chem. Commun. 1998, 853. (c) Price, P. M.; Clark, J. H.; Macquarrie, D. J. J. Chem. Soc., Dalton Trans. 2000, 101. (d) Djakovitch, L.; Rollet, P. Tetrahedron Lett. 2004, 45, 1367. (e) Djakovitch, L.; Rollet, P. Adv. Synth. Catal. 2004, 346, 1782. For recent applications of transition metals immobilized on mesoporous MCM-41 or silica in organic reactions, see: (f) Breynaert, E.; Hermans, I.; Lambie, B.; Maes, G.; Peeters, J.; Maes, A.; Jacobs, P. Angew. Chem. Int. Ed. 2006, 45, 7584. (g) Karimi, B.; Ghoreishi-Nezhad, M.; Clark, J. H. Org. Lett. 2005, 7, 625. (h) Hamza, K.; Abu-Reziq, R.; Avnir, D.; Blum, J. Org. Lett. 2004, 6, 925. (i) Heckel, A.; Seebach, D. Angew. Chem. Int. Ed. 2000, 39, 163. (j) Gelman, F.; Blum, J.; Avnir, D. J. Am. Chem. Soc. 2000, 122, 11999. (k) Crudden, C. M.; Sateesh, M.; Lewis, R. J. Am. Chem. Soc. 2005, 127, 10045. (1) Baleizão, C.; Corma, A.; García, H.; Leyva, A. Chem. Commun. 2003, 606. (m) Mehnert, C. P.; Ying, J. Y. Chem. Commun. 1997, 2215.
- (16) (a) Li, P.; Wang, L. Adv. Synth. Catal. 2006, 348, 681.
  (b) Miao, T.; Wang, L. Tetrahedron Lett. 2007, 48, 95.
  (c) Zhang, L.; Li, P.; Wang, L. Lett. Org. Chem. 2006, 3, 282. (d) Li, P.; Wang, L. Tetrahedron 2007, 63, 5455.
  (e) Li, H.; Wang, L.; Li, P. Synthesis 2007, 1635.
- (17) Scriven, E. F. V.; Turnbull, K. Chem. Rev. 1988, 88, 297.
- (18) Maksikova, A. V.; Serebryakova, E. S.; Tikhonova, L. G.; Vereshagin, L. I. *Chem. Heterocycl. Compd.* **1980**, 1284.
- (19) Feldman, A. K.; Colasson, B.; Fokin, V. V. Org. Lett. 2004, 6, 3897.
- (20) Appukkuttan, P.; Dehaen, W.; Fokin, V. V.; Eycken, E. V. Org. Lett. 2004, 6, 4223.
- (21) Kacprzak, K. Synlett 2005, 943.
- (22) Barral, K.; Moorhouse, A. D.; Moses, J. E. Org. Lett. 2007, 9, 1809.