

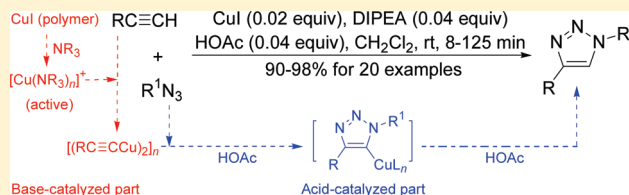
Acid–Base Jointly Promoted Copper(I)-Catalyzed Azide–Alkyne Cycloaddition

Changwei Shao, Xinyan Wang,* Qun Zhang, Sheng Luo, Jichen Zhao, and Yuefei Hu*

Department of Chemistry, Tsinghua University, Beijing 100084, P. R. China

Supporting Information

ABSTRACT: In this novel acid–base jointly promoted CuAAC, the combination of CuI/DIPEA/HOAc was developed as a highly efficient catalytic system. The functions of DIPEA and HOAc have been assigned, and HOAc was recognized to accelerate the conversions of the C–Cu bond-containing intermediates and buffer the basicity of DIPEA. As a result, all drawbacks occurring in the popular catalytic system CuI/NR₃ were overcome easily.



Copper(I)-catalyzed azide–alkyne cycloaddition (CuAAC) has been a prime example of “click chemistry” in the literature¹ since it was reported independently by the groups of Sharpless² and Meldal³ in 2002. Much progress has been made in recent years toward better understanding the mechanism of CuAAC. As shown in Figure 1, a three-step catalytic cycle proposed by Sharpless has been widely accepted.² The copper(I) source has been recognized as one of major factors to influence the efficiency of CuAAC.^{1e,g,h}

It is well-known that CuI is the most often used copper(I) source in catalytic organic reactions, and it also often was used in CuAAC. However, CuI alone was an inefficient catalyst for CuAAC. In most cases, it was used as a combination of CuI/NR₃,⁴ in which the tertiary amine was an essential additive.^{5,6} This results in CuI naturally occurring in a stable polymeric structure that then must be dissociated by amines to yield the “active” Cu(I) species for the formation of copper(I) acetylide (2).

Since the tertiary amine additive functions as both a ligand and a base, it also promotes the coupling of copper(I) acetylide (2) and the substitution of 5-cuprated 1,2,3-triazole (4) to yield undesired byproduct. As shown in Figure 2, Sharpless² has observed that the byproduct diacetylenes, bis-triazoles, and 5-hydroxytriazoles were formed when NEt₃ or DIPEA was used as an additive. Other 5-substituted byproducts⁷ were also reported recently by using different amine additives. This may be the reason that the combination of CuSO₄/NaAsc (used in aqueous *t*-BuOH)² is the most common catalytic system for CuAAC rather than the combination of CuI/NR₃ to date. However, CuI/NR₃ is highly beneficial to be used in nonaqueous or nonprotonic solvents, which is practically important to a range of substrates because they may not tolerate water or protonic solvents. Therefore, CuI/NR₃ is still widely employed in CuAAC despite using a large amount of CuI (up to 2 equiv) and NR₃ (up to 20 equiv) in many cases.⁶

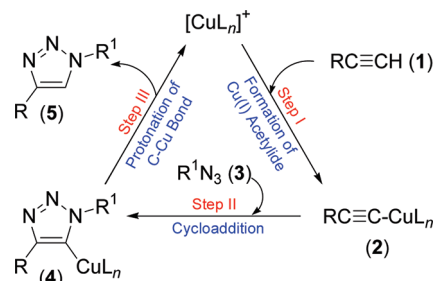


Figure 1. Three-step catalytic cycle for CuAAC.

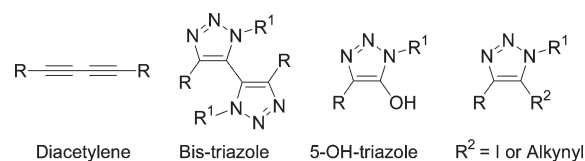


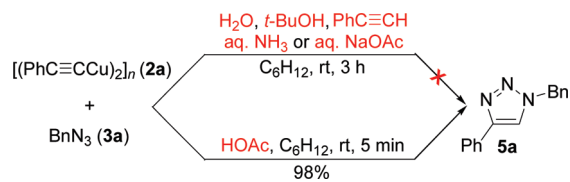
Figure 2. Byproduct formed from the C–Cu bond-containing intermediates.

By carefully monitoring the CuAAC reactions catalyzed by CuI/DIPEA, we observed two phenomena: (a) the intermediate 2 usually was formed very fast, but its conversion into product 5 often proceeded slowly; (b) the amounts of byproduct were increased by prolonging the reaction time. These phenomena clearly indicated that the byproducts were caused by inefficient cycloaddition of 2 and protonation of 4. Therefore, a good strategy to overcome these drawbacks may be to accelerate the conversions of the C–Cu bond-containing intermediates 2 and 4. However, much less attention has been focused on these

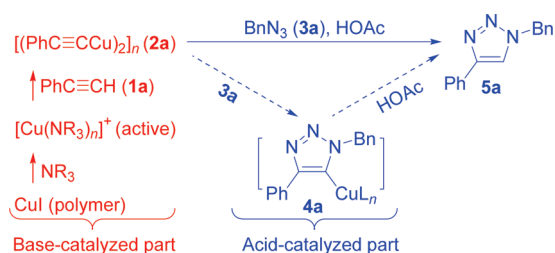
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Scheme 1



Scheme 2



conversions and their influence on the efficiency of CuAAC in literature.

In 2007, Straub⁸ reported that the C–Cu bond in intermediate **4** could be protonated by HOAc within a few minutes. Recently, we^{9,10} reported a highly efficient copper(I) acetate catalyzed CuAAC in which both cycloaddition of **2** and protonation of **4** could be promoted significantly by the in situ formed HOAc. As shown in Scheme 1, the triazole **5a** was obtained in 98% yield within 5 min when the mixture of phenylethyne copper(I) (**2a**) and benzyl azide (**3a**) was treated with HOAc. This was not the case when using other proton sources, such as H₂O, *t*-BuOH, PhC≡CH, ammonia, or aqueous solution of NaOAc.

The results from Straub's work and Scheme 1 strongly imply that CuI/NR₃-catalyzed CuAAC may be enhanced by simple addition of HOAc. Thus, a novel acid–base jointly promoted CuAAC was proposed as shown in Scheme 2, in which NR₃ serves to dissociate the polymeric structure of CuI and accelerate the formation of **2a**. Then, **2a** will be quickly converted into **5a** by our HOAc-promoted CuAAC pathway.^{9,10}

To confirm our hypothesis, a group of control experiments were made as shown in Table 1. As was expected, no desired product **5a** was detected without CuI when the mixture of phenylethyne (**1a**, 1.0 equiv) and benzyl azide (**3a**, 1.05 equiv) in toluene was stirred for 3 h (entry 1). Upon addition of CuI, no **5a** was detected either (entry 2). Upon additions of CuI and HOAc, the same disappointing result was obtained (entry 3). However, when CuI and DIPEA were added into the reaction, the substrates were exhausted in 2.5 h to give **5a** in 84% yield (entry 4). To our delight, in the presence of CuI, DIPEA, and HOAc, **5a** was obtained in 96% yield within 3 min (entry 5).

Then, the neat conditions were used to quickly scan the effect of the amount of CuI and the ratio of CuI/DIPEA/HOAc on the reaction efficiency. As shown in Table 2, the amounts of CuI could be reduced significantly under the neat conditions. In entry 1, the cycloaddition of **1a** and **3a** was finished in 80 min by using 0.01 equiv of CuI and 0.1 equiv of DIPEA. However, in the presence of 0.1 equiv of HOAc, the same reaction was finished within 1 min (entry 2). An excellent result was obtained even by using 0.005, 0.03, and 0.03 equiv of CuI, DIPEA, and HOAc,

Table 1. Effects of DIPEA and HOAc on CuAAC^a

1a + 3a $\xrightarrow[\text{trace-96\%}]{\text{CuI, DIPEA, HOAc, Toluene, rt, 3-180 min}}$ 5a					
entry	CuI (equiv)	DIPEA (equiv)	HOAc (equiv)	time (min)	yield of 5a ^b (%)
1	0	0	0	180	trace
2	0.1	0	0	180	trace
3	0.1	0	2.0	180	trace
4	0.1	2.0	0	150	84
5	0.1	2.0	2.0	3	96

^a A mixture of **1a** (2 mmol) and **3a** (2.1 mmol) in toluene (2 mL) was tested. ^b Isolated yields.

Table 2. Effects of the Ratios of DIPEA and HOAc on CuAAC^a

1a + 3a $\xrightarrow[\text{89-97\%}]{\text{CuI, DIPEA, HOAc, neat, rt, 1-120 min}}$ 5a					
entry	CuI (equiv)	DIPEA (equiv)	HOAc (equiv)	time (min)	yield of 5a ^b (%)
1	0.01	0.1	0	80	89
2	0.01	0.1	0.1	1	94
3	0.005	0.05	0.05	5	95
4	0.005	0.03	0.03	6	96
5	0.005	0.03	0.005	27	95
6	0.005	0.03	0.01	18	96
7	0.005	0.03	0.05	11	96
8	0.005	0.03	0.1	14	97
9	0.005	0.01	0.03	120	92
10	0.005	0.05	0.03	4	96
11	0.005	0.1	0.03	2.5	96

^a A mixture of **1a** (2 mmol) and **3a** (2.1 mmol) was tested. ^b Isolated yields.

respectively (entry 4). The results in entries 4–8 indicated that the 1:1 ratio of DIPEA and HOAc gave the best results by fixing the amount of DIPEA at 0.03 equiv. The results in entries 9–11 indicated that the higher ratios of DIPEA and HOAc gave better results by fixing the amount of HOAc at 0.03 equiv.

To further understand the relationship between structure and promotion activity, different amines and carboxylic acids were tested. As shown in Table 3, tertiary amine gave better results than secondary and primary amines (entries 1–3). Although HOAc, *t*-BuCO₂H, and PhCO₂H (entries 4–6) showed similar promotion activity, TFA and TsOH had lower activity (entries 7 and 8) possibly because they are strong acids. Proline and pyridine-2-carboxylic acid (entries 9 and 10) gave dissatisfied results even though they have both amine and carboxylic acid groups, which may be caused by their tight coordination with Cu(I) ion.^{10,11}

For safety reasons, the catalytic behavior of CuI/DIPEA/HOAc in solvent was tested since CuAAC is a highly exothermic reaction. As shown in Table 4, its catalytic efficiency was reduced significantly in all tested polar solvents (entries 1–4). Nonetheless, it showed excellent catalytic efficiency in nonpolar solvents, and the best results were obtained in cyclohexane (entry 5). The results in entries 5–7 indicated that the 1:2:2 ratios (by mole) of

Table 3. Effects of Different Amines and Acids on CuAAC^a

$1\mathbf{a} + 3\mathbf{a} \xrightarrow[23-97\%]{\text{CuI (0.005 equiv), amine, acid, neat, rt, 6-480 min}}$ $5\mathbf{a}$

entry	amine (0.03 equiv)	acid (0.03 equiv)	time (min)	yield of $5\mathbf{a}^b$ (%)
1	BuNH ₂	HOAc	14	90
2	Bu ₂ NH	HOAc	8	91
3	Bu ₃ N	HOAc	6	96
4	DIPEA	HOAc	6	96
5	DIPEA	<i>t</i> -BuCO ₂ H	12	96
6	DIPEA	PhCO ₂ H	6	97
7	DIPEA	TFA	240	92
8	DIPEA	TsOH	320	67
9	L-proline		480	23
10	Py-2-CO ₂ H		480	31

^a A mixture of $1\mathbf{a}$ (2 mmol) and $3\mathbf{a}$ (2.1 mmol) was tested. ^b Isolated yields.

Table 4. Effects of Solvents on CuAAC^a

$1\mathbf{a} + 3\mathbf{a} \xrightarrow[28-96\%]{\text{CuI, DIPEA, HOAc, solvent, rt, 2-60 min}}$ $5\mathbf{a}$

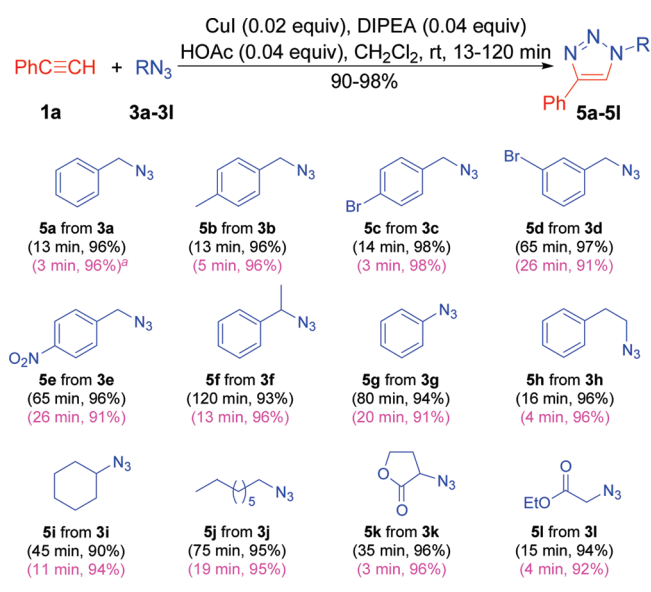
entry	CuI (equiv)	DIPEA (equiv)	HOAc (equiv)	solvent	time (min)	yield of $5\mathbf{a}^b$ (%)
1	0.01	0.02	0.02	H ₂ O	60	28
2	0.01	0.02	0.02	EtOH	60	30
3	0.01	0.02	0.02	THF	60	51
4	0.01	0.02	0.02	MeCN	60	85
5	0.01	0.02	0.02	C ₆ H ₁₂	12	96
6	0.01	0.03	0.03	C ₆ H ₁₂	13	96
7	0.01	0.01	0.01	C ₆ H ₁₂	20	95
8	0.01	0.02	0.02	PhCH ₃	32	94
9	0.01	0.02	0.02	CH ₂ Cl ₂	50	87
10	0.02	0.04	0.04	CH ₂ Cl ₂	13	96
11	0.04	0.08	0.08	CH ₂ Cl ₂	2	96

^a A mixture of $1\mathbf{a}$ (2 mmol) and $3\mathbf{a}$ (2.1 mmol) in different solvents (2 mL) was tested. ^b Isolated yields.

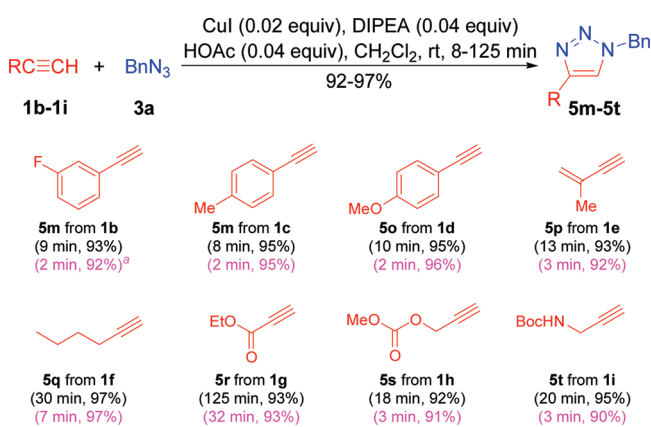
CuI/DIPEA/HOAc was good enough, and large excessive amounts of DIPEA and HOAc were not necessary. The tests in entries 9–11 indicated that an excellent result can be obtained in CH₂Cl₂ (entry 10) by using 0.02 equiv of CuI. When 0.04 equiv of CuI was used, $5\mathbf{a}$ was obtained in 96% yield for 2 min in CH₂Cl₂ (entry 11). Finally, entry 10 was assigned as our standard conditions. In comparison with our previous procedures,^{9,10} this procedure afforded two practical advantages for CuAAC. (a) CuI was used as a copper(I) source to replace the unstable and costly copper(I) acetate $\{[(\text{MeCO}_2\text{Cu})_2]_n\}$ (around 30 times more expensive than CuI). (b) CH₂Cl₂ was used as a solvent to replace the poor solvent cyclohexane or aqueous *t*-BuOH.

To generalize this method, CuAAC between PhC≡CH ($1\mathbf{a}$) and different azides $3\mathbf{b}$ – \mathbf{I} was tested under both standard and neat conditions. As shown in Scheme 3, all tested azides gave excellent results. In the cases of substrates $3\mathbf{a}$ – \mathbf{f} , the electronic and steric effects were observed clearly. As we mentioned in our previous works,^{9,10} β -substituted azides ($3\mathbf{k}$ and \mathbf{I}) usually gave better results. Although the preparation of $5\mathbf{f}$ took for

Scheme 3



Scheme 4



120 min, no coupling or substituted byproduct were detected, possibly because HOAc also has a capability to buffer the basicity of DIPEA.

As shown in Scheme 4, the method has wide scope for alkynes. Interestingly, ethyl propynoate ($1\mathbf{g}$) showed lower reactivity even though it is one of the best dipolarophiles in many 1,3-dipolar cycloadditions. It is plausible that the ring of intermediate $4\mathbf{g}$ is more electron-deficient by substitution of the carboxylate group. Therefore, the protonation of the C–Cu bond on intermediate $4\mathbf{g}$ may be retarded.

CONCLUSION

CuI/NR₃-catalyzed CuAAC is highly beneficial for use in nonaqueous or nonprotonic solvents, but it suffers from byproduct formed by NR₃-catalyzed coupling and substitution of copper(I) acetylide (2) and 5-cuprated 1,2,3-triazole (4). In this study, we showed that these drawbacks can be overcome easily by addition of the catalytic amount of HOAc, which was recognized to accelerate the conversions of the C–Cu bond-containing intermediates 2 and 4 , as well as to buffer the basicity of NR₃.

Finally, the combination of CuI/DIPEA/HOAc was developed as a highly efficient catalytic system for CuAAC. The success of catalytic system CuI/DIPEA/HOAc provides a further evidence for the strategy of carboxylic acids promoted CuAAC.

EXPERIMENTAL SECTION

All spectra of ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) were determined in CDCl_3 using TMS as internal standard.

Typical preparation of 1-benzyl-4-phenyl-1H-[1,2,3]triazole (5a) under Neat Conditions. To a mixture of CuI (1.9 mg, 0.01 mmol, 0.01 equiv), DIPEA (2.6 mg, 0.02 mmol, 0.02 equiv), and HOAc (1.2 mg, 0.02 mmol, 0.02 equiv) was added a mixture of phenylethyne (**1a**, 102 mg, 1 mmol) and benzyl azide (**3a**, 140 mg, 1.05 mmol) at room temperature. The resultant mixture was then stirred until the reaction system had solidified completely (ca. 3 min). After the crude product was diluted with CH_2Cl_2 (5 mL), it was purified by a short chromatography column [silica gel, 30% EtOAc in PE (60–90 °C)] to give 226 mg (96%) of **5a** as an off-white solid.

A similar procedure was used for the preparation of **5b–t** (see Schemes 3 and 4).

Typical Preparation of 1-Benzyl-4-phenyl-1H-[1,2,3]triazole (5a) in CH_2Cl_2 . To a mixture of CuI (3.8 mg, 0.02 mmol, 0.02 equiv), DIPEA (5.2 mg, 0.04 mmol, 0.04 equiv), and HOAc (2.4 mg, 0.04 mmol, 0.04 equiv) in CH_2Cl_2 (1.0 mL) was added a mixture of phenylethyne (**1a**, 102 mg, 1 mmol) and benzyl azide (**3a**, 140 mg, 1.05 mmol) at room temperature. The resultant mixture was stirred until the alkyne disappeared (ca. 13 min). The reaction mixture was purified by a short chromatography column [silica gel, 30% EtOAc in PE (60–90 °C)] to give 227 mg (96%) of **5a** as an off-white solid.

A similar procedure was used for the preparation of **5b–t** (see Schemes 3 and 4).

1-Benzyl-4-phenyl-1H-1,2,3-triazole (5a): white solid; mp 127–128 °C (PE–EtOAc) (lit.¹² mp 129–129.5 °C); ^1H NMR δ 7.82–7.75 (m, 2H), 7.67 (s, 1H), 7.41–7.20 (m, 8H), 5.49 (s, 2H); ^{13}C NMR δ 148.0, 134.6, 130.4, 128.9 (2C), 128.6 (2C), 128.5, 127.9, 127.8 (2C), 125.5 (2C), 119.6, 53.9.

1-(4-Methylbenzyl)-4-phenyl-1H-1,2,3-triazole (5b): white solid; mp 93–95 °C (PE–EtOAc) (lit.¹³ mp 95–97 °C); ^1H NMR δ 7.79–7.76 (m, 2H), 7.64 (s, 1H), 7.40–7.23 (m, 3H), 7.19–7.16 (m, 4H), 5.46 (s, 2H), 2.32 (s, 3H); ^{13}C NMR δ 147.9, 138.4, 131.5, 130.4, 129.6 (2C), 128.6 (2C), 127.9 (3C), 125.5 (2C), 119.4, 53.7, 21.0.

1-(2-Bromobenzyl)-4-phenyl-1H-1,2,3-triazole (5c): white solid; mp 102–104 °C (PE–EtOAc) (lit.¹³ mp 105–106 °C); ^1H NMR δ 7.81–7.78 (m, 3H), 7.62–7.58 (m, 1H), 7.40–7.10 (m, 6H), 5.66 (s, 2H); ^{13}C NMR δ 147.9, 134.1, 133.1, 130.4, 130.2, 130.1, 128.7 (2C), 128.1, 128.0, 125.6 (2C), 123.0, 119.8, 53.7.

1-(3-Bromobenzyl)-4-phenyl-1H-1,2,3-triazole (5d): white solid; mp 91–93 °C (PE–EtOAc) (lit.¹³ mp 94–95 °C); ^1H NMR δ 7.85–7.80 (m, 2H), 7.71 (s, 1H), 7.49–7.20 (m, 7H), 5.50 (s, 2H); ^{13}C NMR δ 148.2, 136.8, 131.8, 130.8, 130.6, 130.3, 128.7 (2C), 128.2, 126.4, 125.6 (2C), 122.9, 119.6, 53.3.

1-(4-Nitrobenzyl)-4-phenyl-1H-1,2,3-triazole (5e): yellow solid; mp 158–159 °C (PE–EtOAc) (lit.¹² mp 156–157 °C); ^1H NMR δ 8.20–8.18 (m, 2H), 7.82–7.79 (m, 3H), 7.43–7.34 (m, 5H), 5.67 (s, 2H); ^{13}C NMR δ 148.5, 147.9, 141.7, 130.1, 128.8 (2C), 128.5 (2C), 128.4, 125.6 (2C), 124.2 (2C), 119.8, 53.0.

4-Phenyl-1-(1-phenylethyl)-1H-1,2,3-triazole (5f):¹⁴ white solid; mp 80–82 °C (PE–EtOAc); ^1H NMR δ 7.81–7.78 (m, 2H), 7.64 (s, 1H), 7.38–7.28 (m, 8H), 5.86 (q, $J = 7.2$ Hz, 1H), 2.02 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR δ 147.7, 139.9, 130.6, 129.0 (2C), 128.7 (2C), 128.5, 128.0, 126.5 (2C), 125.6 (2C), 118.3, 60.2, 21.3.

1,4-Diphenyl-1H-1,2,3-triazole (5g): yellowish solid; mp 182–184 °C (PE–DCM) (lit.¹⁵ mp 184–186 °C); ^1H NMR δ

9.31 (s, 1H), 8.04–7.90 (m, 4H), 7.80–7.32 (m, 6H); ^{13}C NMR (DMSO- d_6) δ 147.3, 136.6, 130.2, 129.9 (2C), 129.0 (2C), 128.7, 128.2, 125.3 (2C), 120.0 (2C), 119.6.

1-(2-Phenylethyl)-4-phenyl-1H-1,2,3-triazole (5h): white solid; mp 141–142 °C (PE–EtOAc) (lit.¹² mp 139 °C); ^1H NMR δ 7.76–7.74 (m, 2H), 7.50 (s, 1H), 7.39–7.32 (m, 2H), 7.28–7.21 (m, 4H), 7.08–7.04 (m, 2H), 4.53 (t, $J = 7.2$ Hz, 2H), 3.16 (t, $J = 7.2$ Hz, 2H); ^{13}C NMR δ 147.1, 136.8, 130.5, 128.6 (4C), 128.4, 128.2, 127.8, 126.8, 125.4 (2C), 119.9, 51.3, 36.4.

1-Cyclohexyl-4-phenyl-1H-1,2,3-triazole (5i): white solid; mp 108–109 °C (PE–EtOAc) (lit.¹⁶ mp 105.8–110 °C); ^1H NMR δ 7.85–7.81 (m, 3H), 7.38–7.35 (m, 2H), 7.32–7.24 (m, 1H), 4.42–4.37 (m, 1H), 2.18–2.11 (m, 2H), 1.84–1.65 (m, 5H), 1.45–1.17 (m, 3H); ^{13}C NMR δ 146.8, 130.7, 128.4 (2C), 127.6, 125.3 (2C), 117.3, 59.8, 33.2 (2C), 24.8 (2C), 24.7.

1-Octyl-4-phenyl-1H-1,2,3-triazole (5j): white solid; mp 78–80 °C (PE–EtOAc) (lit.¹⁵ mp 74–75 °C); ^1H NMR δ 7.88–7.80 (m, 2H), 7.73 (s, 1H), 7.42–7.37 (m, 2H), 7.32–7.26 (m, 1H), 4.34 (t, $J = 7.2$ Hz, 2H), 1.93–1.86 (m, 2H), 1.40–1.24 (m, 10H), 0.86 (t, $J = 5.9$ Hz, 3H); ^{13}C NMR δ 147.5, 130.7, 128.7 (2C), 127.9, 125.5 (2C), 119.4, 50.3, 31.6, 30.2, 28.9, 28.8, 26.1, 22.3, 13.8.

3-(4-Phenyl-1H-1,2,3-triazol-1-yl)dihydrofuran-2(3H)-one (5k): white solid; mp 140–141 °C (PE–EtOAc); IR (KBr) ν 3453, 1780, 1446, 1295, 1166, 1005 cm^{-1} ; ^1H NMR δ 8.81 (s, 1H), 7.88–7.85 (m, 2H), 7.49–7.44 (m, 2H), 7.39–7.31 (m, 1H), 5.98 (t, $J = 22.9$ Hz, 1H), 4.66–4.56 (m, 1H), 4.51–4.42 (m, 1H), 2.98–2.79 (m, 2H); ^{13}C NMR δ 172.3, 146.7, 130.3, 129.0 (2C), 128.1, 125.2 (2C), 121.7, 66.2, 57.8, 29.3; HRMS calcd for $\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}_2$ 229.0851, found 229.0859.

Ethyl 2-(4-phenyl-1H-1,2,3-triazol-1-yl)acetate (5l): white solid; mp 91–92 °C (PE–EtOAc) (lit.⁶ mp 94–95 °C); ^1H NMR δ 7.91 (s, 1H), 7.87–7.84 (m, 2H), 7.46–7.32 (m, 3H), 5.21 (s, 2H), 4.29 (q, $J = 6.9$ Hz, 2H), 1.21 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR δ 166.2, 148.0, 130.3, 128.7 (2C), 128.1, 125.6 (2C), 121.1, 62.3, 50.8, 13.9.

1-Benzyl-4-(3-fluorophenyl)-1H-1,2,3-triazole (5m): yellowish solid; mp 109–110 °C (PE–EtOAc); IR (KBr) ν 3091, 1582, 1450, 1218, 11620, 853 cm^{-1} . ^1H NMR δ 7.77 (s, 1H), 7.53–7.50 (m, 2H), 7.35–7.23 (m, 6H), 5.98–5.89 (m, 1H), 5.48 (s, 2H); ^{13}C NMR δ 162.8 ($J = 243.8$ Hz), 146.6, 134.3, 132.5 ($J = 8.6$ Hz), 130.1 ($J = 8.6$ Hz), 128.8 (2C), 128.4, 127.7 (2C), 121.0 ($J = 2.2$ Hz), 120.1, 114.5 ($J = 20.8$ Hz), 112.0 ($J = 8.6$ Hz), 53.8; HRMS calcd for $\text{C}_{15}\text{H}_{12}\text{FN}_3$ 253.1015, found 253.1019.

1-Benzyl-4-(4-methylphenyl)-1H-1,2,3-triazole (5n): white solid; mp 153–155 °C (PE–EtOAc) (lit.¹⁷ mp 155–157 °C); ^1H NMR δ 7.69–7.60 (m, 3H), 7.33–7.10 (m, 7H), 5.50 (s, 2H), 2.33 (s, 3H); ^{13}C NMR δ 148.0, 137.7, 134.6, 129.3 (2C), 128.8 (2C), 128.4, 127.8 (2C), 127.6, 125.4 (2C), 119.2, 53.8, 21.0.

1-Benzyl-4-(4-methoxyphenyl)-1H-1,2,3-triazole (5o): white solid; mp 143–145 °C (PE–EtOAc) (lit.¹⁵ mp 143–144 °C); ^1H NMR δ 7.73–7.70 (m, 2H), 7.57 (s, 1H), 7.39–7.26 (m, 5H), 6.94–6.91 (m, 2H), 5.55 (s, 2H), 3.82 (s, 3H); ^{13}C NMR δ 159.5, 148.1, 134.7, 129.1 (2C), 128.7, 128.0 (2C), 127.0 (2C), 123.2, 118.7, 114.2 (2C), 55.3, 54.1.

1-Benzyl-4-(prop-1-en-2-yl)-1H-1,2,3-triazole (5p): white solid; mp 84–86 °C (PE/EtOAc) (lit.¹⁸ mp 91–91.5 °C); ^1H NMR δ 7.49 (s, 1H), 7.41–7.22 (m, 5H), 5.68 (s, 1H), 5.51 (s, 2H), 5.11–5.06 (m, 1H), 2.10 (s, 3H); ^{13}C NMR δ 149.2, 134.7, 133.5, 129.0 (2C), 128.6, 127.9 (2C), 119.4, 112.4, 54.0, 20.5.

1-Benzyl-4-butyl-1H-1,2,3-triazole (5q): white solid; mp 64–66 °C (PE/EtOAc) (lit.⁸ mp 61–62 °C); ^1H NMR δ 7.33–7.20 (m, 6H), 5.44 (s, 2H), 2.67 (t, $J = 7.9$ Hz, 2H), 5.51.64–1.56 (m, 2H), 1.38–1.31 (m, 2H), 0.89 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR δ 148.2, 134.7, 128.4 (2C), 127.9, 127.3 (2C), 120.3, 53.2, 31.0, 24.8, 21.8, 13.3.

Ethyl 1-benzyl-1H-1,2,3-triazole-4-carboxylate (5r): yellowish solid; mp 82–83 °C (PE–EtOAc) (lit.¹⁵ mp 83–85 °C); ¹H NMR δ 8.13 (s, 1H), 7.36–7.30 (m, 5H), 5.60 (s, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H); ¹³C NMR δ 160.3, 140.0, 133.7, 128.8 (2C), 128.5, 127.8 (2C), 127.2, 60.7, 53.9, 13.9.

Methyl (1-benzyl-1H-1,2,3-triazol-4-yl)methyl carbonate (5s): yellowish solid; mp 60–62 °C (PE–EtOAc); IR (KBr) ν 3070, 1750, 1450, 1260, 939 cm⁻¹; ¹H NMR δ 7.65 (s, 1H), 7.34–7.22 (m, 5H), 5.50 (s, 2H), 5.22 (s, 2H), 3.74 (s, 3H); ¹³C NMR δ 155.1, 142.1, 134.2, 128.7 (2C), 128.3, 127.7 (2C), 123.5, 60.5, 54.5, 53.7; HRMS calcd for C₁₂H₁₃N₃O₃ 247.0957, found 247.0960.

tert-Butyl (1-benzyl-1H-1,2,3-triazol-4-yl)methylcarbamate (5t): yellowish solid; mp 80–82 °C (PE–EtOAc) (lit.¹⁹ mp 100–102 °C); ¹H NMR δ 7.42 (s, 1H), 7.14–7.05 (m, 5H), 5.86 (t, *J* = 6.0 Hz, 1H), 5.28 (s, 2H), 4.18 (d, *J* = 6.0 Hz, 2H), 1.24 (s, 9H); ¹³C NMR δ 155.3, 145.4, 134.3, 128.3 (2C), 127.8, 127.3 (2C), 121.5, 78.5, 53.1, 34.5, 27.7 (3C).

ASSOCIATED CONTENT

Supporting Information. ¹H NMR and ¹³C NMR spectra for compounds 5a–t. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

*Phone: +86-10-62795380. Fax: +86-10-62771149. E-mail: xinyanwang@mail.tsinghua.edu.cn; yfh@mail.tsinghua.edu.cn.

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