Tetrahedron 67 (2011) 6294–6299

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Highly controlling selectivity of copper(I)-catalyzed azide/alkyne cycloaddition (CuAAC) between sulfonyl azids and normal alkynes or propynoates

Yantao Liu, Xinyan Wang *, Jimin Xu, Qun Zhang, Yi Zhao, Yuefei Hu *

Department of Chemistry, Tsinghua University, Beijing 100084, PR China

ARTICLE INFO

Article history:
Received 13 April 2011
Received in revised form 27 May 2011
Accepted 7 June 2011
Available online 14 June 2011

Keywords:
Copper(I) catalyst
Azide/alkyne cycloaddition
Sulfonyl azids
Copper(II) acetate
2-Aminophenol

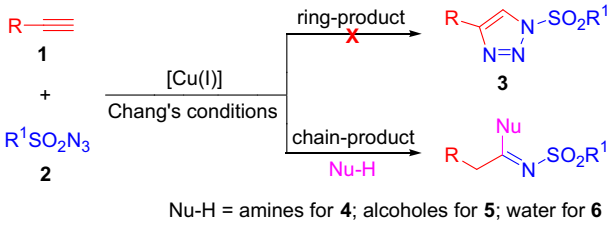
ABSTRACT

In this article, a combination of $Cu(OAc)_2 \cdot H_2O$/2-aminophenol was developed as a highly efficient and controlling catalytic system for sulfonyl azids involved CuAAC. By using this catalytic system, sulfonyl azids reacted with normal alkynes or propynoates to selectively give the ring products or the chain products, respectively, in excellent yields within minutes. HOAc in situ produced in the reaction has been proved to be a super protonation reagent, by which the unstable intermediate 5-cuprated 1,2,3-triazole was protonated efficiently to yield ring-product 1-sulfonyl 1,2,3-trizoles. The control experiments also proved that 2-aminophenol played dual roles as both ligand and reductant, which led to the cheap and chemically stable $Cu(OAc)_2 \cdot H_2O$ being an efficient copper source for our purpose.

1. Introduction

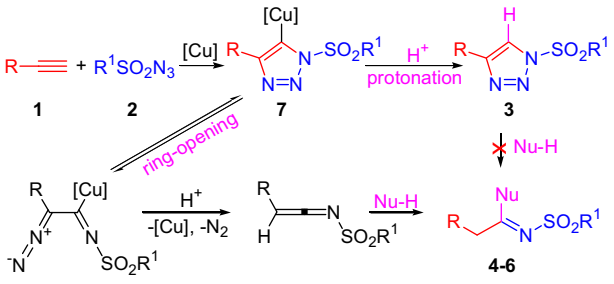
In 2002, the first copper(I)-catalyzed azide/alkyne cycloaddition (CuAAC) was discovered independently by the groups of Sharpless[1] and Meldal,[2] by which 1,4-disubstituted 1,2,3-triazoles were prepared regioselectively under mild conditions.[3] 3 years later, Chang[4] discovered that when an electron-deficient sulfonyl azide (**2**) was used as a substrate, instead of the ring-product 1-sulfonyl-1,2,3-triazole (**3**), a chain-product *N*-sulfonylamidine (**4**) was obtained in the presence of a primary or secondary amine (Scheme 1). His further works proved that the chain-product *N*-sulfonylimidate (**5**)[5a] or *N*-sulfonyl amide (**6**)[5b] could also be synthesized by the similar procedures when alcohol or H_2O was used as a nucleophile, respectively. To date, Chang's reaction and products have widely used in organic synthesis.[6,7]

The mechanism studies reveal that both ring product (**3**) and chain product (**4**–**6**) share the 5-cuprated 1,2,3-triazole (**7**) as a common intermediate. But, the electron-withdrawing substituents on **7** seriously reduce the stability of **7** and cause its N–N bond cleavage to give ring-opening product (Scheme 2).[8] Therefore, although the ring-product **3** have been used as important intermediates[9] or latent diazo precursors[10] in organic synthesis, its efficient synthesis by CuAAC was rarely described in literature.[8a,11] However, the mechanism studies



Scheme 1.

also clearly indicated that the distribution of ring and chain products depended upon the competitive reactions between the protonation and ring-opening of **7**. Thus, highly efficient synthesis of the ring-product **3** might be expected by developing a highly efficient protonation reagent or procedure.



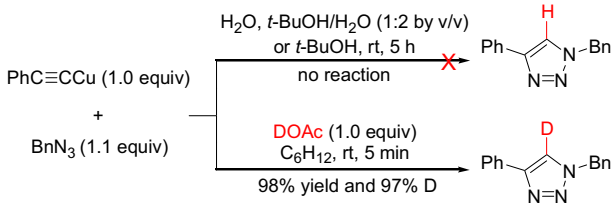
Scheme 2.

* Corresponding authors. Tel.: +86 10 6279 5380; fax: +86 10 6277 1149; e-mail addresses: wangxinyan@mail.tsinghua.edu.cn (X. Wang), yfh@mail.tsinghua.edu.cn (Y. Hu).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.06.017

2. Results and discussion

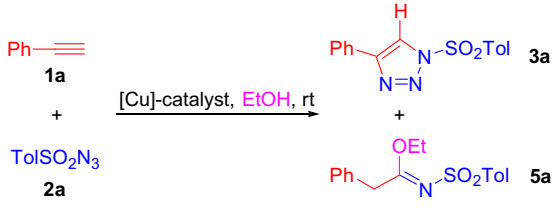
In 2007, Straub[12] reported that the C–Cu bond in 5-cuprated 1,2,3-triazole (as a coordination compound) can be protonated by HOAc within few minutes. Very recently, we reported a novel copper(I) acetate catalyzed CuAAC reaction,[13] in which the C–Cu bond can be protonated within 5 min by the in situ formed HOAc. As shown in Scheme 3, this efficient protonation was indirectly proved by an isotopic labeling experiment. This result strongly encouraged us to develop a copper(I) acetate catalyzed CuAAC for efficient synthesis of the ring-product **3** from the electron-deficient sulfonyl azides (**2**).



Scheme 3.

Thus, a group of control experiments were designed for CuAAC between phenylacetylene (**1a**) and *p*-tolenesulfonyl azide (**2a**). To clearly identify the ring-chain selectivity of the catalysts, EtOH was used as a solvent (Table 1). As was expected, by using the popular catalytic system CuI/Et_3N, the chain-product **5a** was obtained as a major product in 86% yield (entry 1). When the other popular catalytic system $CuSO_4{\cdot}5H_2O$/NaAsc was used, its catalyzed reaction stopped automatically within 2 h. Although it gave a very low conversion, the ring-product **3a** was the major product (entry 2). This is a very exciting result because the in situ formed HAsc behaves as a vinylogous carboxylic acid having pK_a values of 4.10 and 11.79, respectively (pK_a value of acetic acid is 4.76). Interestingly, no H_2O involved product was detected even H_2O was a necessary co-solvent in this reaction.

Table 1
Effects of the catalysts on the ring-chain selectivity[a]



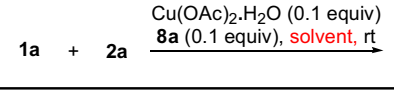
Entry	Cu(I) Catalyst (0.1 equiv)	Time (h)	Yield of **3a**[b] (%)	Yield of **5a**[b] (%)
1	CuI/Et_3N	3	5	86
2[c]	$CuSO_4{\cdot}5H_2O$/NaAsc	24	38	3
3	CuOAc	24	42	5
4	$Cu(OAc)_2{\cdot}H_2O$	24	40	6
5[d]	CuOAc	4	74	8
6[d]	$Cu(OAc)_2{\cdot}H_2O$	16	71	3
7	CuOAc/**8a**	2	76	3
8	$Cu(OAc)_2{\cdot}H_2O$/**8a**	2	77	3
9[e]	$Cu(OAc)_2{\cdot}H_2O$/**8a**	1	68	17

[a] The mixture of **1a** (1.1 mmol), **2a** (1.0 mmol), and catalyst (0.1 mmol) in EtOH (1 mL) was stirred at room temperature.
[b] The isolated yields were obtained.
[c] The mixture of EtOH/H_2O (1:1) was used as a solvent for the reason of the solubility of $CuSO_4{\cdot}5H_2O$ and NaAsc.
[d] The reaction was protected under N_2.
[e] The reaction was proceeded at 50 °C.

Similar to $CuSO_4{\cdot}5H_2O$/NaAsc, both the catalysts CuOAc and $Cu(OAc)_2{\cdot}H_2O$ lost their catalytic activity within 2 h and gave **3a** as a major product in low conversions (entries 3 and 4). However, when the same reactions proceeded under N_2, higher conversions were obtained and CuOAc catalyzed reaction could finish within 4 h (entries 5 and 6). By the addition of some ligands, such as PPh_3, DMAP, DIPEA, $HOCH_2CH_2OH$, $HOCH_2CH_2NH_2$ or $H_2NCH_2CH_2NH_2$, no significant improvements were observed for both conversion and selectivity. To our delight, when 2-aminophenol (**8a**) was used as a ligand, both CuOAc and $Cu(OAc)_2{\cdot}H_2O$ gave similarly good results even without the protection of N_2 (entries 7 and 8). To our surprising, when the mixture of **1a** (1.1 equiv), **2a** (1 equiv), $Cu(OAc)_2{\cdot}H_2O$ (0.1 equiv), and 2-aminophenol (**8a**, 0.1 equiv) in EtOH was heated at 50 °C for 1 h, **3a** was obtained as a major product in 68% yield (entries 9). Thus, the combination of $Cu(OAc)_2{\cdot}H_2O$/**8a** (entry 8) may be an efficient catalytic system with high selectivity for the ring product and with two advantages by comparing with the entries 5–7. (a) In entry 8, the cheap and chemically stable $Cu(OAc)_2{\cdot}H_2O$ was used as a copper source. But, CuOAc was used in entries 5 and 7, which is around 50 times more expensive than $Cu(OAc)_2{\cdot}H_2O$ and chemically unstable for storage. (b) In entry 8, Cu(I) species may be generated from the redox between Cu(II) and 2-aminophenol (**8a**). But, the Cu(I) species was confirmed to be generated from the Cu(II) promoted oxidative coupling of phenylacetylene (**1a**) in entry 6, by which the large amounts of acetylene was wasted and the amount of Cu(I) largely depended upon the reactivity of individual acetylenes.

Then, different solvents were scanned to find their effects on the catalytic activity of $Cu(OAc)_2{\cdot}H_2O$/**8a**. As shown in Table 2, the ring-product **3a** was obtained in excellent yields in all non-protonic solvents (entries 1–5) and the best result was obtained in MeCN (entry 5). The chemoselectivity of $Cu(OAc)_2{\cdot}H_2O$/**8a** was so good that **3a** was formed as a single product even the reaction proceeded in H_2O (entry 6). We found that it was a two-phase reaction and the organic layer was surrounded by H_2O. Therefore, it actually is also a solvent-free reaction and the reactants could contact with H_2O only on the interface.

Table 2
Effects of solvents on the catalytic activity of $Cu(OAc)_2{\cdot}H_2O$/**8a**[a]

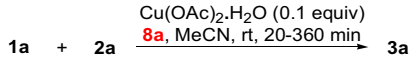


Entry	Solvent	Time (h)	Yield of **3a**[b] (%)
1	PhMe	14	88
2	EtOAc	14	93
3	CH_2Cl_2	5	91
4	THF	2	95
5	MeCN	1	95
6	H_2O	1.2	86

[a] The mixture of **1a** (1.1 mmol), **2a** (1.0 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.1 mmol), and **8a** (0.1 mmol) in solvent (1 mL) was stirred at room temperature.
[b] The isolated yields were obtained.

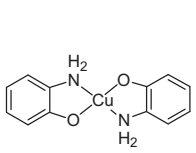
Next, the effects of ratios of $Cu(OAc)_2{\cdot}H_2O$/**8a** on the catalytic activity were tested. As shown in Table 3, although the 1:2 ratio of copper source/ligand usually was employed in the ligand-mediated CuAAC in literature, the worst result was obtained with the 1:2 ratio of $Cu(OAc)_2{\cdot}H_2O$/**8a** (entry 2). This may be caused by the fact that a stable 1:2 coordination product was formed (Chart 1),[14] by which the reduction of Cu(II) and the catalytic cycle of the in situ formed Cu(I) may be retarded. On the contrary, the 2:1 ratio of $Cu(OAc)_2{\cdot}H_2O$/**8a** showed the highest catalytic activity (entry 4). This result suggested that the ligand **8a** may be used to dissociate Cu(II) from the stable dinuclear 'paddle-wheel' coordination structure in $Cu(OAc)_2{\cdot}H_2O$ (Chart 1) or dissociate Cu(I) from the coordination of MeCN, which has been proved to retard the

Table 3
Effects of the ratio of $Cu(OAc)_2 \cdot H_2O$/**8a** on the catalytic activity[a]

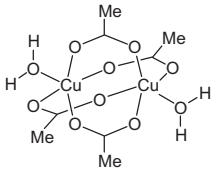


Entry	$Cu(OAc)_2 \cdot H_2O$/**8a** (by mole)	Time (min)	Yield of **3a**[b] (%)
1	1:3	360	74
2	1:2	360	52
3	1:1	60	95
4	2:1	20	95
5	3:1	90	87

[a] The mixture of **1a** (1.1 mmol), **2a** (1.0 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.1 mmol), and **8a** in MeCN (1 mL) was stirred at room temperature.
[b] The isolated yields were obtained.



A stable coordination product from 1:2 ratio of $Cu(OAc)_2 \cdot H_2O$ and **8a**

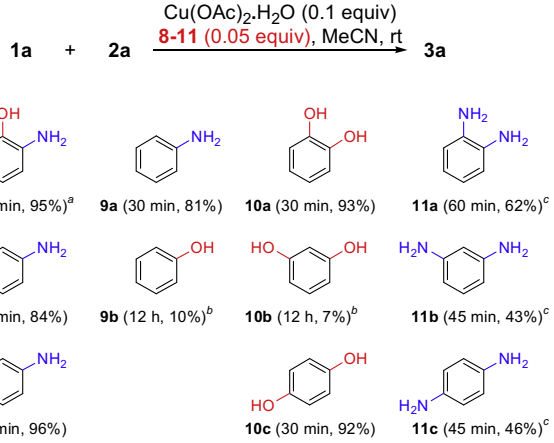


$Cu(OAc)_2 \cdot H_2O$ as a dinuclear coordination compound with stable "paddle-wheel" structure

Chart 1.

catalytic cycle of Cu(I) in our previous works.[13b]Thus, the real catalyst may be a copper coordination compound with mixed ligands including **8a**, acetate anion and/or MeCN.

To further understand the relationship between structure and promotion activity of **8a**, three aminophenol isomers **8a**–**c** were tested as shown in Scheme 4. To our surprise, **8c** showed the same excellent promotion activity as **8a**. Since **8c** is not a chelating ligand, therefore the monodentate ligands aniline (**9a**) and phenol (**9b**) were tested. As was expected, **9a** had the similar promotion activity as **8b**, while **9b** almost had no promotion activity. This result seems that the hydroxyl group had less importance than amine group, but it was not true when benzenediols (**10a**–**c**) and benzenediamines (**11a**–**c**) were evaluated. For example, although **10b** in fact was inert, the promotion activity of **10a** and **10c** was as high as that of **8a** and **8c**. On the contrary, none of **11a**–**c** showed satisfying promotion activity.

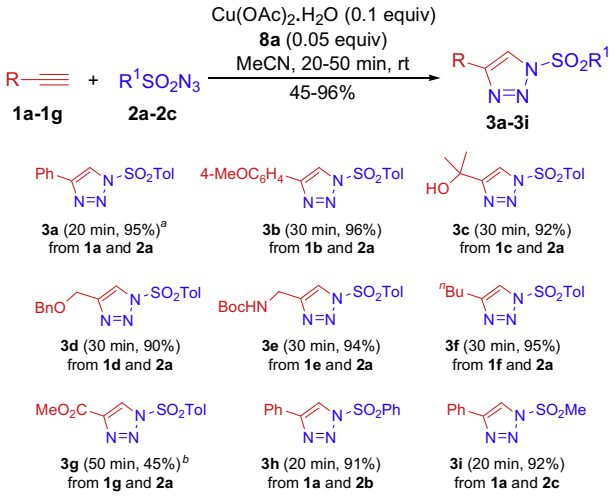


[a]The isolated yields were obtained for all examples. [b]The reaction was quenched at 12 h. [c]The time is that reactant **2a** was exhausted.

Scheme 4.

Based on the results in Table 3 and Scheme 4, we proposed that a satisfying ligand in $Cu(OAc)_2 \cdot H_2O$ catalyzed CuAAC may play dual roles. (a) It was a ligand to loosely coordinate with Cu(II) or Cu(I) species, because unsatisfying results were obtained by using benzenediamines **11a**–**c** or excess amount of **8a**. (b) It was a reductant to reduce Cu(II) into Cu(I) in situ through the formation of 1,2- or 1,4-quinones. This may be the reason that **8b** and **10b** had low or no promotion activity because they could not be converted into quinones.

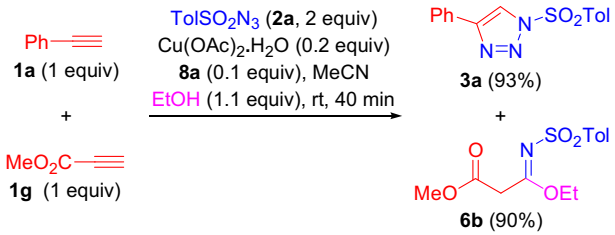
Finally, **8a** was chosen as the ligand for our purpose because it is a nonhygroscopic crystal and $Cu(OAc)_2 \cdot H_2O$/**8a** (2:1 by mole) in MeCN was chosen as the standard conditions. To generalize this method, different alkynes (**1a**–**g**) and sulfonyl azides (**2a**–**c**) were tested under the standard conditions. As shown in Scheme 5, they all gave the desired 1-sulfonyl-1,2,3-triazoles (**3a**–**i**) in excellent yields within minutes. Since the method was performed under extremely mild conditions, many sensitive functional groups stayed intact, such as tertiary alcohol (**3c**), benzyl ether (**3d**), and *N*-Boc protective group (**3e**). When benzenesulfonyl azide (**2b**) or methansulfonyl azide (**2c**) was used as a substrate, **3h** or **3i** was obtained in 91% or 92% yield, respectively.



[a]The isolated yields were obtained. [b]The reaction proceeded at 0 °C.

Scheme 5.

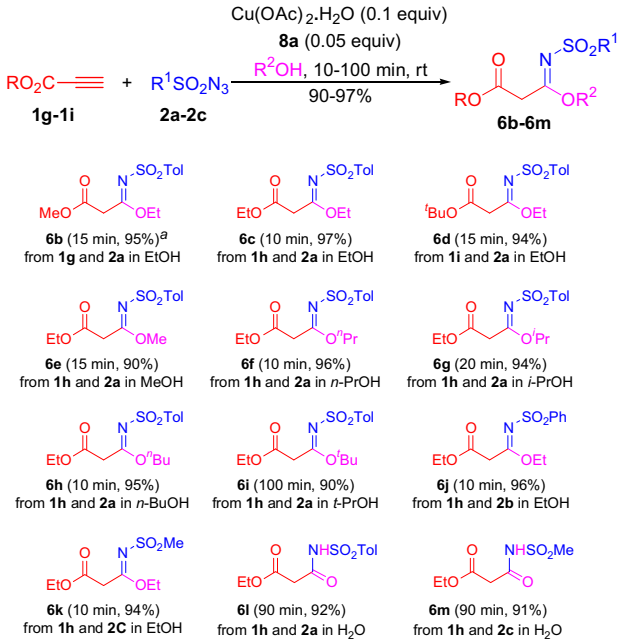
It is very noteworthy that ethyl 1-(toluene-4-sulfonyl)-1*H*-[1,2,3]triazole-4-carboxylate (**3g**, Scheme 5) can be synthesized in 45% yield when methyl propynoate (**1g**) was used as a substrate at 0 °C. This is the first example that [1,2,3]triazole bearing two strong electron-withdrawing groups was prepared by CuAAC. In further studies on **1g**, we found that its reaction with **2a** was very sensitive to the nucleophiles and the chain-product **6b** was produced as a single product in the presence of EtOH. As shown in Scheme 6, when the mixture of **1a**, **1g**, and **2a** in MeCN/EtOH was treated by $Cu(OAc)_2 \cdot H_2O$/**8a**, a highly ring-chain selectivity was achieved to give the corresponding ring-product **3a** and chain-product **6b** in excellent yields.



Scheme 6.

It is well-known that active methylene compounds are the versatile synthones in organic synthesis, therefore, CuAAC reaction between sulfonyl azids and propynoates may afford a practical method for the preparation a series of structurally novel active

methylene compounds. Thus, the reaction between propynoates (**1g**–**i**) and sulfonyl azids (**2a**–**c**) catalyzed by $Cu(OAc)_2 \cdot H_2O$/**8a** was studied in alcohols and H_2O. As shown in Scheme 7, after the mixture of **1g**, **2a**, $Cu(OAc)_2 \cdot H_2O$/**8** in EtOH was stirred at room temperature for 15 min, the desired chain-product **6b** was obtained in 95% yield. It is clear to observe that the size of propynoate had no negative effect on the reaction efficiency (see samples: **6b**–**d**). However, the size of nucleophile showed significant effect on the reaction time (see samples: **6e**–**i**) and the preparation of **6i** took for 100 min in *t*-BuOH. When H_2O was used as a solvent, the corresponding *N*-Ts amides **6l** and **6m** were obtained in excellent yields.



[a] The isolated yields were obtained for all products.

Scheme 7.

3. Conclusion

By using electron-deficient sulfonyl azids as substrates, CuAAC tends to yield chain products in the presence of nucleophiles. Since the mechanism studies proved that the ring and chain products share 5-cuprated 1,2,3-triazole (**7**) as a common intermediate, therefore, it is expected to obtain the ring product by a highly competitive protonation of **7**. We found that the in situ formed HOAc in CuOAc catalyzed CuAAC was a super protonation reagent for 5-cuprated 1,2,3-triazole (**7**), by which the ring product can be obtained as a major product even by using EtOH as a solvent. We also found that CuOAc could be replaced by $Cu(OAc)_2 \cdot H_2O$ as a highly active catalyst in the presence of 2-aminophenol (**8a**). Since the best catalytic result was obtained with the 2:1 ratio of $Cu(OAc)_2 \cdot H_2O$/2-aminophenol (**8a**), this strange phenomenon was further studied to reveal that 2-aminophenol (**8a**) played dual roles as both ligand and reductant. Finally, the combination of $Cu(OAc)_2 \cdot H_2O$/2-aminophenol (**8a**) was developed as a highly efficient and controlling catalytic system for CuAAC. By using this catalytic system, sulfonyl azids reacted with normal alkynes or propynoates to selectively give the ring products or the chain products, respectively. This catalytic system characterized to use cheap and chemically stable $Cu(OAc)_2 \cdot H_2O$ as copper source and all examples were made in excellent yields within minutes.

4. Experimental section

4.1. General

All melting points were determined on a Yanaco melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX spectrometer with KBr. The ^1H NMR and ^{13}H NMR spectra were recorded on a JEOL JNM-ECA 300 spectrometer in $CDCl_3$ with TMS as internal reference. The *J* values are given in hertz. MS (EI) were recorded on a VG-ZAB-MS spectrometer with 70 eV. Elementary analysis data were obtained on a Perkin–Elmer-241C apparatus. PE is petroleum ether (60–90°).

4.2. A Typical procedure for the preparation of ring-product 4-phenyl-1-(toluene-4-sulfonyl)-1*H*-[1,2,3]triazole (3a)

To a stirred solution of phenylacetylene (**1a**, 112 mg, 1.1 mmol), 4-methylbenzenesulfonyl azide (**2a**, 197 mg, 1 mmol), and 2-aminophenol (**8a**, 5.5 mg, 0.05 mmol) in MeCN (1 mL) was added $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol) at room temperature. After **2a** was exhausted (ca. 20 min, monitored by TLC), the solvent was removed off in vacuum. The residue was purified by chromatography (silica gel, 10% EtOAc in PE) to give desired product **3a** as a colorless solid (284 mg, 95%), mp 104–105 °C (EtOAc/PE) (lit.[11a] 105.2–107 °C, lit.[8a] 107–108 °C). ^1H NMR δ 8.32 (s, 1H), 8.03–8.00 (m, 2H), 7.84–7.80 (m, 2H), 7.42–7.36 (m, 5H), 2.43 (s, 3H); ^{13}C NMR δ 147.5, 133.2, 130.6 (2C), 129.2 (2C), 129.1 (2C), 129.0, 128.8 (2C), 126.2 (2C), 119.1, 22.0.

By the similar procedure for the preparation of **3a**, products **3b**–**i** were prepared.

*4.2.1. 4-(4-Methoxy-phenyl)-1-(toluene-4-sulfonyl)-1H-[1,2,3]triazole (**3b**).*[10c] It is a white solid, mp 100–101 °C (EtOAc/PE). ^1H NMR δ 8.22 (s, 1H), 8.02 (d, *J*=8.6 Hz, 2H), 7.75 (d, *J*=8.6 Hz, 2H), 7.38 (d, *J*=7.7 Hz, 2H), 6.95 (d, *J*=8.8 Hz, 2H), 3.84 (s, 3H), 2.44 (s, 3H); ^{13}C NMR δ 160.0, 147.1, 132.9, 130.3 (2C), 128.4 (2C), 127.2 (3C), 121.2, 118.0, 114.2 (2C), 55.1, 21.6.

*4.2.2. 2-[1-(Toluene-4-sulfonyl)-1H-[1,2,3]triazol-4-yl]-propan-2-ol (**3c**).* It is a yellowish solid, mp 120–122 °C (EtOAc/PE) (lit.[8a] 122–123 °C). ^1H NMR δ 8.04–7.98 (m, 3H), 7.40–7.37 (m, 2H), 2.64 (s, 1H), 2.45 (s, 3H), 1.61 (s, 6H); ^{13}C NMR δ 155.1, 147.3, 132.9, 130.4 (2C), 128.7 (2C), 119.1, 68.5, 30.1 (2C), 21.8.

*4.2.3. 4-Benzyloxymethyl-1-(toluene-4-sulfonyl)-1H-[1,2,3]triazole (**3d**).* It is a gray white solid, mp 80–81 °C (EtOAc/PE) (lit.[11a] 85.1–86.7 °C). ^1H NMR δ 8.10 (s, 1H), 7.99 (d, *J*=8.3 Hz, 2H), 7.39–7.33 (m, 7H), 4.66 (s, 2H), 4.60 (s, 2H), 2.45 (s, 3H); ^{13}C NMR δ 147.3, 145.0, 137.2, 132.8, 130.3 (2C), 128.6 (2C), 128.4 (2C), 127.9, 127.8 (2C), 122.2, 72.9, 63.0, 21.7.

*4.2.4. [1-(Toluene-4-sulfonyl)-1H-[1,2,3]triazol-4-ylmethyl]-carbamic acid tert-butyl ester (**3e**).* It is a yellowish solid, mp 111–113 °C (EtOAc/PE) (lit.[8a] 117–118 °C). ^1H NMR δ 8.08 (s, 1H), 8.00–7.97 (m, 2H), 7.40–7.37 (m, 2H), 5.07 (s, 1H), 4.40–4.38 (m, 2H), 2.45 (s, 3H), 1.43 (s, 9H); ^{13}C NMR δ 155.7, 147.3, 145.4, 132.8, 130.4 (2C), 128.6 (2C), 121.7, 79.9, 35.7, 28.2 (3C), 21.7.

*4.2.5. 4-Butyl-1-(toluene-4-sulfonyl)-1H-[1,2,3]triazole (**3f**).* It is a yellowish oil. IR ν 3472, 3134, 2963, 1606, 1455 cm^{-1}; ^1H NMR δ 7.98 (d, *J*=8.6 Hz, 2H), 7.91 (s, 1H), 7.37 (d, *J*=8.6 Hz, 2H), 2.73–2.68 (m, 2H), 2.43 (s, 3H), 1.66–1.61 (m, 2H), 1.39–1.32 (m, 2H), 0.90 (t, *J*=7.2 Hz, 3H); ^{13}C NMR δ 148.1, 146.9, 133.0, 130.2 (2C), 128.3 (2C), 120.2, 30.7, 24.8, 21.9, 21.5, 13.5; MS *m*/*z* (%) 172 (100), 91 (71). Anal.

Calcd. For $C_{13}H_{17}N_3O_2S$: C, 55.89; H, 6.13; N, 15.04. Found: C, 56.11; H, 6.02; N, 15.18.

*4.2.6. 1-(Toluene-4-sulfonyl)-1H-[1,2,3]triazole-4-carboxylic acid methyl ester (**3g**).* It is a white solid, mp 110–112 °C (lit.[15] 115–117 °C). ^{1}H NMR δ 8.63 (s, 1H), 8.02 (d, J=8.6 Hz, 2H), 3.95 (s, 3H), 2.47 (s, 3H); ^{13}C NMR δ 159.9, 148.1, 139.0, 132.1, 130.6 (2C), 128.8 (2C), 127.4, 52.5, 21.8.

*4.2.7. 1-Benzenesulfonyl-4-phenyl-1H-[1,2,3]triazole (**3h**).* It is a white solid, mp 105–107 °C (EtOAc/PE) (lit.[7n] 105–107 °C). ^{1}H NMR δ 8.33 (s, 1H), 8.17–8.15 (m, 2H), 7.84–7.82 (m, 2H), 7.74–7.73 (m, 1H), 7.64–7.61 (m, 2H), 7.44–7.41 (m, 3H); ^{13}C NMR δ 147.4, 136.2, 135.7, 129.8 (2C), 129.1, 129.0 (2C), 128.7, 128.6 (3C), 126.1 (2C), 119.0.

*4.2.8. 1-Methanesulfonyl-4-phenyl-1H-[1,2,3]triazole (**3i**).* It is a white solid, mp 87–89 °C (EtOAc/PE) (lit.[11c] 86–87 °C). ^{1}H NMR δ 8.31 (s, 1H), 7.88–7.85 (m, 2H), 7.47–7.41 (m, 3H), 3.57 (s, 3H); ^{13}C NMR δ 147.4, 129.3, 129.1 (2C), 128.6, 126.1 (2C), 118.9, 42.6.

4.3. A Typical procedure for the preparation of chain-product 3-ethoxy-3-(toluene-4-sulfonylimino)-propionic acid methyl ester (6b)

To a stirred solution of methyl propynoate (**1g**, 93 mg, 1.1 mmol), 4-methylbenzenesulfonyl azide (**2a**, 197 mg, 1 mmol), and 2-aminophenol (**8a**, 5.5 mg, 0.05 mmol) in EtOH (1 mL) was added $Cu(OAc)_2\cdot H_2O$ (20 mg, 0.1 mmol) at room temperature. After **2a** was exhausted (ca. 15 min, monitored by TLC), the solvent was removed off in vacuum. The residue was purified by chromatography (silica gel, 10% EtOAc in PE) to give desired product **6b** as a white solid (284 mg, 95%). It is a colorless oil. IR ν 2982, 1737, 1595, 1462 cm^{-1}; ^{1}H NMR δ 8.02 (d, J=8.6 Hz, 2H), 7.32–7.27 (m, 2H), 4.24 (q, J=6.9 Hz, 2H), 3.95 (s, 2H), 3.75 (s, 3H), 2.43 (s, 3H), 1.28 (t, J=6.9 Hz, 2H); ^{13}C NMR δ 167.5, 166.7, 143.5, 138.3, 129.3 (2C), 126.8 (2C), 65.3, 52.6, 39.7, 21.5, 13.4; MS m/z (%) 299 (M^+, 3.9), 155 (100). Anal. Calcd. For $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.72; N, 4.68. Found: C, 52.41; H, 5.57; N, 4.71.

By the similar procedure for the preparation of **6b**, products **6c**–**k** were prepared. When H_2O was used as a solvent, **6l**–**m** were prepared.

*4.3.1. 3-Ethoxy-3-(toluene-4-sulfonylimino)-propionic acid ethyl ester (**6c**).* It is a colorless oil. IR ν 2989, 1742, 1599, 1450 cm^{-1}; ^{1}H NMR δ 7.82 (d, J=8.3 Hz, 2H), 7.30 (d, J=8.3 Hz, 2H), 4.24–4.19 (m, 4H), 3.93 (s, 2H), 2.42 (s, 3H), 1.29–1.24 (m, 6H); ^{13}C NMR δ 167.8, 166.3, 143.6, 138.5, 129.5 (2C), 126.9 (2C), 65.4, 61.8, 40.1, 21.6, 14.1, 13.6. MS m/z (%) 313 (M^+, 2.3), 155 (100). Anal. Calcd. For $C_{14}H_{19}NO_5S$: C, 53.66; H, 6.11; N, 4.47. Found: C, 53.43; H, 6.02; N, 4.69.

*4.3.2. 3-Ethoxy-3-(toluene-4-sulfonylimino)-propionic acid butyl ester (**6d**).* It is a colorless oil. IR ν 2980, 1740, 1604, 1439 cm^{-1}; ^{1}H NMR δ 7.82 (d, J=8.3 Hz, 2H), 7.31–7.27 (m, 2H), 4.22 (q, J=6.9 Hz, 2H), 3.85 (s, 2H), 2.42 (s, 3H), 1.47 (s, 9H), 1.28 (t, J=7.2 Hz, 2H); ^{13}C NMR δ 168.0, 165.1, 143.2, 138.4, 129.2 (2C), 126.6 (2C), 82.3, 65.0, 41.1, 27.7 (3C), 21.3, 13.4; MS m/z (%) 312 (12), 171 (23), 155 (100). Anal. Calcd. For $C_{16}H_{23}NO_5S$: C, 56.29; H, 6.79; N, 4.10. Found: C, 56.46; H, 6.61; N, 4.23.

*4.3.3. 3-Methoxy-3-(toluene-4-sulfonylimino)-propionic acid ethyl ester (**6e**).* It is a white solid, mp 40–42 °C (EtOAc/PE). IR ν 3449, 3091, 1740, 1620, 1156 cm^{-1}; ^{1}H NMR δ 7.83 (d, J=8.3 Hz, 2H), 7.30 (d, J=8.3 Hz, 2H), 4.20 (q, J=7.2 Hz, 2H), 3.95 (s, 2H), 3.80 (s, 3H), 2.42 (s, 3H), 1.27 (t, J=7.2 Hz, 3H); ^{13}C NMR δ 168.0, 165.8, 143.3, 138.0, 129.1 (2C), 126.5 (2C), 61.4, 55.7, 39.5, 21.2, 13.7; MS m/z (%) 299 (M^+, 6), 91 (100). Anal. Calcd. For $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.72; N, 4.68. Found: C, 52.43; H, 5.57; N, 4.71.

*4.3.4. 3-Propoxy-3-(toluene-4-sulfonylimino)-propionic acid ethyl ester (**6f**).* It is a yellow oil. IR ν 3469, 3196, 1743, 1613, 1320 cm^{-1}; ^{1}H NMR δ 7.81 (d, J=8.3 Hz, 2H), 7.29 (d, J=8.3 Hz, 2H), 4.20–4.13 (m, 4H), 3.95 (s, 2H), 2.40 (s, 3H), 1.70–1.63 (m, 2H), 1.26 (t, J=7.2 Hz, 3H), 0.91 (t, J=7.2 Hz, 3H); ^{13}C NMR δ 167.6, 165.8, 143.2, 138.2, 129.1 (2C), 126.5 (2C), 70.5, 61.4, 39.7, 21.2, 21.1, 13.7, 9.9. MS m/z (%) 286 (22), 172 (18), 155 (100). Anal. Calcd. For $C_{15}H_{21}NO_5S$: C, 55.03; H, 6.47; N, 4.28. Found: C, 55.28; H, 6.36; N, 4.32.

*4.3.5. 3-Isopropoxy-3-(toluene-4-sulfonylimino)-propionic acid ethyl ester (**6g**).* It is a yellowish oil. IR ν 3469, 3196, 1743, 1612, 1318 cm^{-1}; ^{1}H NMR δ 7.81 (d, J=8.3 Hz, 2H), 7.30 (d, J=8.3 Hz, 2H), 5.14–5.10 (m, 1H), 4.22–4.15 (m, 2H), 3.91 (s, 2H), 2.42 (s, 3H), 1.28–1.23 (m, 9H); ^{13}C NMR δ 166.8, 165.8, 143.1, 138.3, 129.0 (2C), 126.3 (2C), 72.7, 61.2, 39.9, 21.1, 20.7 (2C), 13.6; MS m/z (%) 286 (9), 172 (11), 155 (84), 91 (100). Anal. Calcd. For $C_{15}H_{21}NO_5S$: C, 55.03; H, 6.47; N, 4.28. Found: C, 55.31; H, 6.40; N, 4.34.

*4.3.6. 3-Butoxy-3-(toluene-4-sulfonylimino)-propionic acid ethyl ester (**6h**).* It is a yellowish oil. IR ν 3196, 2962, 1744, 1618, 1323 cm^{-1}; ^{1}H NMR δ 7.81 (d, J=8.3 Hz, 2H), 7.29 (d, J=8.3 Hz, 2H), 4.20–4.15 (m, 4H), 3.94 (s, 2H), 2.40 (s, 3H), 1.64–1.60 (m, 2H), 1.36–1.33 (m, 2H), 1.25 (t, J=7.2 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR δ 167.5, 165.7, 143.1, 138.1, 129.0 (2C), 126.4 (2C), 68.7, 61.3, 39.6, 29.6, 21.1, 18.5, 13.6, 13.2; MS m/z (%) 286 (22), 172 (19), 155 (100). Anal. Calcd. For $C_{16}H_{23}NO_5S$: C, 56.29; H, 6.79; N, 4.10. Found: C, 56.48; H, 6.62; N, 4.35.

*4.3.7. 3-tert-Butoxy-3-(toluene-4-sulfonylimino)-propionic acid ethyl ester (**6i**).* It is a yellow oil. IR ν 3529, 3068, 1724, 1597, 1349 cm^{-1}; ^{1}H NMR δ 7.80 (d, J=8.3 Hz, 2H), 7.29 (d, J=8.3 Hz, 2H), 4.18 (q, J=7.2 Hz, 2H), 3.86 (s, 2H), 2.41 (s, 3H), 1.46 (s, 9H), 1.26 (t, J=7.2 Hz, 3H); ^{13}C NMR δ 166.3, 166.0, 143.0, 138.6, 129.2 (2C), 126.3 (2C), 86.1, 61.3, 40.8, 27.4 (3C), 21.3, 13.8; MS m/z (%) 171 (27), 155 (55), 108 (80), 91 (100). Anal. Calcd. For $C_{16}H_{23}NO_5S$: C, 56.29; H, 6.79; N, 4.10. Found: C, 56.47; H, 6.86; N, 4.01.

*4.3.8. 3-Benzenesulfonylimino-3-ethoxy-propionic acid ethyl ester (**6j**).* It is a yellowish oil. IR ν 3467, 3065, 1742, 1614, 1324 cm^{-1}; ^{1}H NMR δ 7.96–7.93 (m, 2H), 7.56–7.50 (m, 3H), 4.26–4.20 (m, 4H), 3.95 (s, 2H), 1.30–1.28 (m, 6H); ^{13}C NMR δ 167.7, 165.8, 141.0, 132.5, 128.5 (2C), 126.4 (2C), 65.1, 61.4, 39.8, 13.7, 13.2; MS m/z (%) 299 (M^+, 0.9), 254 (24), 77 (100). Anal. Calcd. For $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.72; N, 4.68. Found: C, 52.28; H, 5.92; N, 4.47.

*4.3.9. 3-Ethoxy-3-methanesulfonylimino-propionic acid ethyl ester (**6k**).* It is a yellowish oil. IR ν 3468, 2987, 1743, 1622, 1308 cm^{-1}; ^{1}H NMR δ 4.41–4.18 (m, 4H), 3.86 (s, 2H), 3.07 (s, 3H), 1.50–1.22 (m, 6H); ^{13}C NMR δ 168.2, 166.2, 65.2, 61.6, 42.3, 39.9, 13.9, 13.4; MS m/z (%) 237 (M^+, 0.7), 86 (100). Anal. Calcd. For $C_8H_{15}NO_5S$: C, 40.50; H, 6.37; N, 5.90. Found: C, 40.78; H, 6.42; N, 5.76.

*4.3.10. 3-Oxo-3-(toluene-4-sulfonylamino)-propionic acid ethyl ester (**6l**).* Mp 97–99 °C (lit.[15] 97–98 °C). ^{1}H NMR δ 10.07 (s, 1H), 7.96 (d, J=8.3 Hz, 2H), 7.33 (d, J=8.3 Hz, 2H), 4.20 (q, J=7.2 Hz, 2H), 3.35 (s, 2H), 2.43 (s, 3H), 1.27 (t, J=7.2 Hz, 3H); ^{13}C NMR δ 167.4, 163.7, 144.9, 135.1, 129.3 (2C), 128.1 (2C), 61.9, 41.8, 21.3, 13.6.

*4.3.11. 3-Methanesulfonylamino-3-oxo-propionic acid ethyl ester (**6m**).* It is a yellowish solid, mp 57–59 °C (EtOAc/PE). IR ν 3196, 3030, 1738, 1691, 1348 cm^{-1}; ^{1}H NMR δ 9.97 (s, 1H), 4.26 (q, J=7.2 Hz, 2H), 3.47 (s, 2H), 3.32 (s, 3H), 1.32 (t, J=7.2 Hz, 3H); ^{13}C NMR δ 167.7, 164.9, 62.2, 41.7, 41.2, 13.8; MS m/z (%) 209 (M^+, 1), 80

(100). Anal. Calcd. For $C_6H_{11}NO_5S$: C, 34.44; H, 5.30; N, 6.69. Found: C, 34.62; H, 5.38; N, 6.44.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (21072112).

Supplementary data

Supplementary data (^1H and ^{13}C NMR spectra for products **3a**–**i** and **6b**–**m**) associated with this article can be found in the online version at doi:10.1016/j.tet.2011.06.017.

References and notes

1. Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599.
2. Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057–3064.
3. For reviews, see: (a) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302–1315; (b) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952–3015; (c) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51–68.
4. Bae, I.; Han, H.; Chang, S. *J. Am. Soc. Chem.* **2005**, *127*, 2038–2039.
5. (a) Yoo, E. J.; Bae, I.; Cho, S. H.; Han, H.; Chang, S. *Org. Lett.* **2006**, *8*, 1347–1350; (b) Cho, S. H.; Yoo, E. J.; Bae, I.; Chang, S. *J. Am. Chem. Soc.* **2005**, *127*, 16046–16047.
6. For more Chang's works, see: (a) Yoo, E. J.; Park, S. H.; Lee, S. H.; Chang, S. *Org. Lett.* **2009**, *11*, 1155–1158; (b) Cho, S. H.; Chang, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 2836–2839; (c) Kim, J. Y.; Kim, S. H.; Chang, S. *Tetrahedron Lett.* **2008**, *49*, 1745–1749; (d) Yoo, E. J.; Chang, S. *Org. Lett.* **2008**, *10*, 1163–1166; (e) Kim, J.; Lee, Y.; Lee, J.; Do, Y.; Chang, S. *J. Org. Chem.* **2008**, *73*, 9454–9457; (f) Cho, S. H.; Chang, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 1897–1900.
7. For selected references, see: (a) Jin, H.; Xu, X.; Gao, J.; Zhong, J.; Wang, Y. *Adv. Synth. Catal.* **2010**, *352*, 347–350; (b) Lee, M. Y.; Kim, M. H.; Kim, J.; Kim, S. H.; Kim, B. T.; Jeong, I. H.; Chang, S.; Kim, S. H.; Chang, S.-Y. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 541–545; (c) Shang, Y.; Ju, K.; He, X.; Hu, J.; Yu, S.; Zhang, M.; Liao, K.; Wang, L.; Zhang, P. *J. Org. Chem.* **2010**, *75*, 5743–5745; (d) Song, W.; Lu, W.; Wang, J.; Lu, P.; Wang, Y. *J. Org. Chem.* **2010**, *75*, 3481–3483; (e) Yao, W.; Pan, L.; Zhang, Y.; Wang, G.; Wang, X.; Ma, C. *Angew. Chem., Int. Ed.* **2010**, *49*, 9210–9214; (f) Shen, Y.; Cui, S.; Wang, J.; Chen, X.; Lu, P.; Wang, Y. *Adv. Synth. Catal.* **2010**, *352*, 1139–1144; (g) Lu, W.; Song, W. Z.; Hong, D.; Lu, P.; Wang, Y. G. *Adv. Synth. Catal.* **2009**, *351*, 1768–1772; (h) Shang, Y.; He, X.; Hu, J.; Wu, J.; Zhang, M.; Yu, S.; Zhang, Q. *Adv. Synth. Catal.* **2009**, *351*, 2709–2713; (i) Cui, S.; Wang, J.; Wang, Y. G. *Tetrahedron* **2008**, *64*, 487–492; (j) Cui, S.; Wang, J.; Wang, Y. G. *Org. Lett.* **2008**, *10*, 1267–1269; (k) Cui, S.; Wang, J.; Wang, Y. G. *Org. Lett.* **2007**, *9*, 5023–5025; (l) Xu, X.; Cheng, D.; Li, J.; Guo, H.; Yan, J. *Org. Lett.* **2007**, *9*, 1585–1587; (m) Mandal, S.; Gauniyal, H. M.; Pramanik, K.; Mukhopadhyay, B. *J. Org. Chem.* **2007**, *72*, 9753–9756; (n) Cassidy, M. P.; Raushel, J.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2006**, *45*, 3154–3157; (o) Whiting, M.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2006**, *45*, 3157–3161; (p) Cui, S.; Lin, X. F.; Wang, Y. G. *Org. Lett.* **2006**, *8*, 4517–4520.
8. (a) Yoo, E. J.; Ahlquist, M.; Bae, I.; Sharpless, K. B.; Fokin, V. V.; Chang, S. *J. Org. Chem.* **2008**, *73*, 5520–5528; (b) Yoo, E. J.; Ahlquist, M.; Kim, S. H.; Bae, I.; Fokin, V. V.; Sharpless, K. B.; Chang, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 1730–1733.
9. (a) Keith, J. M. *J. Org. Chem.* **2010**, *75*, 2722–2725; (b) Yamauchi, M.; Miura, T.; Murakami, M. *Heterocycles* **2010**, *80*, 177–181.
10. (a) Grimster, N. P.; Zhang, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2010**, *132*, 2510–2511; (b) Chuprakov, S.; Kwok, S. W.; Zhang, L.; Lercher, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2009**, *131*, 18034–18035; (c) Miura, T.; Yamauchi, M.; Murakami, M. *Chem. Commun.* **2009**, 1470–1471; (d) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 14972–14974.
11. (a) Raushel, J.; Fokin, V. V. *Org. Lett.* **2010**, *12*, 4952–4955; (b) Cano, I.; Nicasio, M. C.; Pérez, P. J. *Org. Biomol. Chem.* **2010**, *8*, 536–538; (c) Wang, F.; Fu, H.; Jiang, Y.; Zhao, Y. *Adv. Synth. Catal.* **2008**, *350*, 1830–1834.
12. Nolte, C.; Mayer, P.; Straub, B. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 2101–2103.
13. (a) Shao, C.; Wang, X.; Xu, J.; Zhao, J.; Zhang, Q.; Hu, Y. *J. Org. Chem.* **2010**, *75*, 7002–7005; (b) Shao, C.; Cheng, G.; Su, D.; Xu, J.; Wang, X.; Hu, Y. *Adv. Synth. Catal.* **2010**, *352*, 1587–1592.
14. Ainsdough, E. W.; Bingham, A. G.; Brodie, A. M.; Englebretsen, D. R.; Husbands, J. M. *J. Chem. Res., Synop.* **1988**, 60–61.
15. Huisgen, R.; Knorr, R.; Moebius, L.; Szeimies, G. *Chem. Ber.* **1965**, *98*, 4014–4021.