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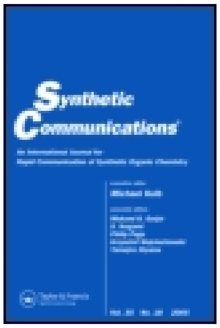

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Cu^I-Catalyzed One-Pot Three-component Huisgen Cycloaddition Reaction of Conjugated Enynes and In Situ Generated Azides

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Abstract

A novel and efficient copper(I)-catalyzed three-component Huisgen cycloaddition reaction of conjugated enynes, alkyl halides and sodium azide has been developed. These reactions were performed in the absence of amide ligands at room temperature and the corresponding mono- and bis-1,2,3-triazoles were obtained in high to excellent yields in a one-pot procedure.

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KEYWORDS: Click chemistry, conjugated enynes, Cu(I) catalysis, triazoles, bis-triazoles

INTRODUCTION

Since the paramount discovery of the Cu(I)-catalyzed 1,3-dipolar azide-alkyne cycloaddition (CuAAC) by the groups of Sharpless and Meldal independently,[1] the

CuAAC reaction has found a myriad of applications in chemical synthesis, biology and material science.[2] Recent efforts to further develop CuAAC have focused on one-pot multicomponent reactions in which azides are obtained in situ prior to the cycloaddition. The attraction of such an approach is that it avoids the isolation and handling of hazardous azides and minimized time-consuming workup and purification protocols. However, in contrast to many examples of one-pot multicomponent alkyne-azide cycloaddition,[3] the Cu(I)-catalyzed three-component cycloaddition of conjugated enynes and in situ generated azides is scarcely reported. To the best of our knowledge, only three examples of three-component cycloaddition of conjugated enynes with in situ generated azides have been reported by the groups of Fokin, Nielsen and Liang, but these reactions need to be operated by heating, microwave heating or the use of mixture ionic liquids and water as reaction media.[4] Herein, we report a copper(I)-catalyzed one-pot three-component Huisgen cycloaddition of conjugated enynes, alkyl halides and sodium azide at room temperature in DMSO-H_2O solvent system.

Over the past decades, the potential of α-oxo ketene-*S,S*-acetals as versatile intermediates in organic synthesis has been recognized.[5] During the course of our studies on the chemistry of functionalized ketene dithioacetals,[6] a series of α-mono-, and di-ethynyl ketene *S,S*-acetals **1** (Tables 1 -3) were prepared in high yields starting from easily available □-oxoketene dithioacetals under mild conditions.[7] As synthetic applications of these electron-rich conjugated enynes, we have described the self-coupling reactions of these conjugated enynes [8] and the addition reactions of these conjugated enynes with o-phenylenediamines[9a] and carboxylic acids,[9b] respectively. Recently, the [4+2] cycloaddition reaction of these enynes with *N*-arylimines was also performed successively in the presence of trifluoromethanesulfonic acid.[10] Encouraged by these results, together with the consideration of importance of the click chemistry,[1-4] we paid our attention to the [3+2] cycloaddition reaction of these electron-rich conjugated enynes **1** with organic azides. Herein, we wish to report the results in this area.

RESULTS AND DISCUSSION

In the present study, initially, the model reaction of enyne **1a** (1.0 equiv), ethyl 2-bromoacetate (1.0 equiv) and NaN_3 (1.2 equiv) was examined to optimized the reaction conditions (Table 1). It was found that, the three-component cycloaddition reaction could easily proceed to give the 1,2,3-triazoles **3a1** in 52% yield in the presence of 3 mol% of CuI in DMSO at room temperature for 8 h under N_2 atmosphere (Table 1, entry 1). To our delight, the yield of **3a1** was raised to 93% with shorter reaction time (1h) when the reaction was performed in a 1:1 mixture of DMSO and H_2O (Table 1, entry 2). However, further decreasing a catalytic amount of CuI led to relatively lower yield of **3a1** (Table 1, entry 3). Among other solvent systems tested, such as DMSO/H_2O (v/v, 1:2) and C_2H_5OH/H_2O (v/v, 1:1), gave lower product yields (Table 1, entries 4 and 5). No reaction was observed when the reaction was carried out in C_2H_5OH or H_2O (Table 1, entries 6 and 7). Meanwhile, when other simple copper salts, such as CuBr and CuCl, were chosen as catalyst for this process, a relatively lower yield of **3a1** was obtained under otherwise identical reaction conditions (Table 1, entries 8 and 9).

Under the optimal conditions, the scope of the reaction was then investigated and the results are summarized in Table 2. It was obvious that this three-component reaction shows wide applicability for various alkyl halides **2**. As a result, various alkyl bromides such as ethyl 2-bromoacetate, 2-bromoacetonitrile, 2-bromoacetophenones with either electron-neutral, electron-deficient, or electron-rich groups, 2-bromo-1-(naphthalen-2-yl)ethanone, 1-(biphenyl-4-yl)-2-bromoethanone, benzyl bromide bearing either electron-neutral, electron-deficient, or electron-rich groups, reacted quickly with **1a** and NaN_3 to give the corresponding 1,2,3-triazoles **3a1-10** in excellent yields (Table 2, entries 1-10). Notably, in the case of benzyl chloride, the three-component reaction also worked well, yielding the desired product **3a8** in 90% yield (Table 2, entry 11). Similarly, the desired 1,2,3-triazole **3b1** could be prepared in 90% yield from the substrate **1b** (Table 2, entry 12). However, 1-bromobutane remained inert to the three-component cycloaddition reaction under otherwise identical reaction conditions (Table 2, entry 13).

With azide-[3+2] cycloaddition reactions of conjugated enynes firmly established, we further examined a potential approach for achieving double cycloadditions to construct novel bis-triazoles. As expected, the bis-1,2,3-triazoles **3c1-5** could be assembled in high yields in a one-pot procedure by reacting conjugated enyne **1c** with various alkyl bromides **2** and NaN_3 at room temperature for 24 h under otherwise identical reaction conditions as above (Table 3, entries 1-5).

On the basis of the above experimental results together with the related reports,[1-4,9] the reaction mechanism for the formation **3** is proposed in Scheme 1. Owing to the strong electron-donating effect of the alkylthio (S-C *sp*^{2}-conjugation), the terminal carbon atom of **1** is believed to be more electron-rich, which favors the formation of copper (I) acetylide **A** even in the absence of amines.[11] Then the azide, generated by the SN2 reaction of NaN_3 with alkyl halides, coordinates to intermediate **A**, leading to the formation of intermediate **B**, wich undergoes an intramolecular cyclization reaction to give the intermediate **D**. Finally, metalated heterocycle **D** undergoes protonolysis, delivering the desired product **3a** and **3b** and regenerating the catalyst (Scheme 1). In the case of diyne **1c**, the monotriazole generated reacts sequentially with another in situ generated azides to give the bis-1,2,3-triazoles **3c** (Scheme 1).[12]

In conclusion, we have demonstrated a novel and efficient copper(I)-catalyzed three-component Huisgen cycloaddition reaction of conjugated enynes, alkyl halides, and sodium azide. These reactions were performed in the absence of amide ligands at room temperature and the corresponding mono- and bis-1,2,3-triazoles were obtained in high to excellent yields in a one-pot procedure. The procedure avoids isolation and handling of organic azide, making this already powerful click process even more user-friendly and safe. Further studies are in progress.

EXPERIMENTAL SECTION

All reagents were commercial and were used without further purification. Chromatography was carried on flash silica gel (300-400 mesh). All reactions were monitored using TLC on silica gel plates. The ^{1}H NMR spectra were recorded at 500 MHz in $CDCl_3$ and the ^{13}C NMR spectra were recorded at 125 MHz in $CDCl_3$ or DMSO-d_6. All coupling constants (*J* values) were reported in Hertz (Hz). IR (KBr) spectra were recorded on in the range of 400~4000 cm^{-1}. High-resolution mass spectra (HRMS) were obtained using a Bruker microTOF II focus spectrometer (ESI).

General Procedure For The Preparation Of 3 (3a1 As Example)

Under a nitrogen atmosphere, CuI (0.03 mmol, 5.7 mg) was added in one portion to a stirred solution of **1a** (1.0 mmol, 214 mg), ethyl 2-bromoacetate (1.0 mmol, 0.11 mL), NaN_3 (1.2 mmol, 78 mg) in DMSO and H_2O (8.0 mL, 1:1). The reaction mixture was stirred for 1.0 h at room temperature. After **1a** was consumed (monitored by TLC), the reaction mixture was poured into water (40 mL) under stirring. The precipitated solid was collected by filtration, and dried in vacuo to afford the crude product, which was purified by a short chromatography column (silica gel, petroleum ether/acetone/dichloromethane = 6/1/1) to give **3a1** (319 mg, 93 %) as a white solid. mp 122–124 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.30 (t, J = 7.0 Hz, 3H), 2.18 (q, J = 7.0 Hz, 2H), 2.89 (t, J = 7.0 Hz, 2H), 3.01 (t, J = 7.0 Hz, 2H), 3.72 (s, 3H), 4.27 (q, J = 7.0 Hz, 2H), 5.19 (s, 2H), 7.66 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.3, 23.8, 29.6, 29.9, 51.2, 52.0, 62.6, 111.5, 125.3, 143.3, 163.6, 165.3, 166.4; IR (KBr, cm-^{1}): 3143, 2928, 1759, 1691, 1480, 1375, 1361, 1219, 1075; HRMS (ESI-TOF) calcd for $C_{13}H_{18}N_3O_4S_2^+$ ($[M + H]^+$): 344.0733, found: 344.0734.

Complete experimental details can be found online in the Supporting Information.

ACKNOWLEDGMENT

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REFERENCES

(1) (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, B. K. A stepwise Huisgen cycloaddition process: copper(I)-catalyzed regioselective“ligation” of azides and terminal alkynes. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599; (b) Tornøe, C. W.; Christensen, C.; Meldal, M. Peptidotriazoles on solid phase: [1,2,3]-triazoles by regiospecific copper(I)-catalyzed 1,3-dipolar cycloadditions of terminal alkynes to azides. *J. Org. Chem.* **2002**, *67*, 3057–3064.

(2) For reviews, see: (a) Meldal, M.; Tornøe, C. W. Cu-catalyzed azide-alkyne cycloaddition. *Chem. Rev.* **2008**, *108*, 2952–3015; (b) Spiteri, C.; Moses, J. E. Copper-catalyzed azide–alkyne cycloaddition: regioselective synthesis of 1,4,5-trisubstituted 1,2,3-triazoles. *Angew. Chem. Int. Ed.* **2010**, *49*, 31–33; (c) Hein, J. E.; Fokin, V. V. Copper-catalyzed azide–alkyne cycloaddition (CuAAC) and beyond: new reactivity of copper(I) acetylides. *Chem. Soc. Rev.* **2010**, *39*, 1302–1315; (d) Kappe, C. O.; der Eycken, E. V. Click chemistry under non-classical reaction conditions. *Chem. Soc. Rev.* **2010**, *39*, 1280–1290; (e) Hänni, K. D.; Leigh, D. A. The application of CuAAC ‘click’ chemistry to catenane and rotaxane synthesis. *Chem. Soc. Rev.* **2010**, *39*, 1240–1251; (f) Le Droumaguet, C.; Wang, C.; Wang, Q. Fluorogenic click reaction. *Chem. Soc. Rev.* **2010**, *39*, 1233–1239; (g) Mamidyala, S. K.; Finn, M. G. In situ click chemistry: probing the binding landscapes of biological molecules. *Chem. Soc. Rev.* **2010**, *39*, 1252–1261; (h) Holub, J. M.; Kirshenbaum, K. Tricks with clicks: modification of peptidomimetic oligomers via copper-catalyzed azide-alkyne [3 + 2] cycloaddition. *Chem. Soc. Rev.* **2010**, *39*, 1325–1337; (i) Ackermann, L.; Potukuchi, H. K. Regioselective syntheses of fully-substituted 1,2,3-triazoles: the CuAAC/C–H bond functionalization nexus. *Org. Biomol. Chem.* **2010**, *8*, 4503–4513; (j) Gil, M. V.; Arévalo, M. J.; López, Ó. Click chemistry – what’s in a name? triazole synthesis and beyond. *Synthesis* **2007**, 1589–1620; (k) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. Cu^{I}-catalyzed alkyne–azide “click” cycloadditions from a mechanistic and synthetic perspective. *Eur. J. Org. Chem.* **2006**, 51–68.

(3) (a) Wang, Y.; Liu, J.; Xia, C. Insights into supported copper(II)-catalyzed azide-alkyne cycloaddition in water. *Adv. Synth. Catal.* **2011**, *353*, 1534–1542; (b) Lal, S.; Díez-González, S. [$CuBr(PPh_3)_3$] for azide-alkyne cycloaddition reactions under strict click conditions. *J. Org. Chem.* **2011**, *76*, 2367–2373; (c) Friscourt, F.; Boons, G.-J. One-pot three-step synthesis of 1,2,3-triazoles by copper-catalyzed cycloaddition of azides with alkynes formed by a Sonogashira cross-coupling and desilylation. *Org. Lett.* **2010**, *12*, 4936–4939; (d) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. Multicomponent synthesis of 1,2,3-triazoles in water catalyzed by copper nanoparticles on activated carbon. *Adv. Synth. Catal.* **2010**, *352*, 3208–3214; (e) Wang, D.; Li, N.; Zhao, M.; Shi, W.; Ma, C.; Chen, B. Solvent-free synthesis of 1,4-disubstituted 1,2,3-triazoles using a low amount of $Cu(PPh_3)_2NO_3$ complex. *Green Chem.* **2010**, *12*, 2120–2123; (f) Yamaguchi, K.; Kotani, M.; Kamata, K.; Mizuno, N. An efficient one-pot three-component reaction to produce 1,4-disubstituted-1,2,3-triazoles catalyzed by a dicopper-substituted silicotungstate. *Chem. Lett.* **2008**, *37*, 1258–1259; (g) Ackermann, L.; Potukuchi, H. K.; Landsberg, D.; Vicente, R. Copper-catalyzed “click” reaction/ direct arylation sequence: modular syntheses of 1,2,3-triazoles. *Org. Lett.* **2008**, *10*, 3081–3084; (h) Molander, G. A.; Ham, J. Synthesis of functionalized organotrifluoroborates via the 1,3-dipolar cycloaddition of azides. *Org. Lett.* **2006**, *8*, 2767–2770; (i) Zhang, X.; Li, H.; You, L.; Tang, Y.; Hsung, R. P. Copper salt-catalyzed azide-[3 + 2] cycloadditions of ynamides and bis-ynamides. *Adv. Synth. Catal.* **2006**, *348*, 2437–2442; (j) Odlo, K.; Høydahl, E. A.; Hansen, T. V. One-pot synthesis of

1,4-disubstituted 1,2,3-triazoles from terminal acetylenes and in situ generated azides. *Tetrahedron Lett.* **2007**, *48*, 2097–2099; (k) Feldman, A. K.; Colasson, B.; Fokin, V. V. One-pot synthesis of 1,4-disubstituted 1,2,3-triazoles from in situ generated azides. *Org. Lett.* **2004**, *6*, 3897–3899; (l) Appukkuttan, P.; Dehaen, W.; Fokin, V. V.; der Eycken, E. V. A microwave-assisted click chemistry synthesis of 1,4-disubstituted 1,2,3-triazoles via a copper(I)-catalyzed three-component reaction. *Org. Lett.* **2004**, *6*, 4223–4225.

(4) (a) Feldman, A. K.; Colasson, B.; Fokin, V. V. One-pot synthesis of 1,4-disubstituted 1,2,3-triazoles from in situ generated azides. *Org. Lett.* **2004**, *6*, 3897–3899; (b) Kočalka, P.; Andersen, N. K.; Jensen, F.; Nielsen, P. Synthesis of 5-(1,2,3-Triazol-4-yl)-2’-deoxyuridines by a click chemistry approach: stacking of triazoles in the major groove gives increased nucleic acid duplex stability. *Chem. Bio. Chem.* **2007**, *8*, 2106–2116; (c) Zhao, Y.-B.; Yan, Z.-Y.; Liang, Y.-M. Efficient synthesis of 1,4-disubstituted 1,2,3-triazoles in ionic liquid/water system. *Tetrahedron Lett.* **2006**, *47*, 1545–1549.

(5) For reviews, see: (a) Dieter, R. K. □-Oxo ketene dithioacetals and related compounds: versatile three-carbon synthons. *Tetrahedron* **1986**, *42*, 3029–3096; (b) Junjappa, H.; Ila, H.; Asokan, C. V. □-Oxoketene-*S,S*-, *N,S*- and *N,N*-acetals: versatile intermediates in organic synthesis. *Tetrahedron* **1990**, *46*, 5423–5506; (c) Elgemeie, G. H.; Sayed, S. H. Synthesis and chemistry of dithiols. *Synthesis* **2001**, 1747–1771; (d) Pan, L.; Liu, Q. [5+1]-Annulation strategy based on alkenoyl ketene dithioacetals and analogues. *Synlett* **2011**, 1073–1080.

(6) (a) Li, Y.; Xu, X.; Tan, J.; Xia, C.; Zhang, D.; Liu, Q. Double isocyanide cyclization: a synthetic strategy for two-carbon-tethered pyrrole/oxazole pairs. *J. Am. Chem. Soc.* **2011**, *133*, 1775–1777; (b) Tan, J.; Xu, X.; Zhang, L.; Li, Y.; Liu, Q. Tandem double Michael addition/cyclization/acyl migration of 1,4-dien-3-ones and isocyanoacetate: a new strategy for stereoselective synthesis of pyrrolizidines. *Angew. Chem., Int. Ed.* **2009**, *48*, 2868–2872; (c) Wang, H.; Zhao, Y.-L.; Ren, C.-Q.; Diallo, A.; Liu, Q. Tandem [5 + 1] annulation-isocyanide cyclization: efficient synthesis of hydroindolones. *Chem. Commun.* **2011**, *47*, 12316–12318; (d) Zhao, Y.-L.; Yang, S.-C.; Di, C.-H.; Han, X.-D.; Liu, Q. Highly efficient synthesis of 3-amino-/alkylthio-cyclobut-2-en-1-ones based on the cyclization of acyl ketene dithioacetals. *Chem. Commun.* **2010**, *46*, 7614–7616; (e) Zhao, Y.-L.; Chen, L.; Yang, S.-C.; Tian, C.; Liu, Q. A synthetic strategy for polyfunctionalized bicyclo[3.3.1]nonanes based on a tandem three-component [3 + 2] cycloaddition of □-cinnamoyl ketene-*S*,*S*-acetals with oxalyl chloride. *J. Org. Chem.* **2009**, *74*, 5622–5625; (f) Piao, C.-R.; Zhao, Y.-L.; Han, X.-D.; Liu, Q. $AlCl_3$-mediated direct carbon–carbon bond forming reaction of □-hydroxyketene-*S*,*S*-acetals with arenes and synthesis of 3,4-disubstituted dihydrocoumarin derivatives. *J. Org. Chem.* **2008**, *73*, 2264–2269; (g) Chen, L.; Zhao, Y.-L.; Liu, Q.; Chen, C.; Piao, C.-R. Domino reaction of α-acetyl-α-carbamoyl ketene dithioacetals with vilsmeier reagents: a novel and efficient synthesis of 4-halogenated 2(1*H*)-pyridinones. *J. Org. Chem.* **2007**, *72*, 9259–9263.

(7) Dong, D.; Liu, Y.; Zhao, Y.-L.; Qi, Y.; Wang, Z.; Liu, Q. Vilsmeier-Haack reaction of α-oxo ketene dithioacetals to α-chlorovinyl/ethynyl ketene dithioacetals. *Synthesis* **2005**, 85–91.

(8) (a) Zhao, Y.-L.; Liu, Q.; Zhang, J.-P.; Liu, Z.-Q. Heteroatom-substituted expanded radialenes: one-pot synthesis and characterization of expanded 1,3-dithiolane[*n*]radialenes. *J. Org. Chem.* **2005**, *70*, 6913–6917; (b) Zhao, Y.-L.; Zhang, W.; Zhang, J.-Q.; Liu, Q. A new route to extended tetrathiafulvalenes from □-acetyl ketene-*S,S*-acetals. *Tetrahedron Lett.* **2006**, *47*, 3157–3159.

(9) (a) Zhao, Y.-L.; Li, D.-Z.; Han, X.-D.; Chen, L.; Liu, Q. Proton-promoted hydroamination of 3-dialkylthiomethylene-1,4-pentadiynes with o-phenylenediamines: a facile route to benzo[b] [1,4]diazepines. *Adv. Synth. Catal.* **2008**, *350*, 1537–1543; (b) Zhao, Y.-L.; Liu, Q.; Zhang, Y.-F.; Sun. S.-G.; Li, Y.-N. Chemo- and regioselective addition of carboxylic acid to the alkylthio activated enyne triple bond in the absence of catalysts. *Synlett* **2006**, 231–234.

(10) Zhao, Y.-L.; Zhang, W.; Wang, S.; Liu, Q. Ethynyl ketene-*S*,*S*-acetals: the highly reactive electron-rich dienophiles and applications in the synthesis of 4-functionalized quinolines via a one-pot three-component reaction. *J. Org. Chem.* **2007**, *72*, 4985–4988.

(11) Shao, C.; Wang, X.; Zhang, Q.; Luo, S.; Zhao, J.; Hu, Y. Acid-base jointly promoted copper(I)-catalyzed azide-alkyne cycloaddition. *J. Org. Chem.* **2011**, *76*, 6832–6836.

(12) Rodionov, V. O.; Fokin, V. V.; Finn, M. G. Mechanism of the ligand-free Cu^I-catalyzed azide–alkyne cycloaddition reaction. *Angew. Chem., Int. Ed.* **2005**, *44*, 2210–2215.

Table 1. Optimization of reactin conditions

Entry	Catalyst (mol%)	Solvent	Time (h)	**3a1** Yield[a] (%)
1	CuI (3)	DMSO	8	52
2	CuI (3)	DMSO-H_2O (v/v, 1/1)	1	93
3	CuI (2)	DMSO-H_2O (v/v, 1/1)	3	81
4	CuI (3)	DMSO-H_2O (v/v, 1/2)	8	61
5	CuI (3)	C_2H_5OH-H_2O (v/v, 1/1)	24	40
6	CuI (3)	C_2H_5OH	24	0
7	CuI (3)	H_2O	24	0
8	CuBr (3)	DMSO-H_2O (1/1)	1	76
9	CuCl (3)	DMSO-H_2O (1/1)	1	82

[a] Isolated yields.

Table 2. One-pot synthesis of 1,2,3-triazoles 3a and 3b from alkyl halides, NaN$_3$, and enynes 1a and 1b[a]

Entry	**1**	R	n	R^1	X	Time (h)	Product	Yield[b] (%)
1	**1a**	CO$_2$Me	2	C$_2$H$_5$OCO	Br	1.0	**3a1**	93
2	**1a**	CO$_2$Me	2	CN	Br	1.0	**3a2**	92
3	**1a**	CO$_2$Me	2	C$_6$H$_5$CO	Br	1.5	**3a3**	90
4	**1a**	CO$_2$Me	2	4-ClC$_6$H$_4$CO	Br	1.5	**3a4**	89
5	**1a**	CO$_2$Me	2	4-CH$_3$OC$_6$H$_4$CO	Br	1.5	**3a5**	86
6	**1a**	CO$_2$Me	2		Br	1.5	**3a6**	92
7	**1a**	CO$_2$Me	2		Br	1.5	**3a7**	90
8	**1a**	CO$_2$Me	2	C$_6$H$_5$	Br	2	**3a8**	95
9	**1a**	CO$_2$Me	2	4-NO$_2$C$_6$H$_4$	Br	1	**3a9**	97
10	**1a**	CO$_2$Me	2	4-CH$_3$C$_6$H$_4$	Br	2	**3a10**	93
11	**1a**	CO$_2$Me	2	C$_6$H$_5$	Cl	5	**3a8**	90
12	**1b**	CONHPh	1	4-ClC$_6$H$_4$CO	Br	1.5	**3b1**	90
13	**1a**	CO$_2$Me	2	CH$_3$CH$_2$CH$_2$	Br	8	**3a11**	0

[a] Reaction conditions: **1** (1.0 mmol), **2** (1.0 mmol), NaN$_3$ (1.2 mmol), 3% CuI in DMSO/H$_2$O (8.0 mL; v/v, 1:1) at room temperature.

[b] Isolated yields.

Table 3. One-pot synthesis of bis-1,2,3-triazoles 3c from alkyl bromides, NaN_3, and enyne 1c[a]

Entry	R^1	Time (h)	Product	Yield[a] (%)
1	C_2H_5OCO	24	**3c1**	85
2	CN	24	**3c2**	88
3	C_6H_5	24	**3c3**	83
4	4-$NO_2C_6H_4$	24	**3c4**	85
5	4-$CH_3C_6H_4$	24	**3c5**	80

[a] Reaction conditions: **1c** (1.0 mmol), **2** (2.0 mmol), NaN_3 (2.2 mmol), 3% CuI in DMSO/H_2O (10.0 mL; v/v, 1:1) at room temperature.

[b] Isolated yields.

Scheme 1. Proposed mechanism for the formation of 3