One-Pot Synthesis of Substituted Furans Using $Cu(OTf)_2$-Catalyzed Propargylation/Cycloisomerization Tandem Reaction

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A convenient one-pot propargylation/cycloisomerization tandem process has been developed for the synthesis of substituted furans derivatives from 1,3-dicarbonyl compounds and enoxysilanes with propargylic alcohols or acetates using copper(II) triflate as a bifunctional catalyst. This method provides a flexible and rapid route to substituted furans.

Introduction

Tandem processes that involve multiple chemical transformations in a single-pot with minimal work up and less waste generation have revolutionized synthetic chemistry in recent years.[1] Especially, the finding and utilization of a single catalyst to promote more than one transformation in a selective manner is a promising area of research.[2] Such direct synthesis routes help to avoid side product formation and loss of starting material as well as to reduce capital investment and operation costs.

Because it has attracted interest for well over a century, the field of furan synthesis is continuously and rapidly developing. In general, substituted furans are accessed via ring derivatization or cyclization of acyclic precursors.[3−5] Among the variety of compounds that can be subjected to cyclization, unsaturated alcohols or ketones are substrates of major interest.[4,5] Recently, efficient propargylation/cycloisomerization sequential reactions of propargylic alcohols with ketones or 1,3-dicarbonyl compounds in the presence of $[Cp^*RuCl(\mu_2\text{-}SMe)_2RuCp^*Cl]/PtCl_2$,[6] CF_3CO_2H/Ru(II),[7] or $TsOH/K_2CO_3$,[8] which lead to the synthesis of substituted furans, have been reported. However, these methods are only applicable to a relatively narrow range of substrates, and that two catalysts are needed. More recently, Tan[9] described an efficient method to synthesize tetrasubstituted furans via In-catalyzed propargylation/cyclization process, but the reaction is performed under N_2 atmosphere and required rather long time for completion. On the other hand, the carbon-centered nucleophiles of In-catalyzed propargylation/cyclization process are limited to 1,3-dicarbonyl compounds. As the results of development on the transition-metal-catalyzed propargylic substitution reaction in our group,[10] herein, we wish to report a highly efficient propargylation/cycloisomerization tandem reaction for the synthesis of substituted furans directly from 1,3-dicarbonyl compounds or enoxysilanes with propargylic alcohols or acetates using copper(II) triflate as catalyst. The process is outlined in Scheme 1. $Cu(OTf)_2$ acts as a bifunctional catalyst and effectively catalyzes two reaction processes in a single reaction vessel under the same conditions. The reaction completes rapidly under mild conditions and air is tolerant. A wide range of secondary propargylic alcohols or acetates bearing not only terminal alkyne group but also internal alkyne group can effectively be employed and a number of functionalities, such as bromo, ester, cyano, and methoxyl, are tolerated under the reaction conditions. In addition, both 1,3-dicarbonyl compounds and enoxysilanes may be used as carbon-centered nucleophiles in this protocol, producing tetrasubstituted furans and trisubstituted furans in good yields.

Results and Discussion

Reaction of propargylic alcohol **1a** (**1** X = OH; R^1 = 1-Naphthyl; R^2 = TMS) with ethyl acetoacetate **3a** (**3** R^3 = Me; R^4 = OEt) under the reaction conditions (5 mol % $Cu(OTf)_2$, toluene, rt), produced only low yield of the coupling product **4a** (**4** R^1 = 1-Naphthyl; R^2 = TMS; R^3 = Me; R^4 = OEt), and no cycloisomerization product **5aa** (**5** R^1 = 1-Naphthyl; R^2 = H; R^3 = Me; R^4 = OEt) was obtained. Gratifyingly, the tandem propargylic substitution/cycloisomerization proceeded well at reflux temperature for 10 min, affording a 30% isolated yield of **5aa** and a 56% isolated yield of **4a**, which could be completely converted to **5aa** by extending the reaction time from 10 to 30 min.

With these conditions in hand, we investigated the reaction of propargylic alcohols **1a**−**1c** (R^1 = 1-Naphthyl) with various 1,3-dicarbonyl compounds. Typical results are shown in Table 1. To our delight, all the secondary propargylic alcohols **1a**−**1c** bearing not only terminal alkyne group but also internal alkyne group participated well in the reaction, producing the propargylation/cycloisomerization products in good yields. The reaction proceeded smoothly under mild conditions and air was tolerant. These were in sharp contrast to the ruthenium catalyzed process,[6,7] where the reactions were performed under N_2 atmosphere and the substrates were limited to propargylic alcohols bearing terminal alkyne group, as well as the reaction required rather long time for completion. In addition, when $TsOH/K_2CO_3$ was employed

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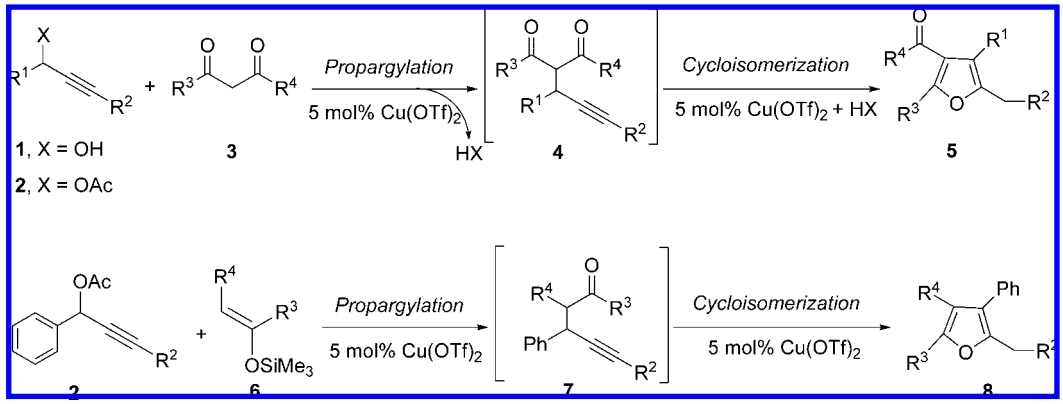
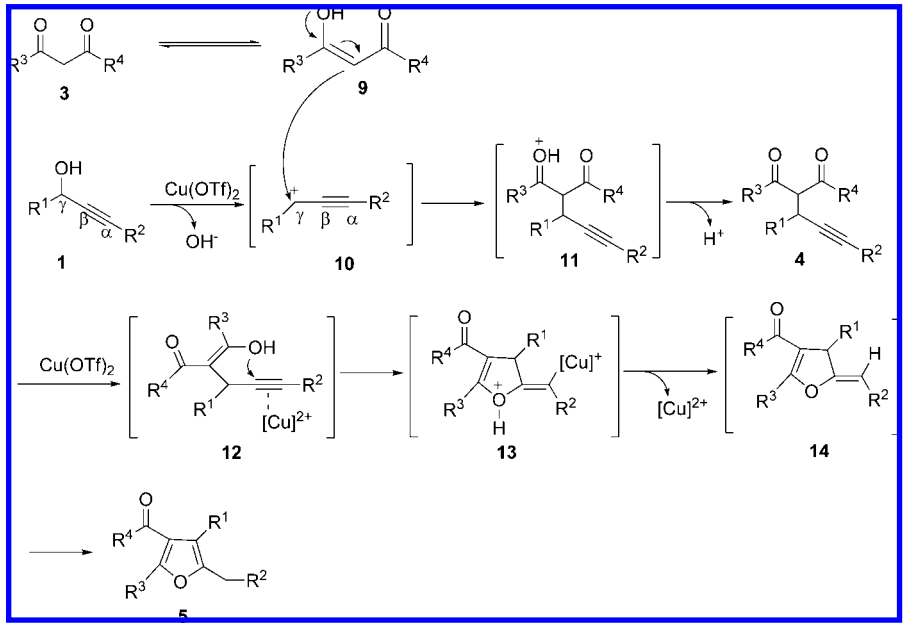
Scheme 1. Sunthesis of Furans from 1,3-Dicarbonyl Compounds or Enoxysilanes with Propargylic Alcohols or Acetates



Scheme 2. Proposed Mechanism for the Propargylation/Cycloisomerization Tandem Reaction

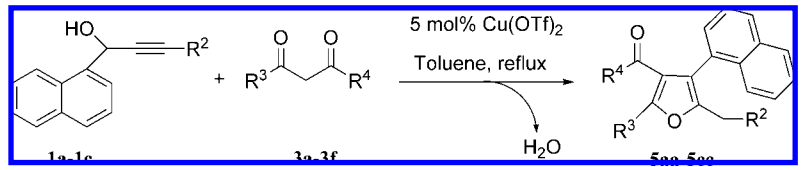


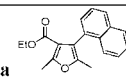
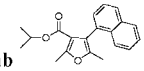
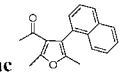
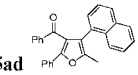
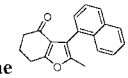
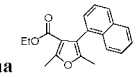
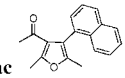
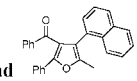
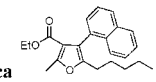
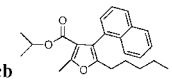
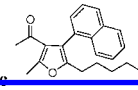
as catalyst, there were only five cases reported and the substrates were limited to propargylic alcohols bearing internal alkyne group.[8]

We propose the sequence outlined in Scheme 2 as the likely mechanism for the propargylation/cycloisomerization tandem reaction. First, the ionization of propargylic alcohols **1** would lead to propargylic cation **10** and the subsequent nucleophilic attack of the enol **9** gives γ-alkynyl ketone **4.** Coordination of cationic copper(II) to the alkyne forms the π-alkyne copper complex **12** and enhances the electrophilicity of alkyne. Subsequent 5-exo-dig nucleophilic attack of the hydroxy group on β-carbon of Cu(II)-alkyne complex **12** would generate the alkenyl-copper derivative **13**. Protonolysis of **13** affords dihydrofuran **14**, which then undergoes isomerization to furan **5**.

This proposed mechanism makes the prediction that the high enol content of 1,3-dicarbonyl compounds favors both propargylic substitution and cycloisomerization process, and therefore, the order of 1,3-dicarbonyl compound reactivity would appear to follow the general trend **3d** > **3c** > **3a**, **3b** > **3f**.[11] Indeed, among the 1,3-dicarbonyl compounds that were examined, β-diketones **3d** and **3c** gave the most desirable result (Table 1, entries 3, 4, 8, 9, and 12), and β-keto esters **3a** and **3b** also gave the propargylation/cycloisomerization products in good yields with complete regioselectivity (Table 1, entries 1, 2, 7, 10, and 11). However, by using diethyl malonate **3f**, none of the furan was observed (Table 1, entry 6). These are in accord with the proposed mechanism. Nevertheless, compared with β-keto esters **3a** and **3b**, 1,3-cyclohexanedione **3e** reacted more sluggishly to give the propargylation/cycloisomerization products in lower yields (Table 1, entry 5 vs entries 1 and 2), possibly because of the steric bulkiness of **3e**. In addition, among the propargylic alcohols that were examined, propargylic alcohol **1a** (R^2 = TMS) gave the most desirable result, providing the furans **5aa**−**5ae** in high to excellent yields (Table 1, entries 1−5). The γ-effect and β-effect of the silicon atom in **1a** may account for its high reactivity in the propargylation/cycloisomerization tandem reaction.[12] However, the trimethylsilyl group could not be tolerated under the acidic condition and had fallen off during workup, so the same product was obtained in the examples involving **1a** and **1b** (Table 1, entries 1−9). Propargylic alcohol bearing internal alkyne group (R^2 = *n*-Bu) **1c** also reacted rapidly with 1,3-dicarbonyl compound (**3a**−**3c**) affording the tetrasubstituted furans **5ca**−**5cc** in good yields (Table 1, entries 10−12).

Table 1. Synthesis of Furans **5aa**−**5cc** from Propargylic Alcohols **1a**−**1c** and 1,3-Dicarbonyl Compounds **3**[a]

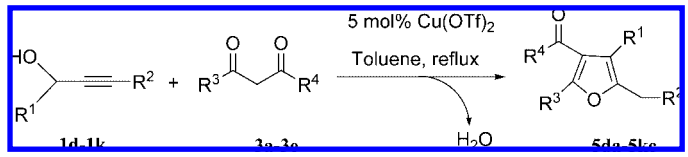


Entry	Propargylic alcohol	1,3-Dicarbonyl compound	Product	Time [h]	Isolated yield [%]
1		**3a:** $R^3 = CH_3$; $R^4 = OEt$	**5aa** 	0.5	86
2		**3b:** $R^3 = CH_3$; $R^4 = O$-*i*-Pr	**5ab** 	0.5	84
3		**3c:** $R^3 = R^4 = CH_3$	**5ac** 	0.2	90
	1a: R^2 = TMS				
4		**3d:** $R^3 = R^4 = Ph$	**5ad** 	0.2	93
5		**3e:** $R^3 = R^4 = -(CH_2)_3-$	**5ae** 	2	73
6		**3f:** $R^3 = OEt$; $R^4 = OEt$	—	24	0[b]
7		**3a:** $R^3 = CH_3$; $R^4 = OEt$	**5aa** 	1	71
8	**1b:** R^2 = H	**3c:** $R^3 = R^4 = CH_3$	**5ac** 	0.8	76
9		**3d:** $R^3 = R^4 = Ph$	**5ad** 	0.5	81
10		**3a:** $R^3 = CH_3$; $R^4 = OEt$	**5ca** 	0.6	75
11	**1c:** R^2 = *n*-Bu	**3b:** $R^3 = CH_3$; $R^4 = O$-*i*-Pr	**5cb** 	0.6	71
12		**3c:** $R^3 = R^4 = CH_3$	**5cc** 	0.5	80

[a] The reactions of propargylic alcohols**1** (0.5 mmol) with 1,3-dicarbonyl compounds **3** (1.5 mmol) were carried out in the presence of $Cu(OTf)_2$ (0.025 mmol) in toluene (2.0 mL) at reflux. [b] Obtained as a complex mixture.

We then extended the scope of the propargylation/cycloisomerization tandem reaction to various propargylic alcohols **1d**−**1k**, and the typical results are summarized in Table 2. A series of benzylic-propargylic alcohols as substrates were treated with 1,3-dicarbonyl compounds (**3a**−**3e**), and the corresponding tetrasubstituted furans (except **5ja** and**5jc**) were obtained in moderate to good yields. In all cases, the reactivity of various 1,3-dicarbonyl compounds followed the same trend (**3d** > **3c** > **3a**, **3b**) shown in Table 1. Furthermore, propargylic alcohol **1d** (R^2 = TMS) presented the same high reactivity as aforementioned propargylic alcohol **1a** (Table 2, entries 1−4). For example, the propargylation/cycloisomerization tandem reaction of propargylic alcohol **1d** with ethyl acetoacetate **3a** was completed rapidly to afford tetrasubstituted furan in high yield, requiring only 5 min for propargylation and 30 min total reaction time for propargylation/cycloisomerization (Table 2, entry 1). In contrast, In-catalyzed propargylation/cyclization reaction of propargylic alcohol **1d** with ethyl acetoacetate **3a** took 10 h for propargylation and 20 h total reaction time for propargylation/cycloisomerization to give tetrasubstituted furan in moderate yield.[9,13] Internal propargylic alcohols (**1f** and **1g**) possessing a phenyl and *n*-Bu group at R^2 gave the desired substituted furans in moderate to high yields (Table 2, entries 8−12). Notably, the use of 1,3-cyclohexanedione as the substrates did not lead to the

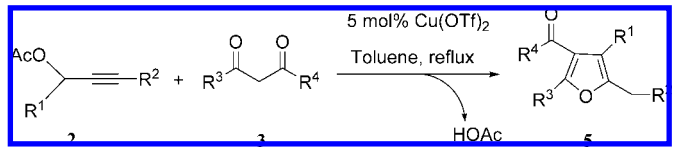
Table 2. Synthesis of Furans **5da**−**5kc** from Propargylic Alcohols **1d**−**1k** and 1,3-Dicarbonyl Compounds **3**[a]



Entry	Propargylic alcohol	1,3-Dicarbonyl compound	Product	Time [h]	Isolated yield [%]
1		**3a**: $R^3 = CH_3$; R^4 = OEt	**5da**	0.5	82
2		**3b**: $R^3 = CH_3$; R^4 = O-*i*-Pr	**5db**	0.6	75
	1d: R^1 = Ph; R^2 = TMS				
3		**3c**: $R^3 = R^4 = CH_3$	**5dc**	0.5	87
4		**3e**: $R^3 = R^4 = -(CH_2)_3-$	**5de**	2	65
5		**3a**: $R^3 = CH_3$; R^4 = OEt	**5da**	2	65
6	**1e**: R^1 = Ph; R^2 = H	**3c**: $R^3 = R^4 = CH_3$	**5dc**	2	71
7		**3e**: $R^3 = R^4 = -(CH_2)_3-$	**5de**	3	53
8		**3a**: $R^3 = CH_3$; R^4 = OEt	**5fa**	1.5	50
9	**1f**: $R^1 = R^2$ = Ph	**3c**: $R^3 = R^4 = CH_3$	**5fc**	0.8	72
10		**3d**: $R^3 = R^4$ = Ph	**5fd**	1	81
11		**3a**: $R^3 = CH_3$; R^4 = OEt	**5ga**	1.5	62
	1g: R^1 = Ph; R^2 = *n*-Bu				
12		**3c**: $R^3 = R^4 = CH_3$	**5gc**	1	73
13		**3a**: $R^3 = CH_3$; R^4 = OEt	**5ha**	2.5	50
	1h: R^1 = 4-Br-C_6H_4; R^2 = *n*-Bu				
14		**3c**: $R^3 = R^4 = CH_3$	**5hc**	2	60
15		**3a**: $R^3 = CH_3$; R^4 = OEt	**5ia**	2	45
	1i: R^1 = 4-COOMe-C_6H_4; R^2 = *n*-Bu				
16		**3c**: $R^3 = R^4 = CH_3$	**5ic**	1.5	58
17		**3a**: $R^3 = CH_3$; R^4 = OEt	**5ja**	2	30
	1j: R^1 = 4-CN-C_6H_4; R^2 = *n*-Bu				
18		**3c**: $R^3 = R^4 = CH_3$	**5jc**	1.5	38
19		**3a**: $R^3 = CH_3$; R^4 = OEt	**5ka**	2	70
	1k: R^1 = 2-MeO-C_6H_4; R^2 = *n*-Bu				
20		**3c**: $R^3 = R^4 = CH_3$	**5kc**	1.5	78

[a] The reactions of propargylic alcohols**1** (0.5 mmol) with 1,3-dicarbonyl compounds **3** (1.5 mmol) were carried out in the presence of $Cu(OTf)_2$ (0.025 mmol) in toluene (2.0 mL) at reflux.

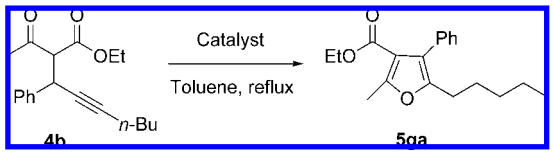
Table 3. Synthesis of Furans from Propargylic Acetates **2d**−**2j** and 1,3-Dicarbonyl Compounds **3**[a]



entry	2	3	5	time [h][b]	isolated yield [%][c]
1	**2d** R^1 = Ph; R^2 = TMS	**3e** $R^3 = R^4 = -(CH_2)_3-$	**5de**	1.5 (2)	81 (65)
2	**2e** R^1 = Ph; R^2 = H	**3a** R^3 = CH_3; R^4 = OEt	**5da**	1.5 (2)	76 (65)
3		**3e** $R^3 = R^4 = -(CH_2)_3-$	**5de**	2 (3)	64 (53)
4	**2f** $R^1 = R^2$ = Ph	**3a** R^3 = CH_3; R^4 = OEt	**5fa**	1 (1.5)	60 (50)
5	**2g** R^1 = Ph; R^2 = *n*-Bu	**3a** R^3 = CH_3; R^4 = OEt	**5ga**	0.8 (1.5)	75 (62)
6	**2h** R^1 = 4−Br-C_6H_4; R^2 = *n*-Bu	**3a** R^3 = CH_3; R^4 = OEt	**5ha**	2 (2.5)	70 (50)
7		**3c** $R^3 = R^4 = CH_3$	**5hc**	1.5 (2)	78 (60)
8	**2i** R^1 = 4-COOMe-C_6H_4; R^2 = *n*-Bu	**3a** R^3 = CH_3; R^4 = OEt	**5ia**	2 (2)	64 (45)
9		**3c** $R^3 = R^4 = CH_3$	**5ic**	1.5 (1.5)	71 (58)
10	**2j** R^1 = 4-CN-C_6H_4; R^2 = *n*-Bu	**3a** R^3 = CH_3; R^4 = OEt	**5ja**	2 (2)	45 (30)
11		**3c** $R^3 = R^4 = CH_3$	**5jc**	1.5 (1.5)	60 (38)

[a] The reactions of propargylic acetates **2** (0.5 mmol) with 1,3-dicarbonyl compounds **3** (1.5 mmol) were carried out in the presence of $Cu(OTf)_2$ (0.025 mmol) in toluene (2.0 mL) at reflux. [b] Values in parentheses are reaction time using the corresponding propargylic alcohols as substrates. See Table 2. [c] Values in parentheses are yields using the corresponding propargylic alcohols as substrates. See Table 2.

Table 4. $Cu(OTf)_2$-Catalyzed Cycloisomerization of **4b**[a]



entry	catalyst	time	isolated yield [%]
1	5 mol% $Cu(OTf)_2$	40 min	79
2	5 mol% $Cu(OTf)_2$/1 equiv of HOAc	30 min	81
3	5 mol% $Cu(OTf)_2$/1 equiv of H_2O	90 min	66
4	1 equiv of HOAc	1 day	nr[b]

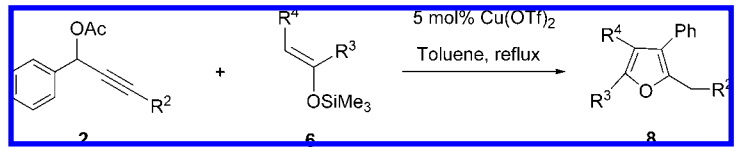
[a] The cycloisomerization reactions of **4b** (0.5 mmol) was carried out in the presence of catalyst in toluene (2.0 mL) at reflux. [b] nr = No reaction.

formation of the 4,6,7,8-tetrahydrochromen-5-one, which were obtained as the main products in the process catalyzed by ruthenium (Table 2, entry 7).[14] Propargylic alcohol **1k** possessing an electron-donating group at the aryl ring reacted smoothly with 1,3-dicarbonyl compounds affording the furans **5ka**−**5kc** in good yields (Table 2, entries 19 and 20). Moreover, substrates **1i** and**1j** possessing strong electron-withdrawing groups (ester and cyano functionalities) at the aryl ring were also successfully employed in the reaction to give the furans **5ia**−**5jc**, albeit in somewhat low yields (Table 2, entries 15−18). Obviously, electron-rich propargylic alcohols provided propargylation/cycloisomerization products in higher yields than electron-poor propargylic alcohols. However, the secondary aliphatic propargylic alcohols, such as 1-methyl-2-propyn-1-ol (R^1 = Me; R^2 = H), failed to afford the desired substituted furan, probably due to the difficult formation of propargylic cation intermediate **10** (Scheme 2). It should be noted that functional groups such as bromo, ester, cyano, and methoxyl in the propargylic alcohols, were readily carried through the propargylation/cycloisomerization tandem reaction, allowing for the subsequent elaboration of the products (Table 2, entries 13−20).

As shown in Table 2, it was remarked that some cases gave the desired furans in somewhat low yields. We reasoned that 1 equiv of water produced in the propargylic substitution would suppress the cycloisomerization reaction. Accordingly, we began searching for an appropriate leaving group, which we thought would readily allow for the propargylation/cycloisomerization tandem reaction. We were pleased to find that replacement of the propargylic alcohols with the corresponding propargylic acetates gave good results in the propargylation/cycloisomerization tandem reaction, and acetic acid produced in the propargylic substitution has no effect on the catalyst activity of $Cu(OTf)_2$. To assess the synthetic utility of propargylic acetates versus propargylic alcohols, comparative experiments were performed. Obviously, increased yields of the desired products were obtained for all cases when propargylic acetates were used as substrates, compared to propargylic alcohols. The typical results are depicted in Table 3. For example, treatment of propargylic acetate **2d** with 1,3-cyclohexanedione **3e** obviously increased the yield of the tetrasubstituted furan **5de** from 65% to 81%, while reducing the reaction time from 2 to 1.5 h (Table 3, entry 1). Most notly, propargylic acetates **2i** and **2j** possessing strong electron-withdrawing groups at the aryl ring were effectively employed in the propargylation/cycloisomerization tandem reaction and sharply increased yields of the furans **5ia**−**5jc** were obtained (Table 3, entries 8−11).

To verify the effects of water and acetic acid on the cycloisomerization reaction, the $Cu(OTf)_2$-catalyzed cycloisomerization of γ-alkynyl ketone **4b** was studied as a model reaction. The results are summarized in Table 4. γ-Alkynyl ketone **4b** underwent smoothly the intramolecular cycloisomerization in the presence of 5 mol% $Cu(OTf)_2$ to give the corresponding furan **5ga** in 79% yield (Table 4, entry 1). The addition of 1 equiv of acetic acid accelerated the intramolecular cycloisomerization and retained good yield (Table 4, entry 2). In contrast, the $Cu(OTf)_2$-catalyzed cycloisomerization of **4b** in the presence of 1 equiv of H_2O afforded **5ga** in 66% yield after 90 min (Table 4, entry 3). The results suggest that water has a obvious negative effect on the $Cu(OTf)_2$-catalyzed intramolecular cycloisomerization of the γ-alkynyl ketone, whereas acetic acid has essentially no effect. The propargylation of 1,3-dicarbonyl compounds with propargylic acetates provided 1 equiv of HOAc, while the reaction with propargylic alcohols provided 1 equiv of

Table 5. Synthesis of Substituted Furans **8** from Propargylic Acetates **2** and Enoxysilanes **6**[a]



Entry	Substrate	Enoxysilane	Product	Time (h)	Isolated yields (%)
1	**2d:** R^2 = TMS	**6a:** R^3 = Ph; R^4 = H	**8da**	2	82
2		**6b**: R^3 = R^4 = -$(CH_2)_4$-	**8db**	4	77
3	**2e:** R^2 = H	**6a:** R^3 = Ph; R^4 = H	**8da**	4	66
4	**2g:** R^2 = *n*-Bu	**6a:** R^3 = Ph; R^4 = H	**8ga**	3	75
5		**6b**: R^3 = R^4 = -$(CH_2)_4$-	**8gb**	4	72

[a] The reactions of propargylic acetates **2** (0.5 mmol) with enoxysilanes **6** (1.5 mmol) were carried out in the presence of $Cu(OTf)_2$ (0.025 mmol) in toluene (2.0 mL) at reflux.

H_2O. Therefore, it is anticipated that the propargylic acetates have higher reactivity than propargylic alcohols in the propargylation/cycloisomerization tandem reaction catalyzed by copper(II) triflate.

We also examined the propargylation/cycloisomerization tandem reaction of enoxysilanes with propargylic acetates and found that the tandem reaction proceeded smoothly without exclusion of moisture or air from the reaction mixture. Typical results are summarized in Table 5. Reactions of enoxysilane **6a** with propargylic acetates afforded corresponding trisubstituted furans in good yields (Table 5, entries 1, 3 and 4). Starting with cyclohexenyloxytrimethylsilane **6b** and propargylic acetates **2d** and **2g,** substituted furans were isolated in 77 and 72% yields, respectively (Table 3, entries 2 and 5). The Nishibayashi team[6] reported novel ruthenium- and platinum-catalyzed sequential reactions to afford the corresponding trisubstituted furans by the direct use of propargylic alcohols as substrates and ketones as carbon-centered nucleophiles under N_2. However, the substrates were limited to propargylic alcohols bearing terminal alkyne group and the reaction required rather long time for completion. In contrast, propargylic acetates bearing both terminal alkyne group and internal alkyne group are available, and the reaction proceeded much more rapidly without inert gases protection in our procedure.

Conclusions

In summary, we have developed a novel and highly efficient procedure for the synthesis of substituted furans directly from 1,3-dicarbonyl compounds and enoxysilanes with propargylic alcohols or acetates using copper(II) triflate as catalyst. Copper(II) triflate operating as a bifunctional catalyst, catalyzes two mechanistically distinct processes in a single-pot under the same reaction conditions. The reaction completes rapidly under mild conditions and air is tolerant. Propargylic alcohols or acetates bearing terminal alkyne group or internal alkyne group are readily available. This method provides a flexible and rapid route to substituted furans. Operational simplicity and minimal waste generation of this process should be beneficial for its large-scale applications. Study on development of the propargylation/cycloisomerization tandem reaction is ongoing in our laboratory.

Experimental Section

A typical experimental procedure for the reaction of 1-(naphthalen-1-yl)-3-(trimethylsilyl)prop-2-yn-1-ol (**1a**) with ethyl acetoacetate (**3a**) catalyzed by 5 mol % of $Cu(OTf)_2$ is described below: to a 5-mL flask were successively added 1-(naphthalen-1-yl)-3-(trimethylsilyl)prop-2-yn-1-ol (**1a**) (127 mg, 0.5 mmol), ethyl acetoacetate (**3a**) (195 mg, 1.5 mmol), toluene (2.0 mL), and $Cu(OTf)_2$ (9 mg, 0.025 mmol), The reaction mixture was stirred at reflux and monitored periodically by TLC. Upon completion, the toluene was removed under reduced pressure by an aspirator, and then the residue was purified by silica gel column chromatography (EtOAc/hexane) to afford 2,5-dimethyl-4-(1-naphthyl)furan-3-carboxylic acid ethyl ester (**5aa**) as a yellow oil (126 mg, 86% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.49 (t, 3H, J = 7.2 Hz), 2.10 (s, 3H), 2.65 (s, 3H), 3.70−3.85 (m, 2H), 7.30−7.48 (m, 4H), 7.65 (d, 1H, J = 8.4 Hz), 7.81 (d, 1H, J = 8.0 Hz), 7.84 (d, 1H, J = 7.6 Hz) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.7, 13.1, 13.9, 59.4, 114.9, 119.1, 125.1, 125.5, 125.7, 126.0, 127.57, 127.58, 128.1, 131.6, 133.3, 133.4, 147.8, 157.8, 164.3 ppm. IR (film): 1707 cm^{-1}. ESI-MS: m/z (%) = 317 (100) [M + Na$^+$].

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Supporting Information Available. Experimental procedures and spectra data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Wasilke, J.-C.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev* **2005**, *105*, 1001, and references cited therein.

(2) Ajamian, A.; Gleason, J. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 3754, and references cited therein.

(3) (a) Kirsch, S. F. *Org. Biomol. Chem.* **2006**, *4*, 2076. (b) Brown, R. C. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 850.

(4) For selected examples, see: (a) Sniady, A.; Durham, A.; Morreale, M. S.; Wheeler, K. A.; Dembinski, R. *Org. Lett.* **2007**, *9*, 1175. (b) Casey, C. P.; Strotman, N. A. *J. Org. Chem.* **2005**, *70*, 2576. (c) Sromek, A. W.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, *127*, 10500. (d) Suhre, M. H.; Reif, M.; Kirsch, S. F. *Org. Lett.* **2005**, *7*, 3925. (e) Imagawa, H.; Kurisaki, T.; Nishizawa, M. *Org. Lett.* **2004**, *6*, 3679. (f) MaGee, D. I.; Leach, J. D.; Setiadji, S. *Tetrahedron* **1999**, *55*, 2847. (g) Brown, C. D.; Chong, J. M.; Shen, L. *Tetrahedron* **1999**, *55*, 14233. (h) Wipf, P.; Rahman, L. T.; Rector, S. R. *J. Org. Chem.* **1998**, *63*, 7132. (i) Hashmi, A. S. K.; Ruppert, T. L.; Knöfel, T.; Bats, J. W. *J. Org. Chem.* **1997**, *62*, 7295. (j) MaGee, D. I.; Leach, J. D. *Tetrahedron Lett.* **1997**, *38*, 8129. (k) D'Souza, D. M.; Müller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095. (l) Calter, M. A.; Zhu, C. *Org. Lett.* **2002**, *4*, 205.

(5) (a) Hou, X. L.; Cheung, H. Y.; Hon, T. Y.; Kwan, P. L.; Lo, T. H.; Tong, S. Y.; Wong, H. N. C. *Tetrahedron* **1998**, *54*, 1955. (b) Jeevanandam, A.; Ghule, A.; Ling, Y.-C. *Curr. Org. Chem.* **2002**, *6*, 841. (c) Hou, X.-L.; Yang, Z.; Yeung, K.-S.; Wong, H. N. C. Furans and benzofurans. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Elsevier: Oxford, 2005; Vol. 17, pp 142−171.

(6) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Milton, M. D.; Hidai, M.; Uemura, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 2681.

(7) Cadierno, V.; Gimeno, J.; Nebra, N. *Adv. Synth. Catal.* **2007**, *349*, 382.

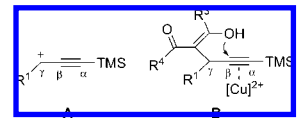
(8) Sanz, R.; Miguel, D.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Org. Lett.* **2007**, *9*, 727.

(9) Feng, X.-B.; Tan, Z.; Chen, D.; Shen, Y.-M.; Guo, C.-C.; Xiang, J.-N.; Zhu, C.-L. *Tetrahedron Lett.* **2008**, *49*, 4110.

(10) (a) Zhan, Z.-P.; Yu, J.-L.; Liu, H.-J.; Cui, Y.-Y.; Yang, R.-F.; Yang, W.-Z.; Li, J.-P. *J. Org. Chem.* **2006**, *71*, 8298. (b) Zhan, Z.-P.; Yang, W.-Z.; Yang, R.-F.; Yu, J.-L.; Liu, H.-J. *Chem. Commun.* **2006**, 3352. (c) Zhan, Z.-P.; Wang, S.-P.; Cai, X.-B.; Liu, H.-J.; Yu, J.-L.; Cui, Y.-Y. *Adv. Synth. Catal.* **2007**, *349*, 2097. (d) Zhan, Z.-P.; Cai, X.-B.; Wang, S.-P.; Yu, J.-L.; Liu, H.-J.; Cui, Y.-Y. *J. Org. Chem.* **2007**, *72*, 9838.

(11) The percentages of the enol content of 1,3-dicarbonyl compounds in CCl_4 follow the order: dibenzoylmethane **3d** (96%) > acetylacetone **3c** (80%) > ethyl acetoacetate **3a** (7.5%) > diethyl malonate **3f** (0.007%). See: (a) Burdett, J. L.; Rogers, M. T. *J. Am. Chem. Soc.* **1964**, *86*, 2105.

(12) The γ-effect of silicon atom stabilizes positive charges in the γ-position of propargylic cation **A** and favors the propargylic substitution. On the other hand, the β-effect of silicon atom is responsible for the polarization (compared to the unsilylated alkynes) of the acetylenic bond of π-alkyne copper complex **B**, and leads to a decrease in the electronic densities on β-carbon, so β-carbon is readily intramolecular nucleophilic attacked by the enolic form of the keto group. Thus, it is anticipated that propargylic alcohol **1a** would be more reactive than propargylic alcohols **1b** and **1c**. See: (a) Antras, F.;



Ahmar, M.; Cazes, B. *Tetrahedron Lett.* **2001**, *42*, 8157. (b) Happ, B.; Bartik, T.; Zucchi, C.; Rossi, M. C.; Ghelfi, F.; Pályi, G.; Váradi, G.; Szalontai, G.; Horváth, I. T.; Chiesi-Villa, A.; Guastini, C. *Organometallics* **1995**, *14*, 809.

(13) We have repeated the propargylation/cyclization of propargylic alcohol **1d** with ethyl acetoacetate in the presence of 10 mol % $InCl_3$ under the tan dard conditions used by Tan. It was found that the propargylation required 10 h for completion.

(14) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Hidai, M.; Uemura, S. *J. Org. Chem.* **2004**, *69*, 3408.

CC8001316