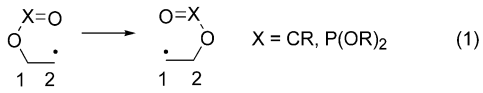
Furan Synthesis

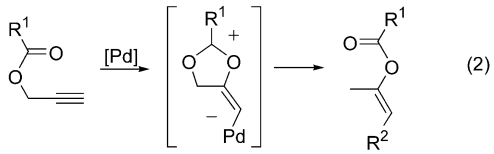
A Novel 1,2-Migration of Acyloxy, Phosphatyloxy, and Sulfonyloxy Groups in Allenes: Efficient Synthesis of Tri- and Tetrasubstituted Furans**

*Anna W. Sromek, Alexander V. Kel'in, and Vladimir Gevorgyan**

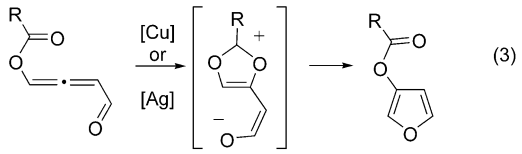
[3,3] Migrations of propargylacyloxy, phosphatyloxy, and sulfonyloxy groups are important transformations in organic synthesis.[1] In addition to these sigmatropic migrations, radical 1,2-acyloxy and -phosphatyloxy migrations [Eq. (1)]



have been used extensively in carbohydrate and nucleoside chemistry.[2] 1,2-Acyloxy migration has also been proposed as a key step in the Pd-catalyzed propargyl–propenyl isomerization [Eq. (2)].[3] In both cases, 1,2-migration of acetate or



phosphate proceeds from an sp^3 carbon. To the best of our knowledge, no 1,2-migrations of the acyloxy, phosphatyloxy, and sulfonyloxy groups from an sp^2 carbon have been disclosed. Herein we wish to report a novel 1,2-migration of the acyloxy, phosphatyloxy, and sulfonyloxy groups in the allenyl system [Eq. (3)]. This unprecedented migration, incorporated into the cycloisomerization reaction, is the key to an efficient synthesis of valuable tri- and tetrasubstituted furans.[4]



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[**] We are grateful to the NIH (GM 64444) for financial support of this work. We also thank D. Yap for technical assistance.

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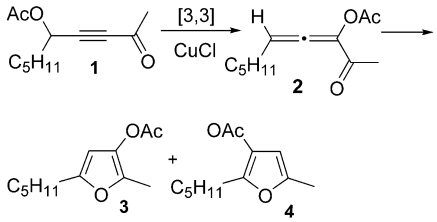
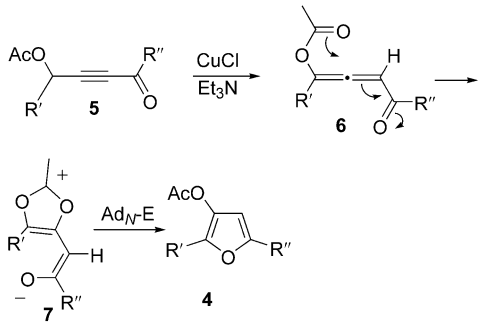
The recently discovered Cu-catalyzed cycloisomerization of alkynyl ketones and imines is an efficient method for the synthesis of up to trisubstituted heterocycles.[5] While attempting to expand the scope of this cycloisomerization reaction, we explored the possibility of utilizing [3,3] acyloxy migration to proceed from **1** to allene **2** en route to acyloxy-substituted furan **3** (Scheme 1). As expected, furan **3** was



Scheme 1. Formation of the unexpected regioisomer **4**.

formed, albeit in moderate yields; however, it was accompanied by traces of the unexpected regioisomer **4**. Addition of triethylamine to the reaction mixture shifted the product distribution toward predominant formation of furan **4**. It was rationalized that **4** arises from initial base-assisted propargyl–allenyl isomerization **5**→**6**[5] (Scheme 2), as opposed to a [3,3]



Scheme 2. Rationale for the formation of the unexpected regioisomer **4**.

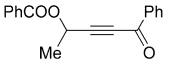
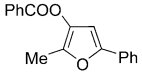
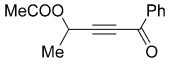
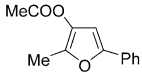
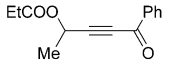
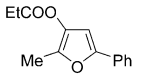
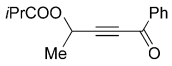
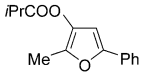
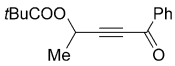
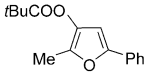
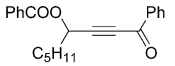
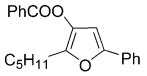
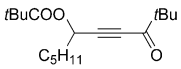
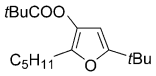
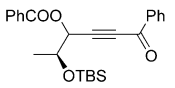
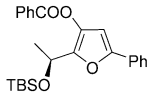
acyloxy shift (Scheme 1). Allene **6** undergoes intramolecular nucleophilic attack to form the aromatic dioxolenylium zwitterion **7**,[6] which is transformed into furan **4** by a subsequent intramolecular Ad_N-E process (Scheme 2).[7]

We were pleased to find that by using phenyl and *tert*-butyl alkynyl ketones, we were able to dramatically improve the regioselectivity and yields of this unusual reaction. Thus, when we employed a series of alkynyl ketones **5** possessing different acyloxy groups, selective cycloisomerization occurred to produce furans **4** as single regioisomers in high yields (Table 1)!

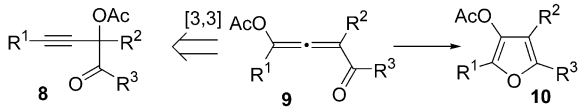
To gain additional support for the proposed allenic intermediate **6** in the formation of furan **4** (Scheme 2), we attempted approaching allenes of type **6** by an independent route. An attractive possibility would be to access acyloxy allene **9** by the [3,3] sigmatropic shift of **8** (Scheme 3). In the event that the sequential cascade transformation of **8** into **9** proves successful, it would not only offer strong support for

  DOI: 10.1002/ange.200353535

Table 1: Cu-catalyzed synthesis of trisubstituted furans.[a]

Substrate		*t* [h]	Product		Yield [%][b]
	**5a**	22		**4a**	82[c]
	**5b**	1		**4b**	81
	**5c**	9		**4c**	69
	**5d**	2		**4d**	90
	**5e**	17		**4e**	86
	**5f**	23		**4f**	80
	**5g**	32		**4g**	80
	**5h**	46		**4h**	83[c,d]

[a] All reactions carried out on a 1-mmol scale. [b] Yields of isolated products. [c] Reactions carried out at 80 °C. [d] TBS = *tert*-butyldimethylsilyl.



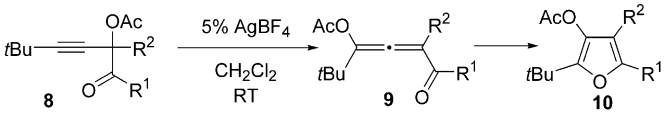
Scheme 3. Different approach to acyloxy allenyl ketones.

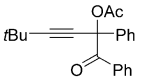
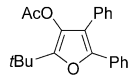
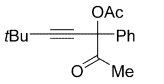
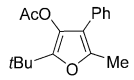
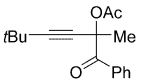
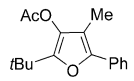
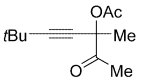
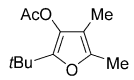
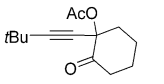
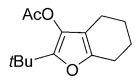
involvement of allenic intermediates **6**/**9**, but would also allow expansion of our cycloisomerization methodology to the synthesis of tetrasubstituted furans **10**. We were thrilled to find that in the presence of $AgBF_4$,[8,9] ketones **8** smoothly underwent the postulated [3,3] shift/1,2-migration/cycloisomerization sequence to directly[10] afford tetrasubstituted furans[11] **10** in excellent yields (Table 2)! Most remarkably, this new mode of cyclization enables facile access to the fused furan **10e**, which was inaccessible by our standard cycloisomerization techniques.[5]

Encouraged by these results, we attempted incorporation of hetero migrating groups into the [3,3] shift/1,2-migration/cycloisomerization cascade. It was found that the phosphatyloxy analogue of **8a**, ketone **11**, underwent cycloisomerization at 60 °C in the presence of 5% $AgBF_4$ to afford furanyl phosphate **12** in 65% yield (Scheme 4). When the reaction was conducted at room temperature, the allenyl phosphate intermediate **13** was isolated in 56% yield. Subjecting the latter to the same conditions as those used for the transformation **11**→**12** led to formation of furan **12** in 77% yield (Scheme 4).

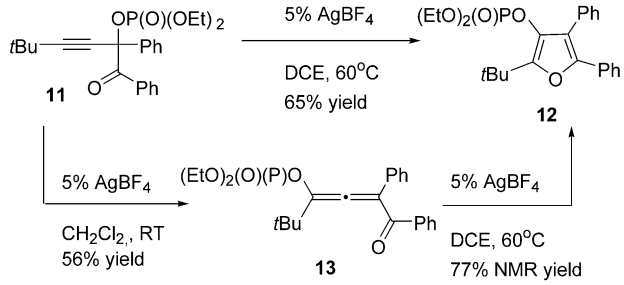
Next, we attempted the analogous transformation with propargyl tosylates **14**. We were pleasantly surprised to find

Table 2: Ag-catalyzed synthesis of tetrasubstituted furans.[a]



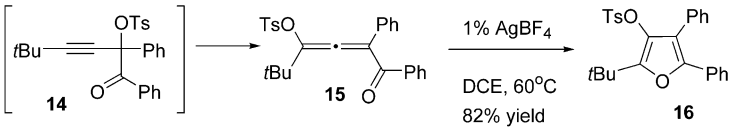
Substrate		*t* [min]	Product		Yield [%][b]
	**8a**	2		**10a**	> 99
	**8b**	15		**10b**	73
	**8c**	15		**10c**	84
	**8d**	15		**10d**	90
	**8e**	10		**10e**	86

[a] Reactions carried out on a 1-mmol scale. [b] Yields of isolated products.



Scheme 4. 1,2-Phosphatyloxy migration. DCE = dichloroethane.

that attempts to synthesize **14**[12] led directly to the formation of tosyl allene **15**, apparently through a thermal [3,3] tosyloxy shift. Allene **15** underwent smooth cycloisomerization at 60 °C in the presence of 1% $AgBF_4$ to produce tosyl furan **16**[13] in 82% yield (Scheme 5). Thus, the successful employment of the phosphatyloxy and sulfonyloxy groups not only expands the scope of the recently found cycloisomerization reaction, but also provides strong support for the involvement of the acyloxy allene intermediate in the formation of acyloxy furans **4** and **10**.



Scheme 5. 1,2-Tosyloxy migration.

In conclusion, a novel 1,2-migration of the acyloxy, phosphatyloxy, and sulfonyloxy groups in allenyl systems has been discovered. Incorporation of this transformation in a

cycloisomerization sequence led to the development of an efficient method for the synthesis of tri- and tetrasubstituted furans.

Received: December 15, 2003 [Z53535]

Keywords: cyclization · furans · homogeneous catalysis · rearrangement · synthetic methods

[1] a) D. G. Oelberg, M. D. Schiavelli, *J. Org. Chem.* **1977**, *42*, 1804; b) H. Schlossarczyk, M. Sieber, M. Hesse, H. J. Hanson, H. Schmid, *Helv. Chim. Acta* **1973**, *56*, 875; c) G. Saucy, R. Marbet, H. Lindlar, O. Isler, *Helv. Chim. Acta* **1959**, *42*, 1945; d) R. Cookson, M. Cramp, P. J. Parsons, *J. Chem. Soc. Chem. Commun.* **1980**, 197; e) D. M. Hollinshead, S. C. Howell, S. V. Ley, M. Mahon, N. M. Ratcliffe, P. A. Worthington, *J. Chem. Soc. Perkin Trans. 1* **1983**, 1579; f) Y. Shigemasa, M. Yasui, S. Ohrai, M. Sasaki, H. Sashiwa, H. Saimoto, *J. Org. Chem.* **1991**, *56*, 910.

[2] a) D. Crich, Q. Yao, *J. Am. Chem. Soc.* **1994**, *116*, 2631; b) Y. Itoh, K. Haraguchi, H. Tanaka, K. Matsumoto, K. Nakamura, T. Miyasaka, *Tetrahedron Lett.* **1995**, *36*, 3867; c) K. Haraguchi, Y. Itoh, K. Matsumoto, K. Hashimoto, K. Nakamura, H. Tanaka, *J. Org. Chem.* **2003**, *68*, 2006; d) L. R. C. Barclay, D. Griller, K. U. Ingold, *J. Am. Chem. Soc.* **1982**, *104*, 4339; e) M. Kira, H. Yoshida, H. Sakurai, *J. Am. Chem. Soc.* **1985**, *107*, 7767; f) H.-G. Korth, R. Sustmann, K. S. Groninger, M. Leisung, B. Giese, *J. Org. Chem.* **1988**, *53*, 4364; g) S. Julia, R. Lorne, *C. R. Seances Acad. Sci. Ser. C* **1971**, *273*, 174.

[3] a) V. Rautenstrauch, U. Burger, P. Wirthner, *Chimia* **1985**, *39*, 225; b) V. Rautenstrauch, *J. Org. Chem.* **1984**, *49*, 950; c) H. Kataoka, K. Watanabe, K. Goto, *Tetrahedron Lett.* **1990**, *31*, 4181; d) R. Mahrwald, H. Schick, *Angew. Chem.* **1991**, *103*, 577; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 593; e) K. Kato, Y. Yamamoto, Y. H. Akita, *Tetrahedron Lett.* **2002**, *43*, 6587.

[4] For naturally occurring products containing 3-alkoxyfuryl fragments see, for example: a) Y. Hayawaka, K. Kawakami, H. Seto, K. Furihata, *Tetrahedron Lett.* **1992**, *33*, 2701; b) C. E. Heltzel, A. A. L. Gunatilaka, T. E. Glass, D. G. I. Kingston, *Tetrahedron* **1993**, *49*, 6757; for biologically active compounds containing 3-alkoxyfuryl fragments see, for example: c) C. P. Miller, M. D. Collins, H. A. Harris, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2399; c) P. C. Unangst, M. E. Carethers, K. Webster, G. M. Janik, L. J. Robichaud, *J. Med. Chem.* **1984**, *27*, 1629.

[5] a) A. V. Kel'in, A. W. Sromek, V. Gevorgyan, *J. Am. Chem. Soc.* **2001**, *123*, 2074; b) A. V. Kel'in, V. Gevorgyan, *J. Org. Chem.* **2002**, *67*, 95; c) J. T. Kim, A. V. Kel'in, V. Gevorgyan, *Angew. Chem.* **2003**, *115*, 102; *Angew. Chem. Int. Ed.* **2003**, *42*, 98; d) J. T. Kim, V. Gevorgyan, *Org. Lett.* **2002**, *4*, 4697.

[6] Dioxolenylium species have been reported: a) A. D. Allen, T. Kitamura, R. A. McClelland, P. J. Stang, T. T. Tidwell, *J. Am. Chem. Soc.* **1990**, *112*, 8873; b) W. Lorenz, G. Maas, *J. Org. Chem.* **1987**, *52*, 375.

[7] For 1,2-migration of the thio group proceeding through a thiirenium intermediate, see ref. [5c].

[8] $AgBF_4$ may participate in either or all steps of the sequence, as silver salts are known to catalyze propargylacyloxy [3,3]-sigmatropic shifts (see ref. [1]) as well as the cycloisomerization of allenyl ketones into furans.[11b,c]

[9] Following a referee's suggestion, we tested the cyclization of **8d** in the presence of $AuCl_3$, which is known to catalyze the cycloisomerization of allenyl ketones.[11f] We found that $AuCl_3$ is as efficient as $AgBF_4$ in catalyzing this transformation.

[10] Most likely, in keeping with earlier proposals (see ref. [5]), the formation of allene **9** is the rate-determining step; therefore, **9** has never been observed in the reaction mixtures.

[11] For a related $AgBF_4$-catalyzed cycloisomerization of allenic alcohols into 2,5-dihydrofurans, see: a) L.-I. Olsson, A. Claesson, *Synthesis* **1979**, 743; for the metal-catalyzed cyclization of allenyl ketones into furans, see: b) J. A. Marshall, X. Wang, *J. Org. Chem.* **1991**, *56*, 960; c) J. A. Marshall, G. S. Bartley, *J. Org. Chem.* **1994**, *59*, 7169; d) S. Ma, J. Zhang, *Chem. Commun.* **2000**, 117; e) S. Ma, L. Lintao, *Org. Lett.* **2000**, *2*, 941; f) A. S. K. Hashmi, L. Schwarz, J. H. Choi, T. M. Frost, *Angew. Chem.* **2000**, *112*, 2382; *Angew. Chem. Int. Ed.* **2000**, *39*, 2285.

[12] See the Supporting Information for details.

[13] Potentially, furanyl tosylates can be used in cross-coupling reactions. For the Pd-catalyzed cross-coupling of aryl tosylates, see: a) H. N. Nguyen, X. Huang, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 11818; b) A. H. Roy, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 8704.

