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A Facile Synthesis of 3-Phenylthio and 3-Methoxy Substituted Furans from 3-Methoxy-1-phenylthio-1-propyne

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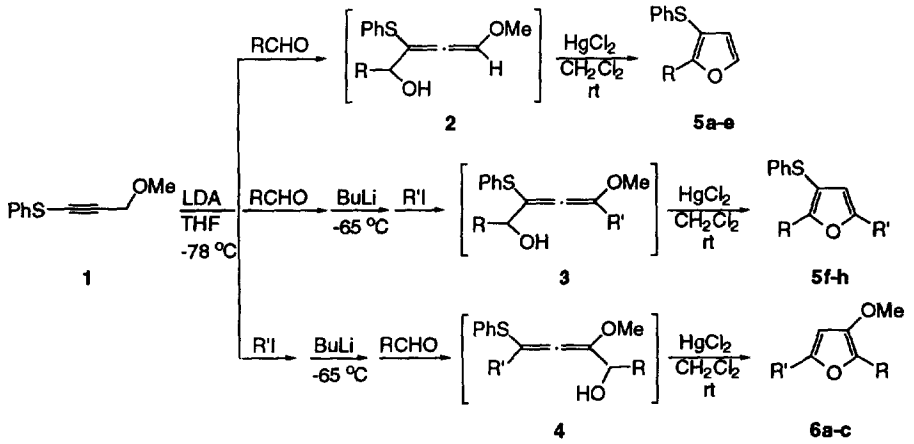
Abstract: A simple route to 3-phenylthio and 3-methoxy substituted furans by way of [3 + 2] annulation of 3-methoxy-1-phenylthio-1-propyne with aldehydes is described. © 1997 Elsevier Science Ltd.

Substituted furans are useful building blocks for the synthesis of natural and non-natural products[1] and new methods leading to this ring systems are of considerable interest.[2] Although, by way of [3 + 2] annulation with aldehydes, several monohetero-substituted acetylenic or allenic derivatives have been described to transform into furans,[3] the use of dihetero-substituted analogues by the same strategy hitherto has not been examined. In a continuation of studying the synthetic utility of the 3-methoxy-1-phenylthio-1-propyne (**1**),[4] we now report that 3-phenylthio and 3-methoxy functionalized furans can be easily obtained from **1** by a sequence of hydroxyalkylation/alkylation and cyclization. Both the methoxy and phenylthio substituents may serve as the leaving group in the $HgCl_2$-catalyzed cycloelimination of allenic intermedates **2-4** (Scheme 1).

Scheme 1



Treatment of compound **1** in anhydrous THF with lithium diisopropyl amide (LDA) (1 equiv.) at -78 °C followed by the addition of acetaldehyde (1.2 equiv.) produced the α-hydroxyalkylated allene **2a** (R = Me) after standard work up. Reaction of the crude **2a** in anhydrous dichloromethane with a catalytic amount of $HgCl_2$ (0.01 equiv.) at room temperature afforded the 2-methyl-3-phenylthio-furan (**5a**) in 69% isolated yield. The n.m.r and ir spectral data of **5a** are identical with those reported.[5] The same strategy is similarly applicable to the synthesis of 3-phenylthio-2,5-disubstituted furans. Reaction of **1** with LDA (1 equiv.), butyraldehyde (1 equiv.), *n*-BuLi (1 equiv.) and ethyl iodide (1.5 equiv.) sequentially in one flask produced the allenic intermediate **3a** (R = *n*-Pr, R' = Et) which was treated with $HgCl_2$ to give the 2-*n*-propyl-3-phenylthio-5-ethylfuran (**5f**) in 50% yield. When the sequence of the hydroxyalkylation and alkylation of **1** in the above reaction was changed, the allenic alcohol **4a** (R = R' = *n*-Pr) was formed. Upon subjection to the $HgCl_2$ catalyzed cyclization, **4a** was transformed into the 3-methoxy-2,5-di-*n*-propylfuran (**6a**) in 52% yield with concurrent generation of thiophenol.[6] Additional experimental results are summerized in Table 1.[7]

Table 1. Synthesis of 3-phenylthio and 3-methoxy substituted furans from **1**§

Aldehydes	Alkyl halides	3-(Phenylthio)furans, yield %	3-Methoxyfurans, yield %
MeCHO		**5a** R = Me 69	
EtCHO		**5b** R = Et 69	
n-PrCHO		**5c** R = *n*-Pr 68	
t-BuCHO		**5d** R = *t*-Bu 60	
PhCHO		**5e** R = Ph 58	
n-PrCHO	EtI	**5f** R = *n*-Pr, R' = Et 50	
t-BuCHO	EtI	**5g** R = *t*-Bu, R' = Et 51	
PhCHO	EtI	**5h** R = Ph, R' = Et 49	
n-PrCHO	*n*-PrI		**6a** R = R' = *n*-Pr 52
PhCHO	*n*-PrI		**6b** R = Ph, R' = *n*-Pr 60
t-BuCHO	*n*-PrI		**6c** R = *t*-Bu, R' = *n*-Pr 53

§ All the furans were isolated by flash chromatography on silica gel and have been fully characterized by ^1H and ^{13}C nmr, ir, and mass spectrometry.·

References and Notes

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2 For some recent developments in furan synthesis, see Frey, H. *Synlett*, **1993**, 905 and references cited therein.

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4 Tso, H. H.; Chen, Y. J. *Heterocycles*, **1995**, *41*, 13.

5 McDougal, P. G.; Oh, Y. I.; VanDerveer, D. *J. Org. Chem.*, **1989**, *54*, 91.

6 For the recent work of synthesis of 2,3,5-trisubstituted furans by the similar methodology, see Marshall, J. A.; Sehon, C. A. *J. Org. Chem.*, **1995**, *60*, 5966.

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