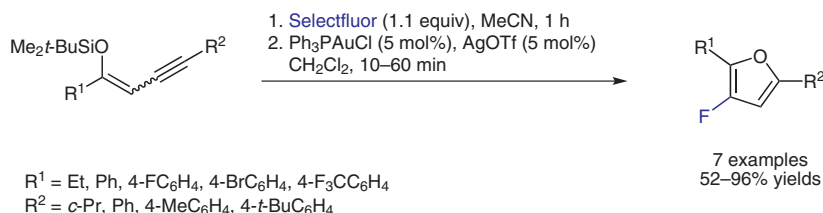


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Thieme

## Au/Ag-Catalyzed Synthesis of 3-Fluorofurans



**Significance:** The synthesis of 2,5-disubstituted 3-fluorofurans from alk(ar)-3-yn-1-ones is reported. The starting ynone requires conversion into its TBDMS enol ether for the monofluorination (step 1). Without this, bisfluorination occurs. Non-halogenated ynones may be cyclized to furans by simple Lewis acid catalysis, but the fluorinated substrates are found to be unreactive under these conditions (step 2). After optimization, the cyclization was found to occur under gold/silver catalysis within short reaction times. Lowering both catalyst loadings to 1 mol% reduced the yield significantly. Although the yields are modest to excellent, the substrate scope was inadequately studied. The starting alk(ar)-3-yn-1-ones are synthesized from the reaction of the corresponding propargyl bromides with aldehydes followed by oxidation.

**Comment:** 2,5-Disubstituted furans exhibit biological activity as illustrated by pentamidine (DB289), a prodrug of furamidine (DB75), efficacious against African trypanosomiasis, pneumonia, and malaria (X. Ming et al. *Drug Metab. Dispos.* **2009**, 37, 424). Fluorine-containing pharmaceuticals have found widespread application in medicinal chemistry (see Book below). The present work combines these aspects in search of new bioactivity of 2,5-disubstituted 3-fluorofurans. Although these compounds may be synthesized from difluorohomopropargyl alcohols by treatment with *t*-BuOK or DBU at elevated temperatures (P. Li, Z. Chai, G. Zhao, S.-Z. Zhu *Synlett* **2008**, 2547), the difluorohomopropargyl alcohols have to be prepared using the Freon gas CBr<sub>2</sub>F<sub>2</sub>. The current procedure proceeds under mild conditions and affords good yields. The only drawback is the lengthy synthesis of starting materials.

**Book:** E. P. Cormier, M. Das, I. Ojima, In *Fluorine in Medicinal Chemistry and Chemical Biology*; I. Ojima, Ed.; Wiley-Blackwell: Chichester, **2009**, 525–603.