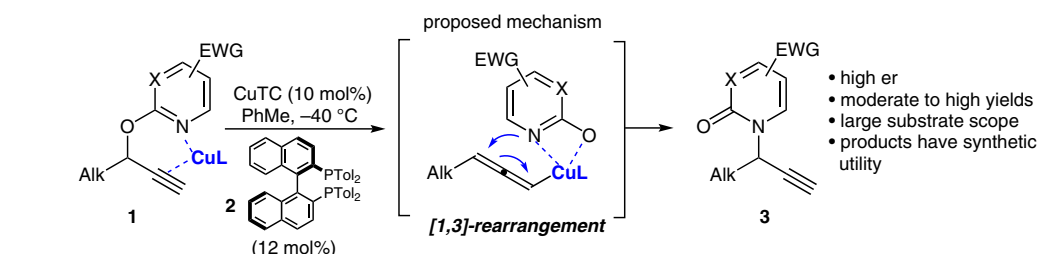


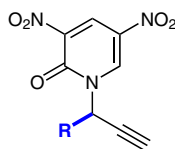
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Enantioselective Propargylic [1,3]-Rearrangements: Copper-Catalyzed O-to-N Migrations toward C–N Bond Formation
Chem. Sci. **2017**, *8*, 4299–4305.

Copper-Catalyzed Enantioselective [1,3]-Rearrangement to Chiral Propargylic Amines

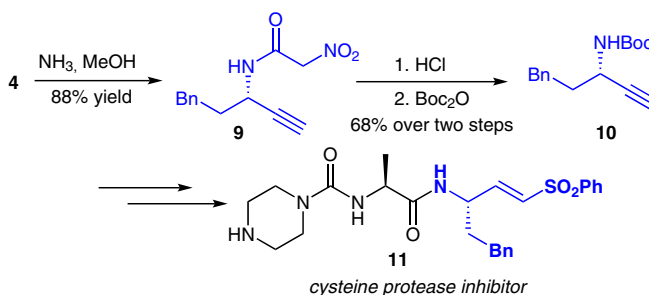


Selected examples:



R = CH₂Bn (**4**), 90% yield, er = 98:2
 R = CH₂OTBS (**5**), 75% yield, er = 97:3
 R = Cy (**6**), 80% yield, er = 96:4
 R = Ph (**7**), 70% yield, er = 85:15
 R = (CH₂)₄CHO (**8**), 89% yield, er = 97:3

Synthetic utility:



Significance: Thermal [3,3]-sigmatropic rearrangements are well preceded and can be achieved at ambient temperature with high levels of enantioselectivity (see, for example: M. P. Watson, L. E. Overman, R. G. Bergman *J. Am. Chem. Soc.* **2007**, *129*, 5031). In contrast, [1,3]-sigmatropic rearrangements are thermally disallowed, but can be promoted at high temperatures with the use of transition-metal catalysts. No examples of [1,3]-rearrangements affording propargylic products or their enantioselective variants have been previously reported.

Comment: The present report details the first example of an enantioselective [1,3]-rearrangement. The alkyne starting materials **1** can be converted into pyridone alkynes **3** with a diverse substrate scope, affording products in high yields and with high er. Detailed mechanistic studies indicate that the reaction proceeds through allene intermediate **2** with copper coordination, followed by a formal [1,3]-rearrangement. The enantioselectivity is derived from a BINAP phosphoryl ligand **2** through CuTC coordination. The synthetic utility of the products was shown by carrying **4** forward to the synthesis of cysteine protease inhibitor **11**. This reaction will find utility due to the mild reaction conditions and the ability to modify the pyridone core to generate chiral amines similar to **10**.

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