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A Concise Synthesis of Alkoxy-Substituted Pyrimidine Derivatives Based upon a Three-Component Access to Functionalized Enamides

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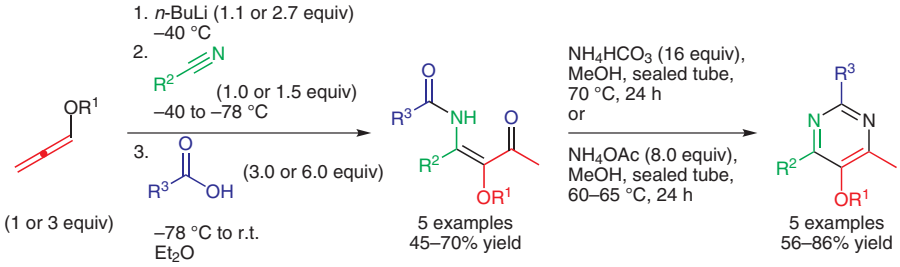
Synthesis of 5-Alkoxy Pyrimidines via Enamides



R^1 = Me, trimethylsilylethyl, Bn
R^2 = *c*-Pr, Ph, 2-thienyl
R^3 = *c*-Pr, Ph

Significance: Reported is the synthesis of substituted 5-alkoxypyrimidines from enamides which are derived through a stepwise three-component reaction of alkoxyallenes, nitriles, and carboxylic acids. The mechanism for this three-component reaction has been previously discussed (H.-U. Reissig and co-workers *Chem. Eur. J.* **2004**, *10*, 4283). Of the two sets of conditions for the final pyrimidine formation, that using ammonium acetate allowed the use of less equivalents of ammonium salt and a slightly lower temperature. However, this was not exclusively employed.

Comment: Pyrimidines are an important class of heteroaromatics which are, or constitute part of, biological molecules and pharmaceuticals. Consequently a large body of literature concerning their synthesis is available (see Book below). The described method is an interesting addition to this lexicon of methodologies. Since the three-component reaction has been previously studied, optimization studies were limited to the formation of the 5-alkoxypyrimidines with respect to solvent, temperature and ammonia source. Additional utility was demonstrated through de-benzylation of the 5-OBn derivative, conversion into the corresponding nonaflate, and subsequent Sonogashira cross-coupling. It was also demonstrated that the 6-Me group was easily oxidized to the corresponding aldehyde.

Book: S. von Angerer, In *Science of Synthesis*, Vol. 16; Y. Yamamoto, Ed.; Thieme: Stuttgart, **2003**, 379-572.

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Category

Synthesis of Heterocycles

Key words

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enamides

multicomponent reaction