T. LECHEL, S. MÖHL, H.-U. REISSIG* (FREIE UNIVERSITÄT BERLIN, GERMANY)

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

Synlett 2009, 1059-1062.

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.

SYNFACTS Contributors: Victor Snieckus, Johnathan Board Synfacts 2009, 8, 0835-0835 Published online: 23.07.2009

 $\textbf{DOI:}\ 10.1055/s\text{-}0029\text{-}1217451; \textbf{Reg-No.:}\ V08009SF$

Category

Synthesis of Heterocycles

Key words

pyrimidines

enamides

multicomponent reaction

