SYNFACTS

Highlights in Current
Synthetic Organic
Chemistry

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Thieme

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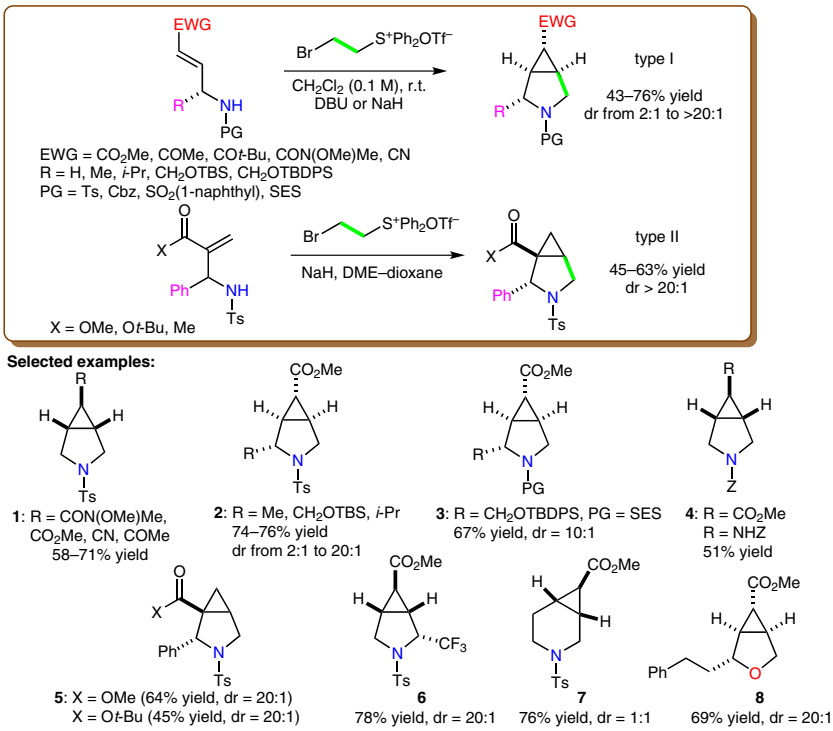
Efficient Synthesis of Cyclopropane-Fused Heterocycles with Bromoethylsulfonium Salt
Chem. Eur. J. **2013**, *19*, 10827–10831.

Category
Synthesis of Heterocycles

Key words
azabicyclohexanes
bromoethyl-sulfonium salt

General Strategy for the Synthesis of Cyclopropane-Fused Heterocycles



Significance: Cyclopropyl-fused heterocycles, in particular the 3-azabicyclo[3.1.0]hexane ring system, are important components in natural products (e.g., duocarymycin A) and pharmaceuticals (e.g., trovafloxacin). The ring system represents a conformationally constrained piperidine and, when substituted with a carboxylic acid, it resembles conformationally restricted glutamate, γ-amino butyric acid and α/β-proline derivatives. Several methods have been developed for the synthesis of 3-azabicyclo[3.1.0]hexanes (see: G. R. Krow, K. C. Cannon *Org. Prep. Proced. Int.* **2000**, *32*, 103) which, however, are usually effective only for one type of ring system. The current work provides a general strategy to obtain a diverse range of substituted and functionalized heterocyclic [3.1.0]-ring systems.

Comment: The present method provides access to a set of 3-azabicyclo[3.1.0]hexanes (compounds **1**–**5**) from the reaction of corresponding allylic amine with bromoethylsulfonium salt. The CF_3-derivative **6** is obtained from the allylic amine and the β-CF_3 vinylsulfonium salt. In addition, a 3-azabicyclo[4.1.0]hexane derivative (**7**) is derived from the reaction of a homoallylic amine and the sulfonium salt, while a 3-oxabicyclo[3.1.0]hexane derivative (**8**) is obtained from the allylic alcohol and the sulfonium salt. The products are obtained with high levels of diastereoselectivity. The chemistry described is certain to find application in the exploration of novel bioactive compounds.

SYNFACTS Contributors: Victor Snieckus, John I. Trujillo (Pfizer)
Synfacts 2013, 9(11), 1159 Published online: 18.10.2013
DOI: 10.1055/s-0033-1340007; **Reg-No.:** V13013SF