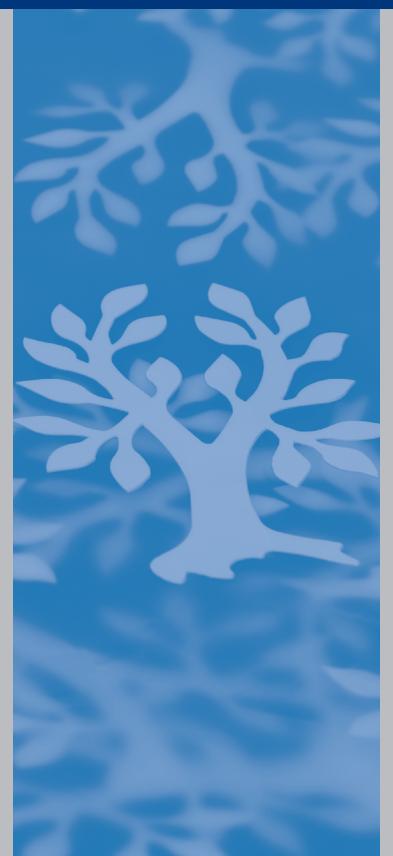
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SYNFACTS Highlights in Current Synthetic Organic Chemistry

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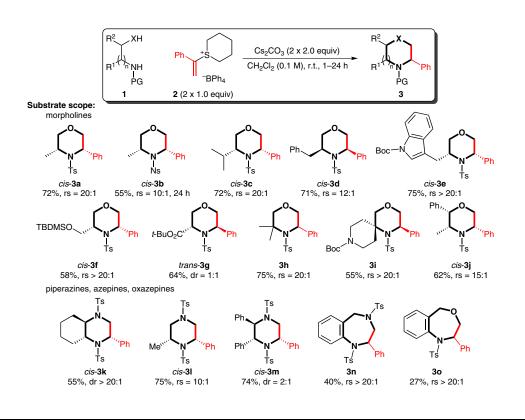


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Synthesis of 6- and 7-Membered N-Heterocycles Using α -Phenylvinylsulfonium Salts *Org. Lett.* **2015**, *17*, 5044–5047.

Synthesis of Six- and Seven-Membered Heterocycles



Significance: Reported is a highly regio- and diastereoselective synthesis of morpholines **3** from N-protected amino alcohols **1** (PG = protecting group) and the α -phenylvinylsulfonium salt **2**; the method can also be used to prepare piperazines, azepines, or oxazepines. Cs₂CO₃ was required for high diastereoselectivity, the optimum yields being obtained by batchwise addition of both the base and salt **2**. No desired product was formed when PG = Boc, Cbz, Troc, Bn, or COCF₃, whereas PG = nosyl led to a lower yield and regioselectivity. A variety of R¹ groups were well tolerated, whereas R² = Me led to diminished diastereoselectivity. The structure of *cis*-**3a** was confirmed by single-crystal X-ray analysis.

SYNFACTS Contributors: Victor Snieckus, Michael E. Dalziel Synfacts 2015, 11(12), 1249 Published online: 17.11.2015 DOI: 10.1055/s-0035-1560892; Reg-No.: V13815SF Comment: Given the importance of six- and seven-membered heterocycles in pharmaceutically relevant compounds, the development of synthetic routes to compounds of type 3 is desirable (R. Wijtmans, M. K. S. Vink, H. E. Schoemaker, F. L. van Delft, R. H. Blaauw, F. P. T. Rutjes Synthesis 2004, 641). The method described has advantages over previous methods and involves simple operations. In this regard, a comparable yield and selectivity were observed in a gram-scale synthesis of cis-3a (72%, rs = 20:1), without the need for anhydrous conditions. Furthermore, deprotection of cis-3a and cis-3b to the corresponding hydrochloride salts was demonstrated in high yields (86-92%). A plausible rationale for the observed selectivity is provided.

Category

Synthesis of Heterocycles

Key words

sulfonium salts

morpholines

piperazines

oxazepines

asymmetric synthesis