SYNFACTS

Highlights in Current
Synthetic Organic
Chemistry

REPRINT

Thieme

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An Efficient Synthesis of Azetidines with (2-Bromoethyl)sulfonium Triflate
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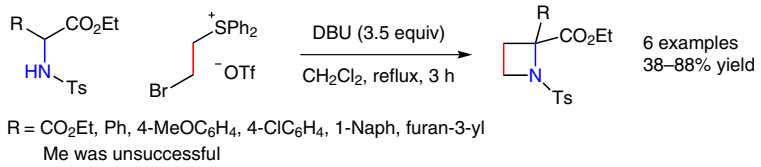
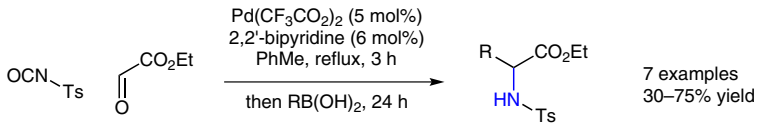
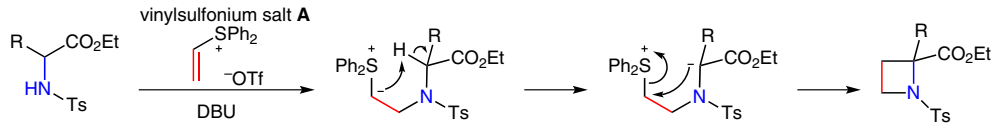
Synthesis of Azetidines from Glycine Esters and a Vinylsulfonium Salt





Proposed mechanism:



Significance: Reported is the synthesis of C2-substituted azetidines from the reaction of *N*-tosyl glycine esters and vinylsulfonium salt **A**, which was generated in situ by the reaction of (2-bromoethyl)diphenylsulfonium triflate with DBU. The starting glycine esters were synthesized using tosyl isocyanate, ethyl glyoxylate, and a boronic acid according to the previously published procedure of Lu and co-workers (H. Dai, M. Yang, X. Lu *Adv. Synth. Catal.* **2008**, *350*, 249). The proposed mechanism for azetidine formation is, in part, supported by the apparent importance of the acidity of the proton α to the ester; when R^1 = methyl the reaction fails.

Comment: Azetidines are both biologically important molecules and useful as synthetic intermediates, yet their synthesis can prove problematic, all of which is adroitly illustrated in the introduction to the current work. The presented method is an expansion of the previous work by Aggarwal and coworkers concerning the synthesis of heterocycles involving the use of the in situ generated vinylsulfonium salt **A**. It benefits from operational simplicity, reasonable yields and inexpensive or easily accessible starting materials. The reaction was optimized with respect to nitrogen protecting group, base, solvent, temperature, and ester. The substrate scope was modestly studied and the reaction seems to be tolerant to an ester in addition to sterically bulky, electron-poor, and electron-rich aromatic substitution. The yield of azetidine product in the reaction where R^1 = furan-2-yl was poor, possibly for the same reason that R^1 = alkyl failed: reduced acidity of the ester α hydrogen.

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Category
Synthesis of Heterocycles

Key words
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annulation
cyclization