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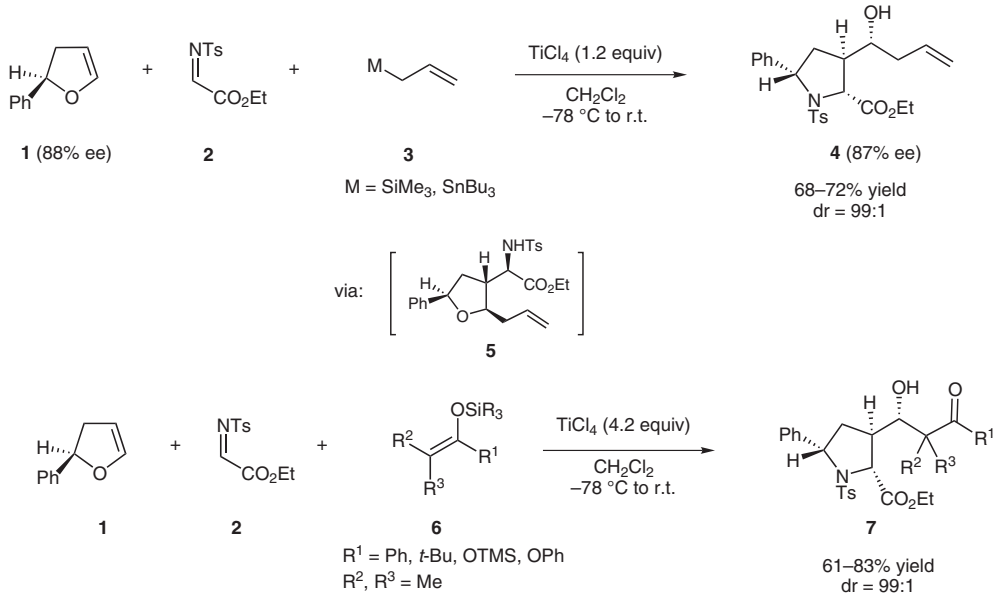
Asymmetric Multicomponent Reactions: Diastereoselective Synthesis of Substituted Pyrrolidines and Prolines
Org. Lett. **2006**, *8*, 4509-4511.

Diastereoselective Synthesis of Pyrrolidines and Prolines



Significance: The report constitutes one of the few multicomponent reactions (MCR) that generate multiple stereocenters. The method created three contiguous stereocenters in a single operation. The rearrangement of furan adduct **5** to pyrrolidine **4** is an extension of a method developed previously by the same group (A. K. Ghosh, C.-X. Xu, S. S. Kulkarni, D. Wink *Org. Lett.* **2005**, *7*, 7-10). The reaction can be halted at the THF adduct **5** in the presence of MeCN as an additive. In all cases, the MCR yielded highly substituted proline derivatives **4** and **7** with excellent diastereoselectivity.

Review: D. J. Ramon, M. Yus *Angew. Chem. Int. Ed.* **2005**, *44*, 1602-1634.

Comment: The proposed mechanism for the conversion of **5** into **4** invokes formation of a benzylic carbocation promoted by $TiCl_4$. It is noteworthy that an almost perfect retention of the stereochemistry was observed. An S_N2 attack of the tosylamine on the activated benzylic ether was proposed to explain the observed stereochemical outcome. It should be noted that hydrides instead of allyl nucleophiles (**3**) were also effective (Et_3SiH = 69%, Bu_3SnH = 53%), but the selectivity was reduced (90:10 and 85:15, respectively). When enolsilanes or ketene acetals **6** were used as one component, an excess of Lewis acid was necessary to get full conversion into pyrrolidine derivatives **7**.

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