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 TiCl₄. 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 (Et₃SiH = 69%, Bu₃SnH = 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**.

Category

Metal-Catalyzed
Asymmetric
Synthesis and
Stereoselective
Reactions

Key words

multicomponent
reaction

pyrrolidines

tetrahydrofuran

titanium
tetrachloride

Lewis acids

allylsilanes

allylstannanes

aldols

N-tosyl imino esters

SYNFACT
of the month