New frontiers in Castagnoli–Cushman Reaction
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Introduction and Aim

Thorough exploration of chemical space relevant for medicinal chemistry requires synthetic methods, which open access to potential lead compounds in an efficient manner. Multicomponent reactions are especially promising in this view since they provide sufficient diversity of the compound libraries with minimum synthetic efforts required. In particular, Castagnoli-Cushman reaction (CCR), i.e. condensation of imines with cyclic anhydrides, has been considered as an efficient tool for synthesis of pyrrolidones and piperidones, as well as their fused and heteroatom-substituted analogues.

Like in the case of many other multicomponent reactions, the use of CCR has been limited to the construction of five- and six-membered heterocycles. Cyclic systems of larger size such as seven-membered rings are considered as less accessible by analogous condensations, but could be in principle obtained since adipic anhydride and its corresponding benzo analogue are analogous condensations, but could be in principle obtained since adipic anhydride and its corresponding benzo analogue are known and stable compounds.

Scope and limitation

Conditions A: 14k′ 15a = 0.1 (LCMS)
Conditions B: 14k′ 15a = 1.6 (LCMS)

Diastereoselectivity

Conditions: A 16a 16b = 0.12 4 (LCMS)
Conditions B: 16a 16b = 1.0 2.3 (LCMS)

References


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