J. PEDRONI, N. CRAMER* (ECOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE, SWITZERLAND) Enantioselective C-H Functionalization-Addition Sequence Delivers Densely Substituted 3-Azabicyclo[3.1.0]hexanes

Enantioselective C–H Functionalization–Addition Sequence Delivers Densely Substituted 3-Azabicyclo[3.1.0]hexanes J. Am. Chem. Soc. **2017**, 139, 12398–12401.

Enantioselective Modular Approach to 3-Azabicyclohexanes



Significance: 3-Azabicylo[3.1.0]hexanes are present in a wide range of bioactive compounds. Besides many common methods to access this scaffold, the 1,3-dipolar cycloaddition of azomethine ylides to cyclopropenes (A. S. Filatov et al. *J. Org. Chem.* 2017, *82*, 959) and multicomponent reactions in water (M. Ghorbani et al. *Org. Lett.* 2016, *18*, 4759) have recently been described. The present work takes advantage of the high electrophilic character of the intermediate alkylfluoro-substituted ketamine 2 to produce highly substituted 3-azabicyclo[3.1.0]hexanes 3 by addition of nucleophiles. The presence of the strained cyclopropane ring ensures the diastereoselective control of the addition.

Comment: Reported is the enantioselective palladium-catalyzed cyclization of imidoyl chlorides 1 to produce cyclopropane-fused dihydropyrrole 2. The scope of this transformation is broad, and 1 with various substituents gave products 2 in high yields and high enantioselectivities. When $R^2 = H$, the reaction proceeded with low yield, although the er was unaffected. Cyclopropane C-H functionalization was observed exclusively in the presence of an aryl substituent ($R^1 = Ar$), to give dihydropyrroles 2. However, switching the ligand to Ph₃P reversed the chemoselectivity to aryl C–H functionalization, producing spirocyclic dihydroisoquinolines 4. The reaction of electrophilic ketimines 2 with various nucleophiles gave pyrrolidines 3 diastereoselectively. Moreover, 3 can be accessed directly from 1 in a one-pot manner without any significant loss in enantioselectivity.

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