Chiral γ-Lactams by Enantioselective Cyclopropane Functionalization

Significance: Cyclopropanes are important components of many biologically active molecules and they can be found fused to a pyrrolidine ring in certain medicines. The authors present a new approach to this ring system using an enantioselective C–H functionalization of a cyclopropane, enabled by a Pd/TADDOL catalyst. This work constitutes a notable advance in the field of C(sp^3)–C(sp^3) bond formation by C–H activation.

Comment: The reaction shows good functional group tolerance and allows the synthesis of a library of diverse cyclopropane-fused pyrrolidines in high yield and with high enantioselectivity. The substrates can be accessed in a sequence by using a variant of the Kulinkovich reaction. The authors also demonstrate that the catalyst can efficiently activate methyl C–H groups in other substrates.

Selected examples:

Additional examples:

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