Regio- and Diastereoselective [3 + 2] Annulation of Aliphatic Aldimines with Alkenes via β-C(sp^3)−H Activation by Scandium Catalysts

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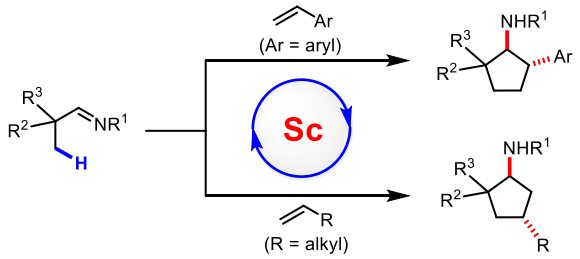
The catalytic [3 + 2] annulation of aliphatic aldimines with alkenes via β-C(sp^3)−H activation is of much interest and importance for the synthesis of multi-substituted aminocyclopentanes, which are important components in many natural products, bioactive molecules and pharmaceuticals. However, such transformation has remained a challenge to date because of the lack of suitable catalysts.[1-3] Here we report for the first time the regio- and diastereoselective [3 + 2] annulation of a wide range of aliphatic aldimines with alkenes via the activation of an unactivated β-C(sp^3)−H bond by half-sandwich scandium catalysts.

This protocol offers a straightforward and atom-efficient route for the synthesis of a new family of multi-substituted aminocyclopentane derivatives from easily accessible aliphatic aldimines and alkenes. The annulation of aldimines with styrenes exclusively afforded the corresponding 5-aryl-*trans*-substituted 1-aminocyclopentane derivatives with excellent diastereoselectivity (d.r. > 19:1) through the 2,1-insertion of a styrene unit. In the annulation of aldimines with aliphatic alkenes, the alkene insertion took place in a 1,2-fashion, selectively affording the corresponding 4-alkyl-*trans*-substituted 1-aminocyclopentane products. The addition of a catalytic amount of an appropriate amine such as adamantylamine (AdH_2) or dibenzylamine (Bn_2NH) showed significant effects on the catalyst activity and stereoselectivity. Some key reaction intermediates were isolated to elucidate the reaction mechanism.



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