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Enantioselective Intramolecular Hydroacylation of Unactivated Alkenes: An NHC-Catalyzed Robust and Versatile Formation of Cyclic Chiral Ketones

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Intramolecular Hydroacylation of Unactivated Alkenes by NHC Catalysis

Category

Organo- and Biocatalysis

Key words

hydroacylation

NHC catalysis

unactivated alkenes

quaternary stereocenters

Synfact
of the month

Selected examples:

Significance: Glorius and co-workers report a highly enantioselective intramolecular N-heterocyclic carbene catalyzed hydroacylation of unactivated alkenes **1** to afford ketones **2** which bear an α -quaternary stereocenter. By employing pre-catalyst **A**, both aliphatic and aromatic aldehydes reacted smoothly to afford the desired products, by 5- or 6-exo-trig cyclization, in good to excellent yields and enantioselectivities. The scalability of the reaction was also proven by running the reaction on a two-gram scale (99% yield, er = 99:1).

Comment: Enantiopure ketones bearing an α -quaternary stereocenter (**2**) are important motifs in biologically active molecules. The authors report an asymmetric approach to synthesize these compounds by employing simple unactivated olefins as starting materials. The methodology shows a strong functional group tolerance, proven by a 'robustness screening' and a broad substrate scope. A current limitation of the protocol is represented by the instability of products bearing an α -tertiary stereocenter; they racemize under the basic reaction conditions. Previous mechanistic studies (*Angew. Chem. Int. Ed.* **2011**, 50, 4983) from the same group on salicylaldehyde-derived substrates suggest a protonation of the alkene from the Breslow intermediate followed by C–C bond formation.

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