

Asymmetric Synthesis of 1,2,3-Substituted Cyclopropanes

Category

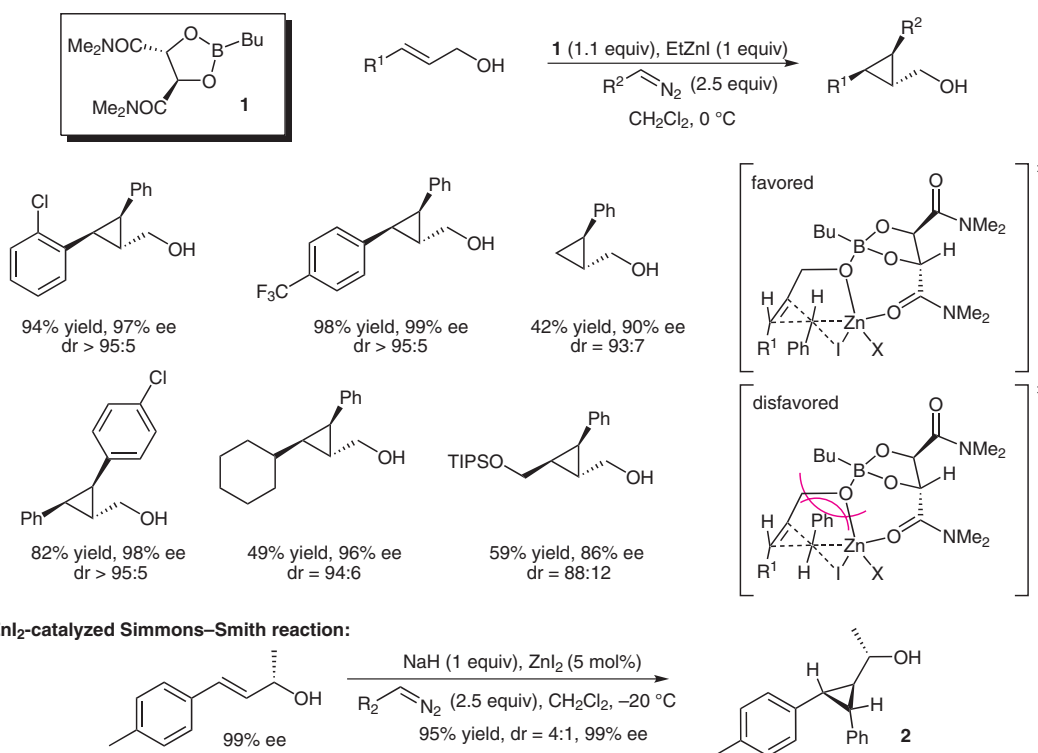
Metal-Catalyzed
Asymmetric
Synthesis and
Stereoselective
Reactions

Key words

cyclopropanation

Simmons–Smith
reaction

diazo compounds



Significance: The established approaches to 1,2,3-substituted cyclopropanes usually involve the formation of the preactivated ring followed by introduction of the third substituent. The recent work of Charette and co-workers (*J. Am. Chem. Soc.* **2009**, *131*, 15624) describes a highly enantioselective method based on this concept. Herein, this group reports a *direct* approach, representing the first enantioselective cyclopropanation of alkenes by zinc carbenoids generated in situ from diazo compounds. A number of products was obtained with a wide range of yields (42–98%), good to excellent enantioselectivities (86–99% ee) and dr values up to >95:5. In addition, the first Simmons–Smith reaction using a catalytic amount of zinc salt is reported, which furnished **2** with 95% yield and a dr of 4:1.

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Comment: The asymmetric induction was achieved by the use of a stoichiometric amount of chiral ligand **1**. EtZnI was found to be the optimum base for the deprotonation of the allylic alcohol. Cinnamyl alcohol derivatives reacted with phenyldiazomethane with complete conversions and excellent enantioselectivities (92–99% ee); the exclusive formation of only one diastereomer was observed. *Para*- and *ortho*-aromatic halogens were tolerated. The use of alkyl-substituted allylic alcohols resulted in somewhat inferior results. Primary, secondary, and functionalized alkyl groups were tolerated. Other aryl diazo reagents were also successfully employed.