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Rhodium-Catalyzed Intramolecular, Anti-Markovnikov Hydroamination. Synthesis of 3-Arylpiperidines
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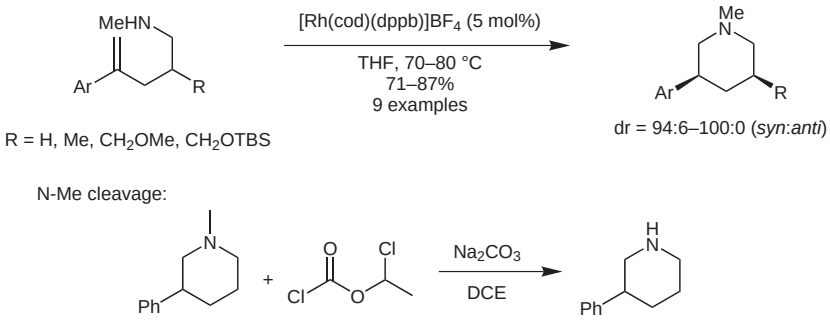
Syn-Selective anti-Markovnikov Intramolecular Hydroamination



Significance: Using a Rh(I)/DPPB catalyst system, aminoolefins undergo a remarkably selective anti-Markovnikov hydroamination reaction to generate 3-arylpiperidines in good yields. When the aminoolefin is appropriately substituted (R ≠ H), products are obtained with high degrees of *syn*-selectivity; presumably due to equatorial placement of the substituents in a chair-like transition state. The *N*-methyl substituent is necessary for the reaction to proceed; however, this group can be easily cleaved (see scheme).

Comment: Hydroamination reactions have been studied for decades, with many advances improving the efficiency of the reaction. However, the main limitation of hydroamination is a lack of Markovnikov/anti-Markovnikov selectivity (see review below), which is overcome using the rhodium catalyst system reported. The products of this reaction are medicinally interesting, as 3-arylpiperidines have found activity as dopamine autoreceptor antagonists which stimulate dopamine turnover without inducing hypoactivity. Development of an enantioselective anti-Markovnikov hydroamination would provide rapid access to this class of bioactive compounds.

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Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

rhodium(I)

anti-Markovnikov

hydroamination