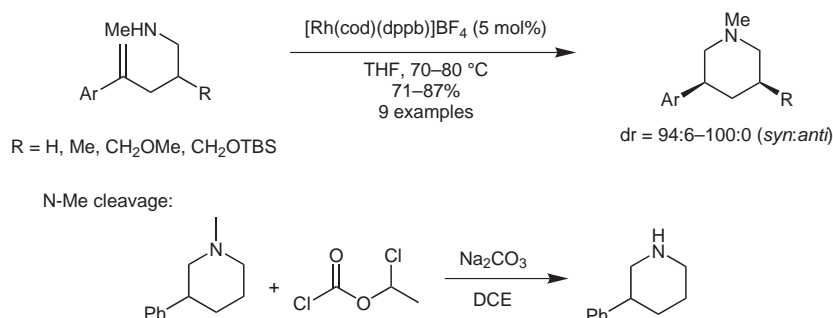


Syn-Selective anti-Markovnikov Intramolecular Hydroamination



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 ($R \neq H$), 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 medically 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.

Review: S. Hong, T. J. Marks *Acc. Chem. Res.* **2004**, *37*, 673-686.