Stereoselective Reactions

anti-Markovnikov

hydroamination

Key words rhodium(l)

Category

Syn-Selective anti-Markovnikov Intramolecular Hydroamination

$$\begin{array}{c} \text{MeHN} \\ \text{Ar} \\ \text{R} \end{array} \begin{array}{c} \text{[Rh(cod)(dppb)]BF}_4 \text{ (5 mol\%)} \\ \text{THF, 70-80 °C} \\ \text{71-87\%} \\ \text{9 examples} \end{array}$$

$$\text{dr} = 94.6-100:0 \text{ (syn:anti)} \\ \text{N-Me cleavage:} \\ \text{Ph} \end{array}$$

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 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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