Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

enantioselectivity

chiral α-amines

one-pot reaction

multicomponent reaction

copper

imines

dialkylzinc

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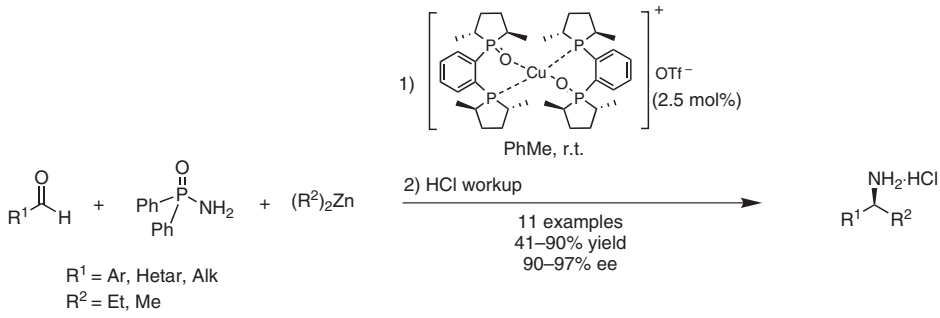
Multicomponent One-Pot Procedure for the Synthesis of Free α-Chiral Amines from Aldehydes
J. Org. Chem. **2005**, *70*, 10864-10867.

Three-Component, One-pot Procedure for α-Chiral Amine Synthesis



Significance: This one-pot process afforded chiral α-amine hydrochlorides in excellent enantioselectivities and moderate to excellent yields from an aldehyde, diphenylphosphinoylamide, and excess dialkylzinc. This protocol should replace the previously described three-step reaction including imine formation, enantioselective nucleophilic addition, and deprotection. A one-step process that can potentially be adapted to combinatorial techniques is now available. A number of aldehydes including different electronic and steric properties are tolerated using catalytic amounts of BozPHOS·CuOTf complex. Two commercially available dialkylzinc reagents (Et_2Zn and Me_2Zn) were used, the latter yielding to poorer yield and slightly lower enantioselectivities.

Comments: Chiral α-amines are very common in the nature and among pharmaceuticals, hence synthetic methods leading to enantioenriched products are very important (see reviews below). Previously, Charette developed an enantioselective addition of dialkylzinc to *N*-phosphinoylimines to form N-protected amines in excellent enantioselectivities (A. A. Boezio, J. Pytkowicz, A. Côté, A. B. Charette *J. Am. Chem. Soc.* **2003**, *125*, 14260-14261). Drawbacks were the extra imine formation and deprotection steps. This new procedure uses the dehydration power of dialkylzinc (5 equiv) in the formation of the imine, and an HCl workup for deprotection to greatly simplify the chiral amine preparation. It would be advantageous if more functionalized dialkylzinc compounds (preferably from commercially available alkylzinc halide) was tested, even though previous work has shown that some of them worked well on the imine addition step.

Reviews: R. Bloch *Chem. Rev.* **1998**, *98*, 1407-1438; S. Kobayashi, H. Ishitani *Chem. Rev.* **1999**, *99*, 1069-1094.

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