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Highly Enantioselective Insertion of Carbenoids into N–H Bonds Catalyzed by Copper Complexes of Chiral Spiro Bisoxazolines

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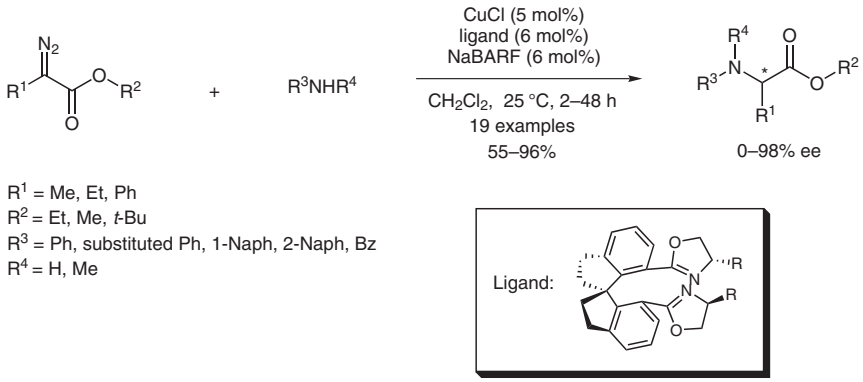
Copper-Catalyzed Enantioselective N–H Insertion Reactions



Significance: A highly enantioselective catalytic insertion of α-diazoesters into N–H bonds is reported. The catalyst is prepared from a Cu(I) source, a spiro-bisoxazoline ligand, and a BARF counterion. A wide range of substituted anilines and naphthalenamines could be used for the insertion reaction with complete conversions observed within two hours and high yields and enantioselectivities were obtained. However, an electron-donating group in the *para* position of a phenyl-substituted aniline or a halogen at the *ortho* position resulted in slightly lower enantioselectivities for unknown reasons. The ester group on the diazoester could be changed with negligible effect; however, the diazo substituent is more sensitive and can lead to lower yields or ee values. No enantioselectivity was induced with *N*-methylaniline and benzamide, and cyclohexylamine was inert under the reported conditions.

Comment: Although significant effort has been focused on diazoesters over the years, a highly enantioselective catalytic N–H insertion has remained elusive until the present communication. The authors note that the spiro-bisoxazoline ligand, which was developed in their labs, provided optimal enantioselectivities compared to other spiro bisoxazolines, with one diastereomer of the ligand exhibiting a matched combination of chiralities. Also, the nature of the counterion significantly affects the reaction; the catalyst with the BARF counterion has high enough activity that only 1 mol% of the catalyst is needed. Copper(II) could also be used as the catalyst precursor; however, it provides lower ee values. Chloroform and benzene could also be used as solvents, though using acetonitrile resulted in significantly longer reaction times.

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