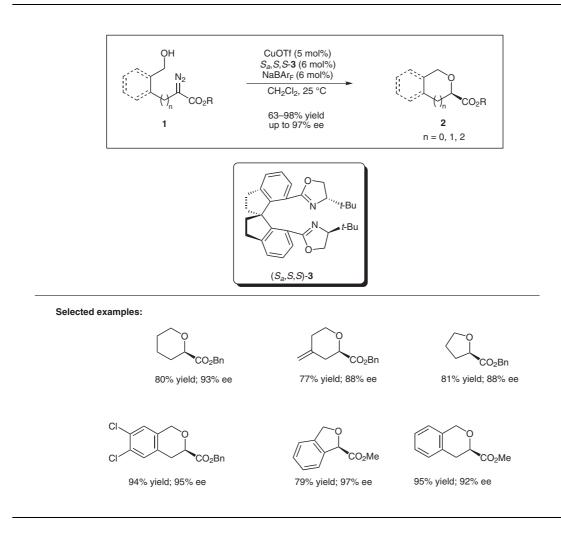
S.-F. ZHU, X.-G. SONG, Y. LI, Y. CAI, Q.-L. ZHOU* (NANKAI UNIVERSITY, TIANJIN, P. R. OF CHINA) Enantioselective Copper-Catalyzed Intramolecular O–H Insertion: An Efficient Approach to Chiral 2-Carboxy Cyclic Ethers

J. Am. Chem. Soc. 2010, 132, 16374-16376.

Enantioselective Synthesis of 2-Carboxy Cyclic Ethers



Significance: The formation of new carbonheteroatom bonds using transition-metalcatalyzed carbene insertion reactions into X–H bonds (X = O, N, S) is a useful synthetic tool. While highly enantioselective variants of intermolecular O–H insertions are known, selective intramolecular versions have not been developed. Herein, the authors present the first highly enantioselective copper-catalyzed O–H insertion approach used for the preparation of chiral 2-carboxy cyclic ethers of type **2**.

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 Synfacts 2011, 2, 0165-0165
 Published online: 19.01.2011

 DOI: 10.1055/s-0030-1259338; Reg-No.: L17010SF

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Comment: Starting from readily available ω -hydroxy- α -diazo esters **1**, a number of chiral cyclic ethers of type **2** with various ring sizes could be prepared in good to excellent yields and high enantioselectivities. The combination of CuOTf and the chiral spiro bisoxazoline ligand (S_a ,S,S)-**3** in the presence of catalytic amounts of NaBAr_F in non-coordinating solvents like methylene chloride was found to be crucial to achieve high selectivities. The products formed in this transformation are useful building blocks since the 2-carboxylic cyclic ether substructure can be found in several natural products and pharmaceuticals.

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

asymmetric O-H insertion

cyclic ethers

copper