Enantioselective Synthesis of 2-Carboxy Cyclic Ethers

**Significance:** The formation of new carbon–heteroatom bonds using transition-metal-catalyzed 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.

**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,S,S)-3 in the presence of catalytic amounts of NaBARF 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.

![Reaction Scheme](image-url)