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N-Heterocyclic Carbene Catalyzed Asymmetric Hydration: Direct Synthesis of \(\alpha\)-Protio and \(\alpha\)-Deutero \(\alpha\)-Chloro and \(\alpha\)-Fluoro Carboxylic Acids


## Asymmetric Synthesis of \(\alpha\)-Halo Carboxylic Acids from \(\alpha,\alpha\)-Dihalo Aldehydes

**Significance:** The enantioselective hydration of \(\alpha,\alpha\)-dichloro aldehydes and \(\alpha\)-fluoro enals catalyzed by N-heterocyclic carbene 1 has been reported. \(\alpha\)-Fluoro and \(\alpha\)-chloro carboxylic acids 2 and 3 were obtained in good yields with high enantioselectivity. The developed reaction enables incorporation of an \(\alpha\)-deuterium to give rise to enantioenriched \(\alpha\)-deutero \(\alpha\)-halo acids using D₂O as the deuterium source.

**Comment:** Enantioenriched \(\alpha\)-halo carbonyls are valuable synthetic intermediates. Current approaches to these compounds rely on the asymmetric generation of \(\alpha\)-halo aldehydes or esters. Rovis and colleagues previously demonstrated that chiral N-heterocyclic carbene catalyzes the enantioselective reaction of \(\alpha,\alpha\)-dichloro aldehydes and phenol leading to \(\alpha\)-chloro aryl esters (N. T. Reynolds, T. Rovis* J. Am. Chem. Soc. 2005, 127, 16406). This approach is based on the enantioselective protonation of catalytically generated chiral enolates A. Utilizing the same principle and employing water as the nucleophile instead of phenol enabled a direct approach to \(\alpha\)-halo carboxylic acids.