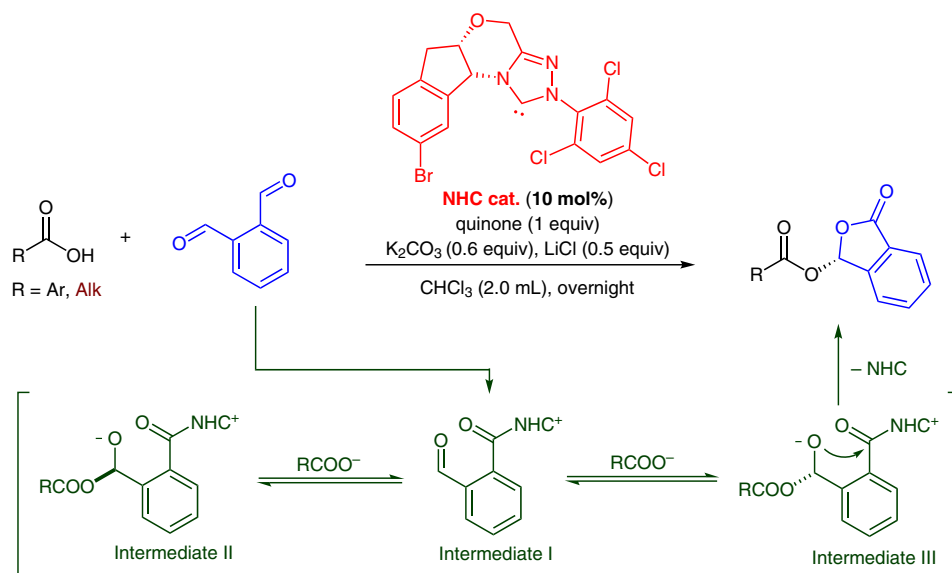
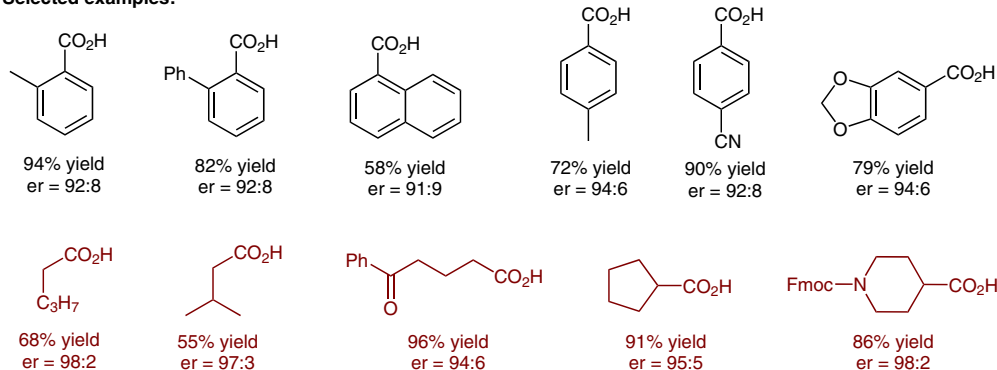


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Catalytic Asymmetric Acetalization of Carboxylic Acids for Access to Chiral Phthalidyl Ester Prodrugs
Nat. Commun. **2019**, *10*, 1675.

Phthalidyl Ester Prodrugs by Catalytic Asymmetric Acetalization of Carboxylic Acids



Selected examples:



Significance: The authors report an NHC-catalyzed asymmetric acetalization of carboxylic acids that provides efficient access to chiral phthalidyl ester prodrugs. Phthalidyl esters are conventionally prepared by treating carboxylic acids with 3-bromophthalides, but this standard approach exhibits poor stereoselective control over the newly created chiral center.

Comment: Interestingly, higher average enantioselectivities were obtained with aliphatic acid substrates than with aromatic acid substrates. However, stronger acids such as trifluoroacetic acid proved to be poor substrates for this transformation due to the lower nucleophilicities of their corresponding anions and the poor stabilities of the subsequent reaction intermediates.