Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

enamides

titanium

BINOLs

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Catalytic Asymmetric Difunctionalization of Stable Tertiary Enamides with Salicylaldehydes: Highly Efficient, Enantioselective, and Diastereoselective Synthesis of Diverse 4-Chromanol Derivatives

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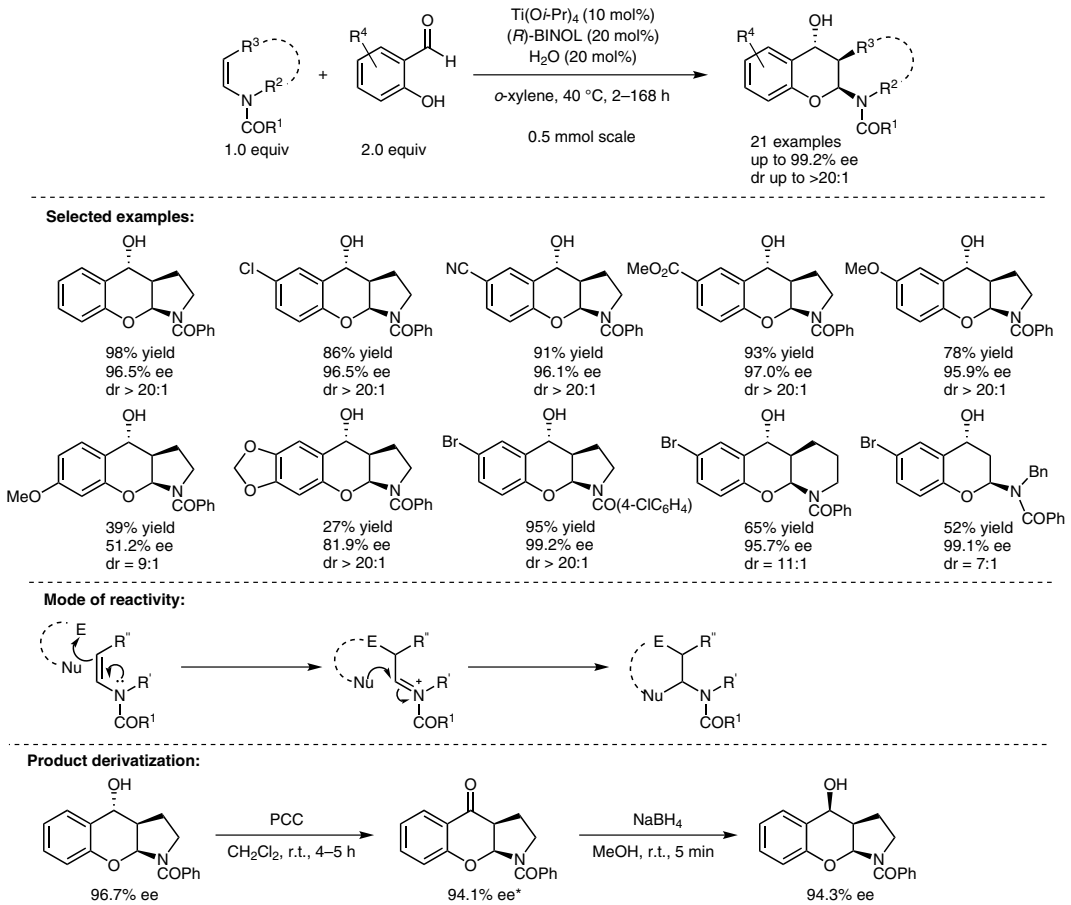
Enantioselective Reaction of Tertiary Enamides with Salicylaldehydes



*Slight loss in ee is explained by the presence of a minor amount of the opposite diastereomer of lower ee in starting material.

Significance: Tertiary enamides are related to enamines by replacement of an *N*-alkyl substitutent with an electron-withdrawing group. Despite this change, they remain nucleophilic. Taking advantage of this characteristic and of the electrophilicity of the transient iminium, the authors developed a modular titanium(IV)-catalyzed synthesis of 4-chromanol derivatives, by reaction with salicylaldehydes.

Comment: The use of a titanium–(*R*)-BINOL complex enabled the synthesis of diverse 4-chromanol products with good to excellent enantio- and diastereoselectivity. Water was found to have a marked effect on enantioselectivity: under anhydrous conditions, the ee decreased to 50.8%, whereas it was measured at 96.5% in the presence of 20 mol% water, in the model reaction. The exact mechanism remains to be elucidated.

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