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A Highly Reactive and Enantioselective Bifunctional Organocatalyst for the Methanolytic Desymmetrization of Cyclic Anhydrides: Prevention of Catalyst Aggregation

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A New Catalyst for the Desymmetrization of Cyclic Anhydrides

Significance: A new hydrogen-bonding cinchona alkaloid based organocatalyst was designed by focusing on the prevention of catalyst self-aggregation. Due to the lack of this deactivation mode, the resulting bifunctional chiral sulfonamide **1** showed unprecedented catalytic activity in the methanolytic desymmetrization of *meso*-anhydrides. The reaction proceeds at room temperature within few hours in excellent yields (88–97%) and enantioselectivities (er = 95.5:4.5 to 98.5:1.5).

Review: Y. Cheng, P. McDaid, L. Deng *Chem. Rev.* **2003**, 103, 2965-2984.

Comment: The alcoholytic desymmetrization of *meso*-anhydrides with cinchona catalysts is a well established reaction in organocatalysis although turnover numbers are frequently moderate (see Review). Unfortunately, previously introduced hydrogen-bonding catalysts suffer from self-aggregation, coming along with lower reactivity and strongly temperature- and concentration-dependent enantioselectivities. Since **1** was especially designed to avoid this phenomenon, the catalyst showed an unprecedented reactivity beside excellent enantioselectivities. The application of **1** in other organocatalytic transformations seems promising.

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