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Sequential and Modular Synthesis of Chiral 1,3-Diols with Two Stereogenic Centers: Access to All Four Stereoisomers by Combination of Organo- and Biocatalysis *Angew. Chem. Int. Ed.* **2009**, *48*, 9355-9358.

organocatalysis biocatalysis QН QН 1 (5 mol%) (S)-ADH, buffer solvent-free, r.t., 20 I >95% conversion >95% conversion NADH NAD dr (anti) up to 11:1 er up to 90:10 er up to > 99.5:0.5catalyst co-factor regeneration ΗÌ OH (S,S)-1 Рń ЮH 25% v/v

Combining Organo- and Biocatalysis

Significance: The authors report a chemoenzymatic reaction sequence towards 1,3-diols. The reported route consists of the amine-**1**-catalyzed aldol addition of acetone to aromatic aldehydes with a subsequent alcohol dehydrogenase (ADH) catalyzed ketoreduction. The co-factor NADH or NADPH, depending on the involved enzyme, respectively, was used in only catalytic amounts, enabled by a substrate-coupled regeneration process. The stereochemical outcome of the reaction could be fully controlled. With the four possible combinations of (*S*,*S*)-**1**, (*R*,*R*)-**1** and (*S*)-ADH, (*R*)-ADH all diastereoisomers of each product could be obtained with excellent diastereo- and enantiocontrol. **Comment:** The preparation of 1,3-diols is a challenging synthetic task, often achieved via metal catalysis or enzymatic reactions relying on dynamic kinetic resolution. The elegance of the present procedure is that it enables the synthesis of all four possible diastereoisomers of the desired diols by simple variation of the catalyst combination. Furthermore, the involved catalysts and the reaction conditions are fully biocompatible, enabling 'green chemistry'. Since the combination of bioand metal catalysis has already been achieved (see Review below), the present work closes a gap, disclosing that in principle all three types of catalyses are compatible.

Review: O. Pàmies, J.-E. Bäckvall *Chem. Rev.* **2003**, *103*, 3247-3262.

Category

Organo- and Biocatalysis

Key words

1.3-diols

enzymatic reduction

aldol addition

chemoenzymatic sequence



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