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Enantioselective Reduction of Ketones with "Designer Cells" at High Substrate Concentrations: Highly Efficient Access to Functionalized Optically Active Alcohols
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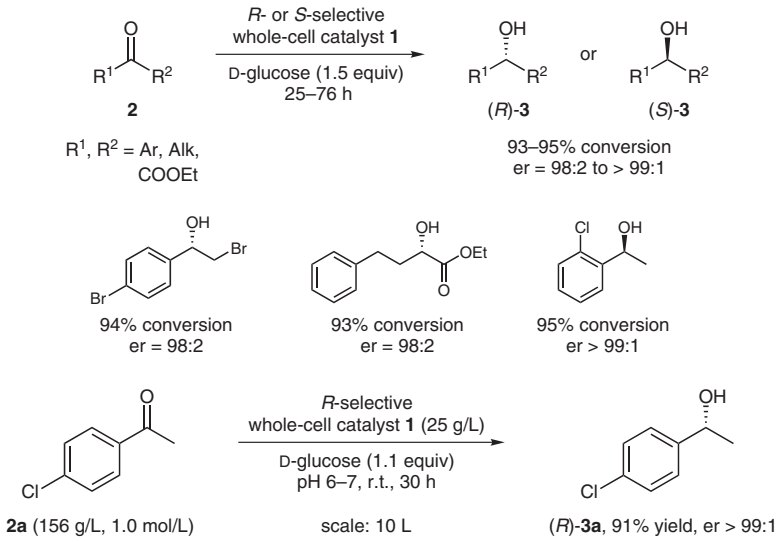
Biocatalytic Asymmetric Reduction of Ketones Using Designer Cells



Significance: Designer cells have been developed as catalysts for the asymmetric reduction of ketones. Whole-cell catalysts **1** mediate the reduction of carbonyl compounds **2** in the presence of D-glucose to give (*R*)- or (*S*)-alcohols **3** in high conversions and excellent enantioselectivities. Both aromatic and aliphatic substrates as well as α-keto esters can be used. Furthermore, one example of a ketone (**2a**) has been demonstrated to undergo the reduction on a technical scale in good yield and with essentially perfect stereocontrol.

Comment: Although alcohol dehydrogenases are valuable biocatalysts for the asymmetric reduction of ketones (see for example: S. Shimizu et al. *Appl. Microbiol. Biotechnol.* **2003**, *62*, 437-445), only a few industrial applications have been described. Whole-cell catalysts **1** contain not only an alcohol dehydrogenase to reduce ketones **2**, but also $NAD(P)^+$ and a glucose dehydrogenase, which regenerates the cofactor $NAD(P)H/H^+$ in situ. Instead of adding any costly external cofactor, the present method allows for the use of inexpensive D-glucose to regenerate the reducing agent. Moreover, the reaction can be carried out in pure aqueous media at high substrate concentrations. Therefore, an attractive practical feature of this process could be the extension to the preparation of various optically active alcohols on a technical scale.

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