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Ru(II)-Catalyzed Asymmetric Transfer Hydrogenation of α-Alkyl-β-Ketoaldehydes via Dynamic Kinetic Resolution

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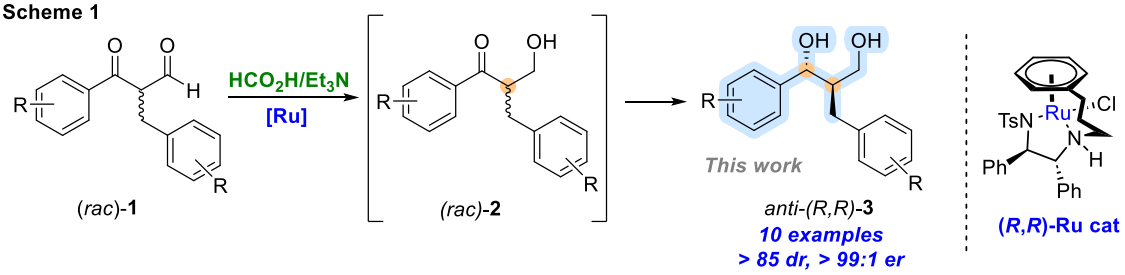
ABSTRACT

The 2-alkyl-1-phenylpropane-1,3-diols are structural motifs containing two adjacent stereocenters that are prevalent in various natural products. Notable examples include the lignans (-)-podophyllotoxin and (-)-sesaminone, as well as the flavonoid (+)-homoferrugenone [1–3]. The transition metal (TM)-catalyzed asymmetric hydrogenation (AH) of α-alkyl-β-ketoesters stands out as a straightforward approach to access these key intermediates. This method allows for the creation of two contiguous stereocenters in one single step through a dynamic kinetic resolution (DKR) [4–6]. However, the α-alkyl-β-ketoesters pose challenges in TM-AH-DKR reactions when compared to cyclic β-ketoesters or acyclic α-heteroatom-substituted β-ketoesters.

In this work, the (*R*,*R*)-Teth-TsDPEN-Ru(II) complex promoted the one-pot double C=O reduction of α-alkyl-β-ketoaldehydes through asymmetric transfer hydrogenation/dynamic kinetic resolution (ATH-DKR) under mild conditions. In this process, ten *anti*-2-benzyl-1-phenylpropane-1,3-diols (85:15 to 92:8 dr) were obtained in good yields (41-87%) and excellent enantioselectivities (>99% ee for all compounds) (Scheme 1).

Scheme 1



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