Asymmetric Hydrogenation of α-Amino Esters through Dynamic Kinetic Resolution Catalyzed by Ruthenabicyclic Complexes (RUCY®)

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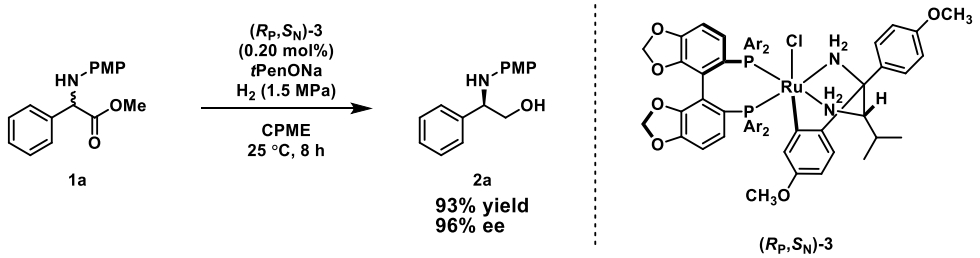
Optically active β-substituted β-aminoethanols have been frequently utilized in the synthesis of a wide variety of bioactive compounds, including natural products, medicines, and agrochemicals. Reduction of enantiomerically enriched α-amino esters into the β-amino alcohols with maintenance of the enantiopurity by metal hydride reagent or transition metal catalyst is well-known methods. [1] However, these procedures are required to prepare the corresponding enantiomerically enriched α-amino esters in advance. We herein report asymmetric hydrogenation of racemic α-substituted α-amino esters into the enantiomerically enriched β-amino alcohols through dynamic kinetic resolution with chiral ruthenabicyclic complexes (RUCY®). [2]

N-PMP (PMP = *p*-methoxyphenyl) protected phenylglycine methyl ester **1a** was selected as a substrate for optimization of catalyst structure and reaction conditions, and the RuCl[(*S*)-daipena][(*R*)-dm-segphos] (R_P,S_N)-**3**/*t*PenONa system was successfully catalyzed the hydrogenation of **1a** to give **2a** in 96% ee. The scope of the reaction was also examined, and a variety of β-aryl- and β-heteroaryl-substituted β-aminoethanols was obtained in high ee (up to 97%). The mechanistic deuteration experiments suggested that the reaction is not a simple ester hydrogenation, but proceeds with 1,2-hydride migration of the α-amino acetalate intermediate into the α-hydroxy imine.



1) See for example: (a) W. Kuriyama *et al*., *Adv. Synth. Catal*. **2010**, *352*, 92–96. (b) B. M. Widegren *et al.*, *Org. Lett*. **2018**, *20*, 2654–2658.
2) K. Matsumura *et al. J. Am. Chem. Soc*. **2011**, *133*, 10696–10699.