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Convergent Asymmetric Disproportionation Reactions: Metal/Brønsted Acid Relay Catalysis for Enantioselective Reduction of Quinoxalines
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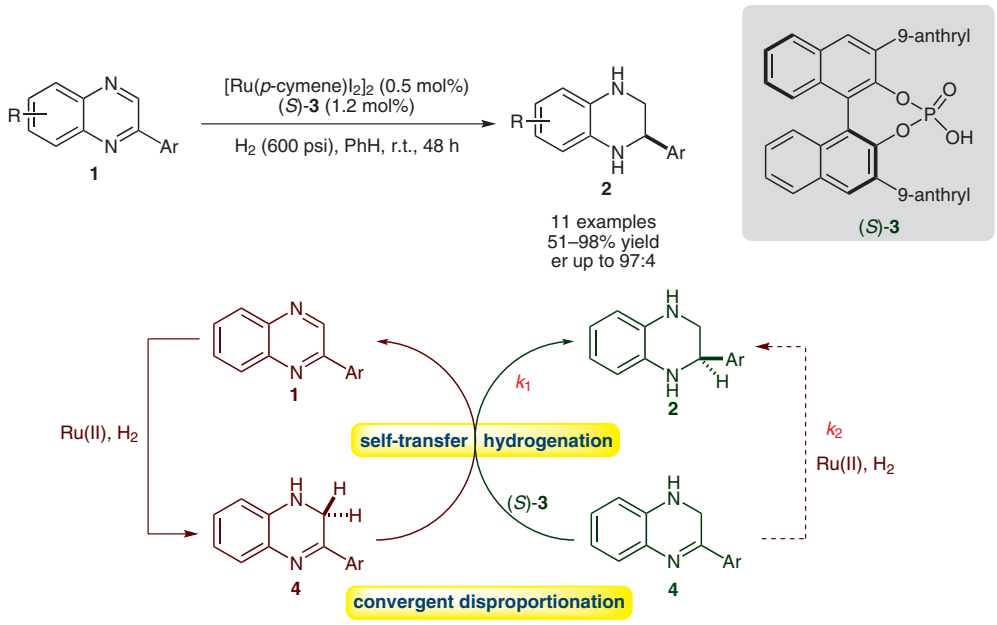
Reduction of Quinoxalines: A Convergent Disproportionation Reaction



Significance: The authors report an elegant transition metal/Brønsted acid relay catalytic system for the asymmetric reduction of quinoxalines **1**, where a convergent disproportionation reaction of the dihydroquinoxaline intermediates **4** is involved. With Ru(II) as the catalyst for the initial reduction of **1** to dihydroquinoxalines **4** with H_2 and phosphoric acid catalyst **3** for subsequent asymmetric disproportionation reactions of **4**, tetrahydroquinoxaline products **2** were obtained generally in high yields and enantioselectivities. The detection of dihydroquinoxaline intermediates **4** in the hydrogenation of **1** without the addition of the Brønsted acid suggested that the first hydrogenation process catalyzed by Ru(II) was the rate-determining step. The higher reaction rate of the chiral acid catalyzed reaction (k_1) compared to the undesired side reaction (k_2) catalyzed by Ru(II) is crucial to the observed high enantioselectivities.

Comment: The same asymmetric transformation has been realized by Rueping and co-workers using Brønsted acid (*R*)-**3** as the catalyst and Hantzsch dihydropyridines as the hydride source (*Chem. Eur. J.* **2010**, *16*, 2688). Interestingly, a dramatic reversal of enantioselectivity was observed in the current asymmetric disproportionation reaction, which was attributed to the different steric demands in the 1,2- and 1,4-hydride transfer pathways. The use of hydrogen gas as the reductant makes the convergent disproportionation an ideal atom-economical process.

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Category
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reduction
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