Enantioselective Synthesis of Cyclic Dipeptides by Iridium-Catalyzed Hydrogenation

**Significance:** The 2,5-dioxopiperazine motif, also known as a cyclic dipeptide, is found in compounds possessing biological activity, such as retosiban and fumitremorgin C (see first Review below). In addition, the motif has found utility in asymmetric synthesis as a chiral auxiliary or organocatalyst (see second Review below; C. Becker et al. *Eur. J. Org. Chem.* 2005, 1497). The synthesis of the ring system is usually accomplished by careful cyclization of protected acyclic peptide precursors. Other methods exist, including asymmetric alkylation of 2,5-diketopiperazines and, to a limited degree, asymmetric reduction of compounds similar to 1 by cobalt catalysis in the total synthesis of an alkaloid (S. Takeuchi et al. *Heterocycles* 1990, 31, 2073).

**Comment:** In the current method, the asymmetric reduction of compounds 1 to give dioxopiperazines 3 in high yields with ee values of up to 98% and exclusive formation of the cis diastereomer. The optimal catalyst [SpinPHOX/Ir(I)] was identified by screening a series of ligands. The scope of the reduction is exemplified by products 3a–e. A mechanism that rationalizes the high ee values observed is proposed in which two C=C double bonds of the substrate are hydrogenated successively while bound to the iridium center.