Synthesis of (R)-Ofloxacin

Significance: The key step in the small-scale synthesis of (R)-ofloxacin depicted here is the first step, a chiral Brønsted acid catalyzed transfer hydrogenation in which the hydride source is the dihydropyridine C. These reactions give excellent enantiofacial discrimination with low catalyst loadings under mild conditions. A synthesis of the simpler fluoroquinolone antibiotic flumequine is also described.

Comment: Ofloxacin is a DNA gyrase inhibitor that was initially marketed as a racemate. The (S)-(−)-enantiomer, levofloxicin, is more active than the (R)-enantiomer and has now supplanted the racemate for the treatment of life-threatening bacterial infections.

Review: For a review about asymmetric Brønsted acid catalyzed transfer hydrogenations, see: M. Rueping, E. Sugiono, F. R. Schoepke *Synlett* 2010, 852-865.