Abstract

Over the last 20 years, asymmetric synthesis has seen considerable progress, particularly in the field of catalysis. In addition to enzyme catalysis and transition metal catalysis, organocatalysis, catalysis using small organic molecules also plays an important role in the asymmetric synthesis. Chiral organocatalysts allow the preparation of structurally interesting and optically pure molecules via various activation modes.

This work is focused on the use of organocatalysis based on the formation of hydrogen bonds in organic synthesis. Our study was devoted to the enantioselective organocatalytic reactions of ketimines leading to the formation of chiral vicinal centers.

The first part deals with the organocatalytic enantioselective addition reaction of α-fluoro(phenylsulfonyl)methanes to ketimines derived from isatin. The reaction utilizes catalysis of a commercially available quinoline alkaloid cinchonine. A series of enantiomerically pure compounds were prepared containing two neighboring stereocenters in good yields of up to 97%, with diastereoselectivity up to 6: 1 *dr* and with enantiomeric excesses of 70-98% *ee*. In most cases pure diastereomers were obtained.

In the second part of the work a method of enantioselective orgnocatalytic synthesis of bis-spirocompounds containing two neighboring chiral spiroatoms was developed. The transformation involves an organocatalytic Mannich reaction between isatin-derived ketimines and propargylated pyrazolones followed by a hydroamination reaction. The Mannich reaction was successfully catalyzed by the *epi*-quinine-derived chiral bifunctional Rawal´s amide. The synthesized optically active adducts with vicinal stereocenters were prepared in good yields of 63-97 %, with diastereoselectivity >20:1 *dr* and enantiomeric excesses of 97-99 % *ee*. The hydroamination reaction of the prepared adducts was catalyzed by a carbene gold catalyst in the presence of $AgNTf_2$ as silver salt. The desired bis-spiro compounds were obtained in good yields of up to 51 % and with high enantiomeric excesses of up to 99 % *ee*.