ENANTIOSELECTIVE SYNTHESIS OF (S)-(+) PRAZIQUANTEL (PZQ)

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Praziquantel is an generally known anthelmintic drug. Although several approaches for the synthesis of Praziquantel have appeared in the literature [1, 2] and in patents, only one stereoselective method have been reported [3]. To the stereoselective synthesis of Praziquantel we proposed the Bischler-Napieralski/asymmetric transfer reduction pathway as key steps in our synthetic strategy [4].

The basic strategy of our synthesis (Fig. 1) involves the Bischler-Napieralski cyclization and asymmetric hydrogen transfer with chiral ruten catalyst (*S,S*)-**8** [4, 5].

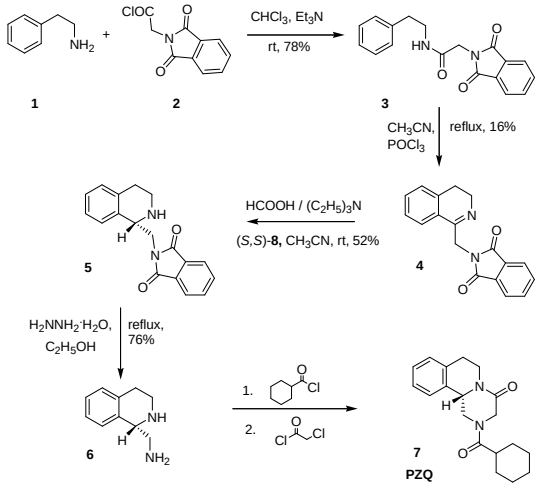
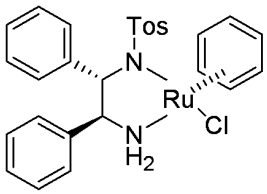


Fig. 1. The synthetic sequence.

We obtained the 3,4-dihydroisoquinoline **4** under known procedure [6] modified by transformation of imine into hydrochloride and unblocked to free imine. The unreacted amide was recovered. Asymmetric reduction of imine **4** with the chiral Ru complex (*S,S*)-**8** and triethylamine-formic acid azeotrope as hydrogen source gave amine **5** in good yield and excellent enantiopurity. The structural formula of the ruthenium catalyst is shown in Fig. 2.

The amine **5** was transsformed into (R)-Mosher acid derivative **9** in order to determine the diastereomeric ratios in ^{1}HNMR. The contamination of the second diastereoisomer was not observed. The Mosher's amide (1*S*)-**9** was obtained in a form of single crystal suitable for X-ray crystallography that served for unambiguous stereochemistry assignment (Fig. 3).



(*S,S*)-**8**

Fig. 2. The Ruthenium catalyst.

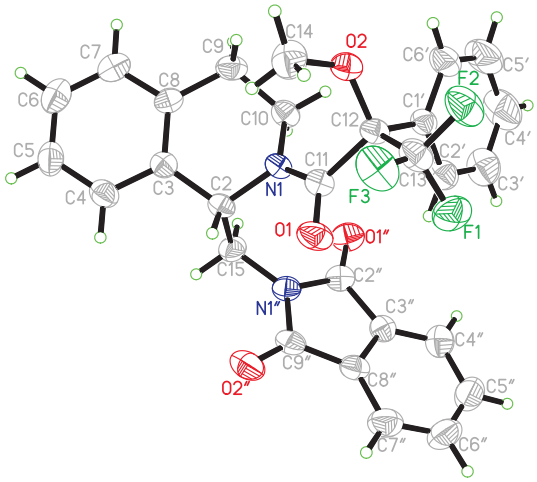


Fig. 3. Absolute configuration of the molecule.

References

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