Catalytic asymmetric synthesis of chiral tetrahydroisoquinoline derivatives

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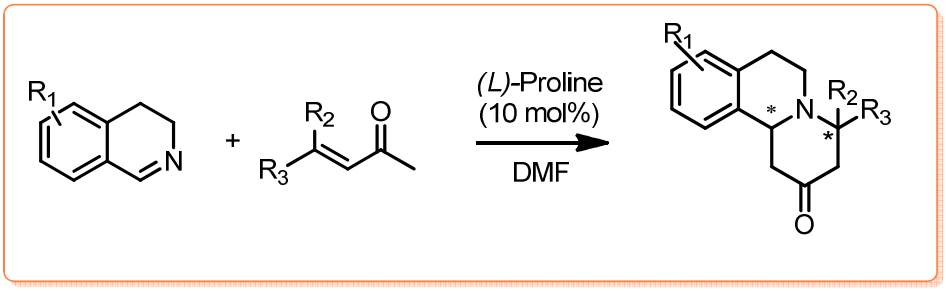
The C1-substituted tetrahydroisoquinoline motif has been an important target for organic chemists for many years,[1] due to its ubiquitous presence in alkaloid and modern pharmaceuticals. A number of different approaches have been developed to construct this ring system; and one of the most important objectives is to obtain enantiomeric pure compounds.[2]

Our approach towards the synthesis of C1 substituted tetrahydroisoquinoline is based on a proline catalyzed cascade reaction between dihydroisoquinoline and α,β-unsaturated enones. For the purpose of our studies, we investigated a range of reaction conditions, (solvents, catalyst loading etc.), in order to optimize the reaction, with respect to the percentage conversion of the substrate and enantioselectivity of the product.



The best results were achieved using DMF as solvent and (*L*)-Proline as the catalyst. The advantage of using (*L*)-Proline as catalyst is that it is a relatively inexpensive and has been shown to catalyze this type of reaction with good yields and enantioselectivities.

In conclusion, we have developed an organocatalytic asymmetric synthetic procedure for a variety of stereochemically complex benzoquinolizidine building blocks. Studies on the mechanism of this reaction are ongoing.

[1] Bentley K.W. *Nat. Prod. Rep.* **2004**, *21*, 395-424.

[2] (a) Rozwadowska, M. D. *Heterocycles* **1994**, *39*, 903–931. Recent progress in diastereoselective syntheses