[AL] [10/10/2003(Fri) 16:30-17:30/ASEM Hall]

Asymmetric Synthesis in Pharmaceutical Manufacturing Chemistry

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Organic compounds play an important role in the area of pharmaceutical, agrochemical, and other materials, which possess useful biological activities. Generally, such biological activities are come from the interaction of the organic compounds with the receptors in biological system, such as enzymes. Such receptors are composed of the chiral building blocks such as amino acid or carbohydrate, which means the biological active sites of receptors are chiral.

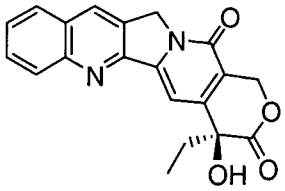
The discovery of chirality, during the last century, enforced chemists to concern themselves with developing methods to obtain enantioenriched substances. The important of chirality is understood by the fact that nearly all natural products are chiral and their physiological or pharmacological properties depend upon their recognition by chiral receptor. The chirality of receptors has the ability to differentiate between two enantiomers of organic compounds that possess more than one chiral center. The two enantiomers may have different level of biological activity or may show quite different type of activity. Usually, one enantiomer is far more active than the other one. The inactive enantiomer may give little or no activity, but only provides undesirable side effect. In addition, the enantiomers can be metabolized ether different rate or different pathway because the metabolizing enzymes are also chiral. To overcome the potential problems is to use single enantiomer.

There are several methods to get single enantiomeric compounds: a) Resolution of racemate; b) Using chiral starting material; c) asymmetric synthesis. The first two methods are currently used now but both are not popular as a general method. The unwanted enantiomer, obtained by resolution method, usually raised the cost of production and evoke environmental pollution problem. Also there are not enough available chiral starting materials for all interested biologically active compounds.

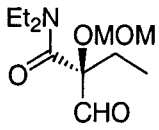
Within the past 20 years asymmetric synthesis has been the forefront of organic chemistry. A massive of new synthetic methods has been reported so far. There is a lot efficient

enantioselective synthetic method for practical application. In this symposium, I would like to introduce a few efficient asymmetric synthetic methods to prepare some useful chiral intermediates and its application for the biologically active compounds, which have been performed in the last few years in our laboratory.

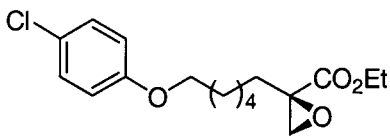
Asymmetric halolactonization



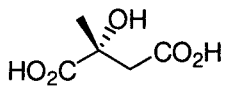
Camptothecin



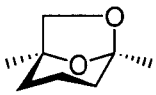
Intermediate for Camptothecin



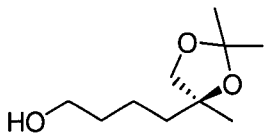
(R)-(+)-etomoxir



(R)-(-)-Citramalic acid

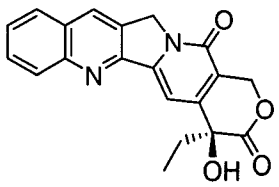


(1S,5R)-(-)-Frontalin

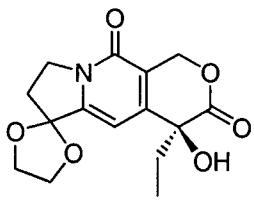


Intermediate for frontalin

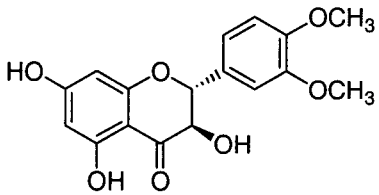
Asymmetric Dihydroxylation



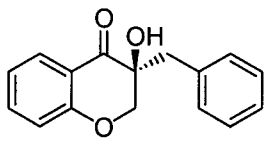
Camptothecin



Intermediate for Camptothecin

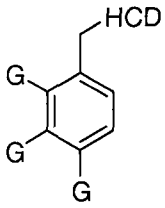


(3R,4R)-O-dimethyltaxifolin

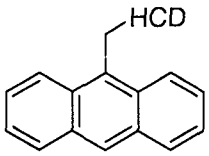


(S)-Eucomol

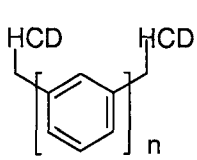
Asymmetric Phase-transfer Catalytic Alkylation.



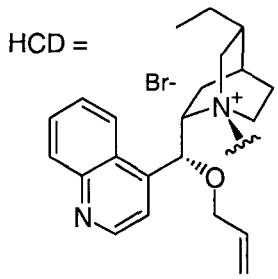
1 a G = H
b G = F

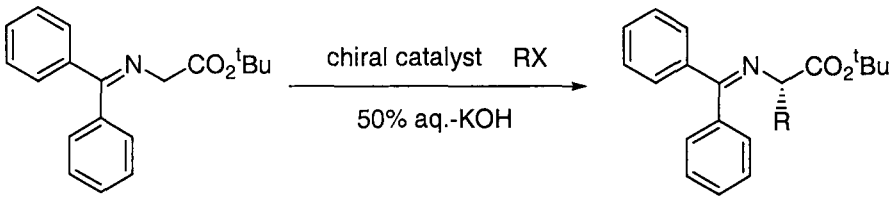


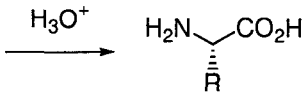
2



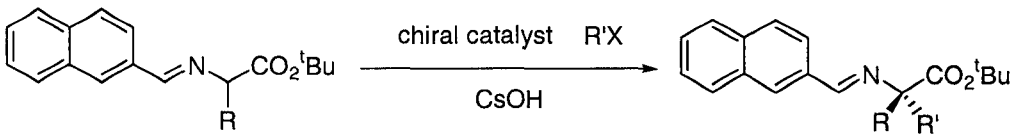
3 a n = 1
b n = 2

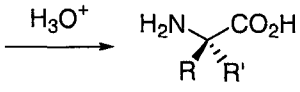






α–amino acid





α,α–dialkylamino acid