

## Chiral organic molecules at work with epoxides: two arms drive the asymmetric transformations

Many organic compounds, including natural aminoacids and sugars, are chiral molecules. They can exist in two not superimposable forms, the enantiomers, having identical chemical formulae and bond connections, but likewise our hands, being mirror - images. As in the case of chiral pharmaceuticals, it is often necessary to synthesize only one of the two enantiomers, which can show very different biological activities or in the worst case, one of the two enantiomers if administered could have a dangerous effect for the health.

Over the last fifteen years, we have assisted to the exponential growth of asymmetric organocatalysis, namely a new convenient and sustainable tool for the preparation of enantiomers. A variety of small organic chiral molecules, the organocatalysts, derived from readily accessible natural sources such as quinine and L-proline to cite two of the most renowned, are able to catalyse asymmetric transformations affording the desired products preferentially in one of the two enantiomeric forms, rather than in equal amounts as a racemic mixture. Chiral non racemic epoxides are three-membered heterocycles to be considered among the most useful class of organic molecules. Besides showing a wide spectrum of biological activities, among others as anticancer drugs as Neocarzinostatin, Epothilones and Ovalicin, they proved to be also highly versatile intermediates in several total syntheses of natural and non-natural compounds (Fig. 1.). Their importance has been recognized in 2001 with Nobel prize won by Sharpless for his work on oxidations, including asymmetric epoxidation reactions.

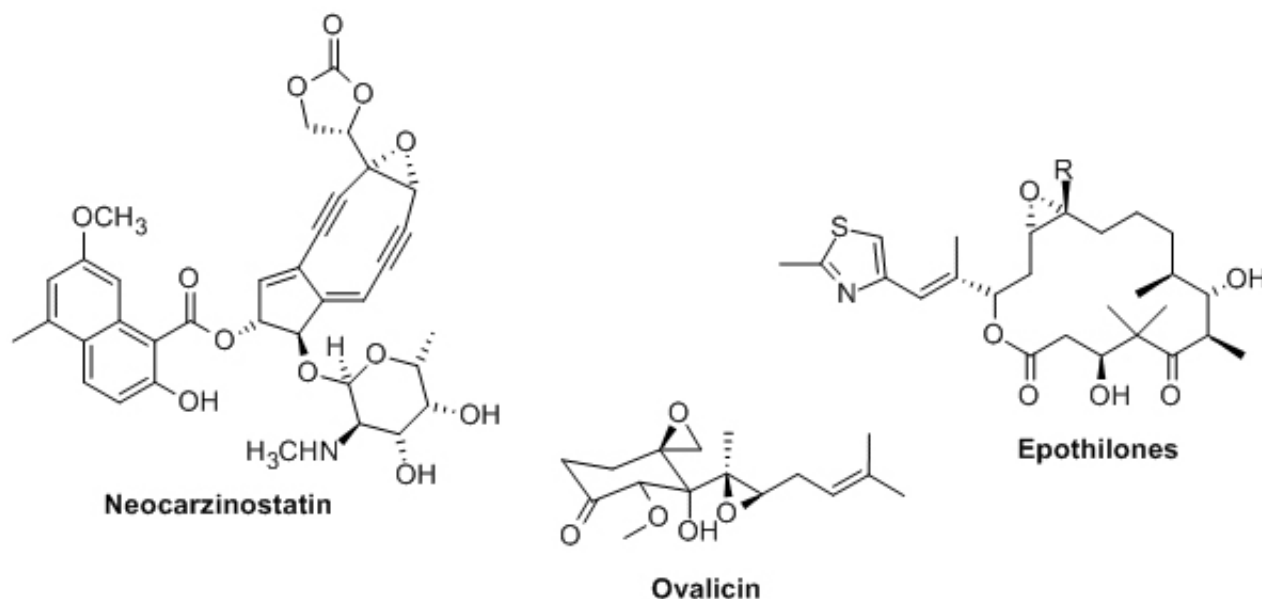


Fig. 1. Naturally occurring epoxides with anticancer activity.

Synthetic organic chemists are interested in developing simple and effective methodologies to manipulate racemic or *meso*-epoxides (achiral) via ring-opening reactions to obtain pure enantiomers of the starting epoxides or several other valuable functionalised products in one enantiomeric form (or enantiomerically enriched form). Major ways of producing derivatives of interest are the desymmetrization of *meso*-epoxides by using heteroatom centred nucleophiles (NuH) (Fig. 2.). The organocatalyst facilitates the attack of a nucleophile at one of the two carbons of a *meso*-epoxide. The preferential ring-opening reaction will give an enantioenriched product. Additionally, in a kinetic resolution of racemic epoxides, the organocatalyst will favour a faster conversion of one of the two enantiomers of the epoxide to a product, thus leaving the other unreacted and isolable from the reaction mixture. These processes allow the synthesis of enantioenriched representative compounds: 1,2-amino alcohols, 1,2-diols, 2-hydroxy sulfides, allylic alcohols, nitroepoxides, carbonyl compounds. In our contribution, written for a special issue to celebrate Women in Chemistry, "Organocatalytic Asymmetric Reactions of Epoxides: Recent Progress", we reviewed the asymmetric strategies cited above, applied by others and our group, to produce either enantioenriched functionalised products or epoxides by using enantiopure bifunctional organocatalysts. This class of promoters bear two closely located arms in their scaffold, i. e. Brønsted/Lewis basic and Brønsted acid groups, able to synergistically and efficiently activate the reagents mainly through hydrogen-bonding interactions. Indeed, they work as greatly simplified biocatalysts, able to mimicking the activation of reagents provided by high molecular weight, structurally much more complex and expensive enzymes.

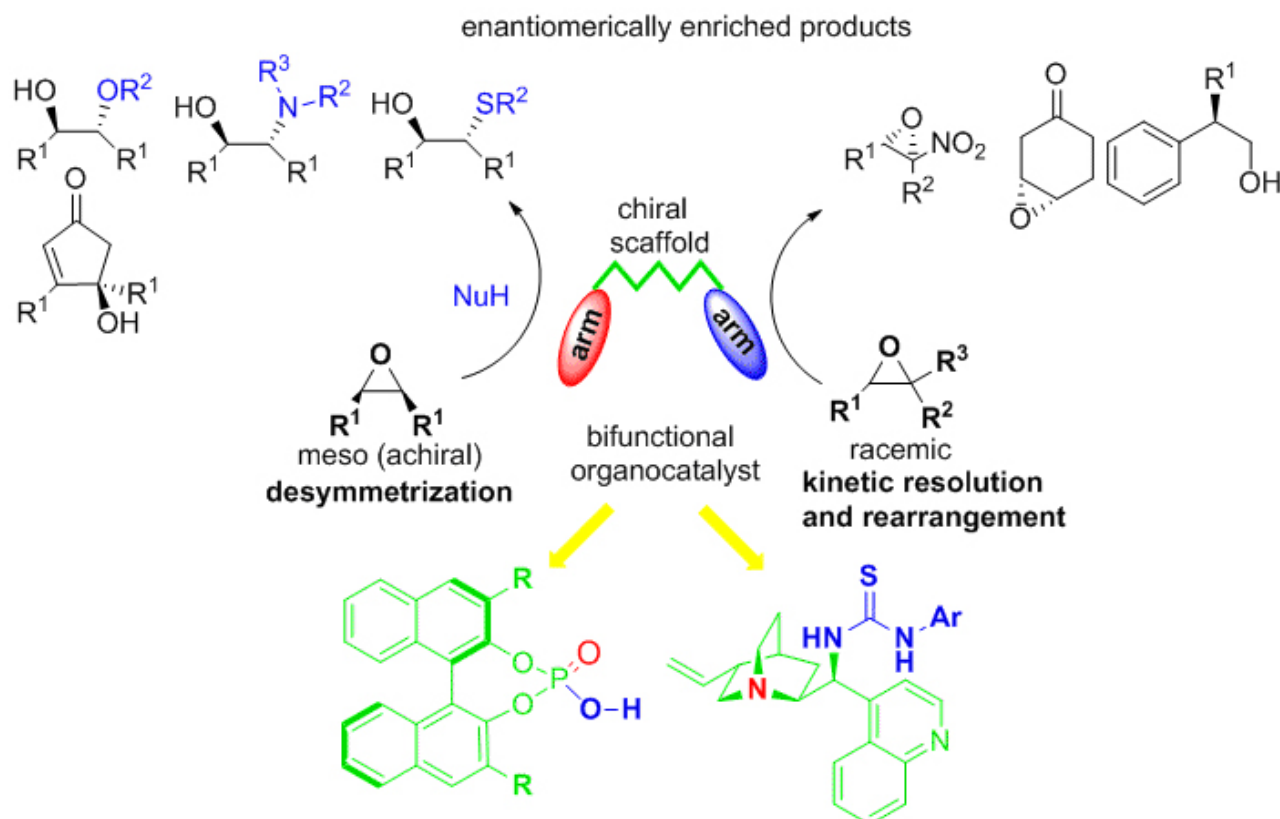


Fig. 2. Asymmetric transformations of meso and racemic epoxides promoted by two representative bifunctional organocatalysts.

From these studies emerges the great potential of bifunctional organocatalysts to access a variety of useful enantioenriched products, exploiting easily accessible and low cost racemic or achiral epoxides as starting material. In the near future, we expect major improvements in terms of their catalytic efficiency and extension of either epoxide scope and nucleophiles arena. It can be envisaged organocatalysed ring-opening reactions of epoxides will occupy a significant role in academia, and likely in the industry as an additional or exclusive synthetic tool to well-established metal-based chiral complex catalysis and biocatalysis mediated by enzymes.

***Sara Meninno and Alessandra Lattanzi***

*Dipartimento di Chimica e Biologia "A. Zambelli", Università di Salerno  
Italy*

## Publication

[Organocatalytic Asymmetric Reactions of Epoxides: Recent Progress.](#)

Meninno S, Lattanzi A.

*Chemistry*. 2016 Mar 7