

3 Asymmetric Epoxidation

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3.1 INTRODUCTION

The stereoselective oxidation of organic compounds is dominated by studies of epoxidation (Figure 3.1). Epoxides are useful in organic synthesis, they are versatile intermediates and easily undergo stereoselective ring-opening reactions to form bifunctional compounds^[1]. This explains the development of many methods for the synthesis of the enantiomerically pure epoxides. We will describe in Chapters 4–6 different methods of asymmetric epoxidation of functionalized and unfunctionalized alkenes. This chapter expands the information given in Chapter 1 and forms a consolidated introductory section for the next three chapters

In 1980 a useful level of asymmetric induction in the epoxidation of some alkenes was reported by Katsuki and Sharpless^[2]. The combination of titanium (IV) alkoxide, an enantiomerically pure tartrate ester and *tert*-butyl hydroperoxide was used to epoxidize a wide variety of allylic alcohols in good yield and enantiomeric excess (usually >90%). This reaction is now one of the most widely applied reactions in asymmetric synthesis^[3].

Concerning the oxidation of electron-deficient alkenes such as chalcone derivatives, in 1980, Juliá *et al.* reported an example of a highly stereoselective epoxidation of an electron deficient alkene using a triphasic catalysis system. This method involves alkaline aqueous hydrogen peroxide, an organic solvent and an insoluble polyamino acid.^[4–7] A refined method now employs a biphasic system consisting of an oxidant, a non-nucleophilic base, a polyamino acid and an organic solvent^[8].

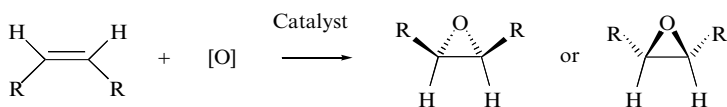


Figure 3.1 Catalytic asymmetric epoxidation of alkenes.

A new method of asymmetric epoxidation of α , β -unsaturated ketones using a stoichiometric amount of *N*-methylpseudoephedrine as a chiral source in the presence of diethylzinc and oxygen to afford the α , β -epoxy-ketones with good yield and enantiomeric excess was developed by Enders and co-workers^[9]. Shibasaki^[10] reported an efficient catalytic asymmetric epoxidation of enones using lanthanoid complexes, which give epoxides with enantiomeric excesses between 83 and 94 %. This last method will be reported in another volume of this series.

New methods for asymmetric epoxidation of alkenes, bearing no functionality to precoordinate the catalyst, have also been developed successfully in the past few years^[11]. Among these methods, Jacobsen *et al.*^[12] were able to epoxidize monosubstituted, disubstituted *Z*- and trisubstituted alkenes with good asymmetric induction, using cationic (salen)manganese(III) complexes. Shi *et al.*^[13] reported a method of epoxidation using dioxirane generated *in situ* from potassium peroxomonosulfate and a chiral fructose-derived ketone as catalyst. Using this method high enantioselectivity can be obtained for the epoxidation of unfunctionalized *E*-alkenes.

Other methods of epoxidation were described; for example in 1979, Groves *et al.*^[14] reported the first example of alkene epoxidation by a chloroferritetraphenylporphyrin catalyst. By adding an optically active group on to this catalyst, they obtained optically active chiral epoxides but generally with a low enantiomeric excess^[14]. A number of metalloporphyrins have been used for the epoxidation of unfunctionalized alkenes^[15] (see Chapter 6.3). Asymmetric epoxides can also be obtained using enzymes. Peroxidases^[16, 17] and monooxygenases^[18–20] catalyse the synthesis of nonracemic chiral epoxides. A kinetic resolution of racemic epoxides can be catalysed by epoxide hydrolases.^[21–23] Those methods (using enzymes) will not be described in this chapter since enzymatic epoxidation has been reviewed previously^[24].

Chapters 4–6 present an overview and a comparison between the various existing strategies for asymmetric epoxidation of unfunctionalized alkenes, α , β -unsaturated ketones and allylic alcohols.

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