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# PORPHYRIN SYMMETRY AND CHIRAL CATALYSIS IN WATER

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*Fields of interest:* Catalysis, chirality, bioinorganic, enantioselective recognition.

*Publications:* with Bondon, A. (2005) Mechanism of electron transfer in heme proteins and models: the NMR approach, *Chemical Reviews*, 105, 2627-2646; with Le Maux, P., Ferrand, Y. and Rault-Berthelot, J. (2006) Asymmetric heterogeneous catalysis by metalloporphyrins, *Coordination Chemistry Reviews*, 250, 2212-2221; with Srour, H., Le Maux, P. (2012) Enantioselective manganese-porphyrin-catalyzed epoxidation and C-H hydroxylation with hydrogen peroxide in water/methanol solutions, *Inorganic Chemistry*, 51, 5850-5856; with Srour, H., Le Maux, P., Chevance, S. and Carrie, D. (2014) Metalloporphyrin symmetry in chiral recognition and enantioselective catalysis, *Symmetry*, 6, 210-221;

**Abstract:** *Chiral metalloporphyrins (ruthenium, iron and manganese) have been developed in solution. Both effective chiral recognition and asymmetric catalysis using optically active macrocycles were observed. Asymmetric oxidation and carbene transfer showed potential pharmaceutical applications.*

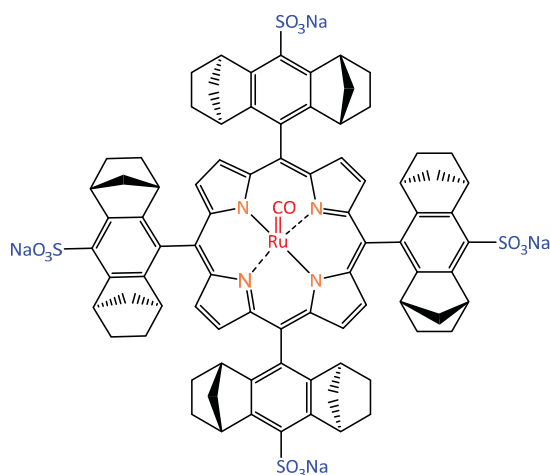
**Keywords:** chiral recognition, asymmetric catalysis, metalloporphyrins, asymmetric oxidation, carbene transfer.

## 1 INTRODUCTION

Chiral molecules containing symmetry elements are of special interest for chiral recognition (Moberg, 1998) and asymmetric catalysis. These areas play an important role in biological systems. Natural proteins throughout evolution are made up of L-amino acids. Therefore the interest in these processes is largely determined by chiral recognition and catalysis in water because it is desired to mimic physiological conditions (Borovkov et al., 2006). Over the years, our group has been interested in chiral

recognition (Galardon et al., 1999) and asymmetric catalysis (Galardon et al., 2000) in organic solvents. More recently, we have engaged in a research program aimed at expanding the scope of water-based organic synthesis and protein conjugation, (Srouf et al., 2015) using water-soluble metalloporphyrins as hosts or chiral catalysts. The present investigation will illustrate how symmetry plays a fundamental role in these reactions.

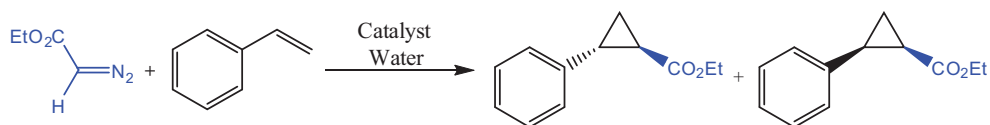
## 2 CHIRAL RECOGNITION OF AMINO ACIDS



**Figure 1:** Structure of chiral ruthenium complexes.

Our strategy (Nicolas et al., 2008) for studying selectivity for amines and amino acids involves the use of ruthenium porphyrins. As a simple model for chiral recognition of amino acid derivatives, we decided to use Halterman's porphyrin (Halterman et al, 1991) which is a rigid ligand bearing aliphatic substituents on the arenes without any functional groups. Since this ruthenium porphyrin has no hydrogen bond donor site, the chiral recognition should be due to other interactions. In organic solvent, aliphatic amino esters showed weak chiral recognition (ee ~ 20%) whereas aromatic amines and aromatic amino esters exhibited much higher chiral recognition (ee up to 60%). The ee enhancements of aromatic substrates suggest that aryl-aryl interactions may stabilize the complex with the preferred enantiomer. Similar results were obtained in methanol. The reaction of optically active Halterman's porphyrin with sulphuric acid (95%) provided the expected water-soluble para-tetrasulfonated porphyrin in 82% yield. The metalloporphyrin complexes were prepared by metal insertion (iron in the case of asymmetric catalysis) or direct sulfonation of the chiral ruthenium porphyrin (Figure 1).

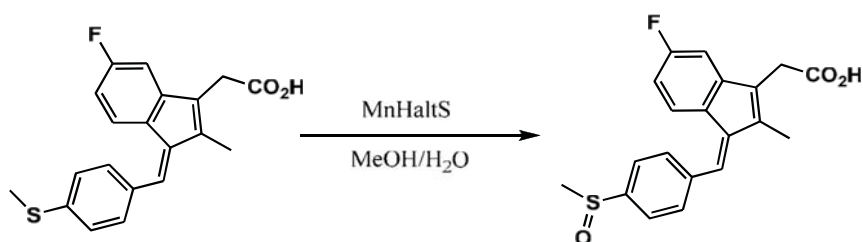
### 3 ASYMMETRIC CATALYSIS



**Figure 2:** Asymmetric cyclopropanation of styrene.

The asymmetric addition of diazoacetate to styrene derivatives to give optically active trans cyclopropyl esters (ee up to 86%) was carried out in water (Nicolas et al., 2008) by using chiral iron or ruthenium porphyrins with a possible reuse due to the high solubility and stability in aqueous solution (Figure 2).

An efficient asymmetric oxidation of sulfides catalyzed by a water-soluble chiral manganese porphyrin was carried out in presence of cheap and environmentally benign oxidant  $\text{H}_2\text{O}_2$  at  $25^\circ\text{C}$  (Srouf et al., 2013). Prochiral sulfides were converted to respective sulfoxides with up to 100% conversion. The present study demonstrated the necessity of water as solvent and imidazole as co-catalyst. Application to the preparation of the optically drug, sulindac, was demonstrated (82% enantiomeric excess) (Figure 3).



**Figure3:** Preparation of sulindac using manganese sulfonated Halterman's porphyrin (MnHaltS) as catalyst.

### 4 SUMMARY

Metalloporphyrins possess a number of structural features that make them attractive for chiral recognition and metal-catalyzed asymmetric reactions in water. Ongoing work includes the synthesis of new water-soluble zinc diazoporphyrin esters with good yields offering a general access to original symmetric porphyrins. Studies on the application of the insertion reaction into N-H and S-H bonds for bioconjugation of these potentially fluorescent probes to proteins are in progress.

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