Enantioselective Olefin Epoxidation with Chiral Manganese/1,4,7-Triazacyclononane Complexes[1]

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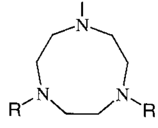
Abstract: Complexes prepared *in situ* from chiral *N*-substituted 1,4,7-triazacyclononanes and manganese(II) acetate catalyze the asymmetric oxidation of unfunctionalized olefins with hydrogen peroxide to give optically active epoxides under mild reaction conditions.

The introduction of new methodologies for the asymmetric epoxidation of olefins not bearing directing groups still stands as a main challenge in organic synthesis.[2] In the past years, the use of chiral transition metal complexes as catalysts has extensively been studied and the best results have been obtained with manganese complexes bearing tetradentate C_2-symmetric salen ligands.[3] In this communication we report a new approach demonstrating that enantioselective epoxidation of olefins can also be achieved by the use of complexes prepared *in situ* from optically active 1,4,7-triazacyclononanes and manganese(II) acetate. Most interestingly, 30% aqueous hydrogen peroxide is the oxidant in this system.[4]

1,4,7-Triazacyclononanes **1** have a rich coordination chemistry and the properties of various transition metal complexes have been investigated by structural and spectroscopic means.[5] In 1994, researchers from *Unilever* showed that manganese complexes of these cyclic triamines were highly effective catalysts for the bleaching of stains by H_2O_2 at low temperature.[6, 7] They also demonstrated that these complexes catalyzed the oxidation of simple olefins to give the corresponding epoxides. *Bein* and coworkers optimized the reaction procedure[8] and introduced 1,4,7-triazacyclononane/manganese-containing zeolites as epoxidation catalysts.[9, 10] We now describe the first *enantioselective* epoxidation using catalysts derived from the readily available C_3-symmetric ligands **2**.[5, 11]



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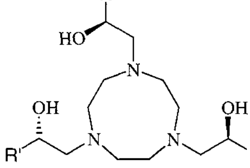
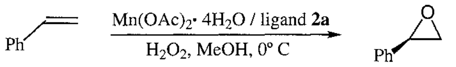


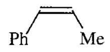
2a: R' = Me
2b: R' = *i*Pr

As first test reaction we chose the epoxidation of styrene (**3**). A variety of conditions had to be examined to identify the optimal reaction protocol. Enantioselective oxidation of **3** with 30% aqueous H_2O_2 (2 equiv.) was achieved in methanol solution using 3 mol% of manganese(II) acetate and *(S,S,S)*-**2a** as ligand in a ratio of 1:1.5 giving *(R)*-styrene oxide (**4**) with 43% enantiomeric excess *(ee)*.[12] However, even under these optimized reaction conditions the conversion of **3** remained low (≈15% after 5 h at 0 °C). Longer reaction times, higher temperature, more catalyst and larger quantities of H_2O_2 gave higher conversion of **3**, but the *ee* of **4** was decreased. Presumably, the chiral catalyst was decomposed during the reaction giving rise to other catalytically active species which yielded racemic product. Attempts to use *ent*-**2b** as ligand having the sterically more demanding isopropyl substituents resulted in the formation of *(S)*-configured epoxide with enantioselectivities in the range of 13-38% *ee*.



3 *(R)*-**4**

Next, we investigated the epoxidation of *cis*-β-methylstyrene (**5**). This substrate is of particular interest because it can serve as mechanistic probe to distinguish between concerted and stepwise radical addition processes to the double bond.[3a, 13] Using the same catalyst composition [**2a**/Mn(II)], 3 equiv. of 30% H_2O_2 and otherwise identical reaction conditions as described above for the oxidation of styrene, complete conversion of the starting material was now observed after 3 h at 0 °C.[12] Two isomeric epoxides were formed in a ratio of about 7:1. The major product was *1R,2R*-configured epoxide *trans*-**6** which was formed with 55% *ee*. The minor compound was identified as *cis*-**6** having 13% *ee*.[14]



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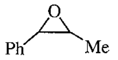
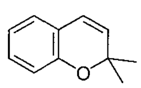
trans-**6**



cis-**6**

Chromene **7**, a compound with a fixed *cis*-double bond was also oxidized enantioselectively. With *(S,S,S)*-**2a** as ligand, **7** gave epoxide *(3R,4R)*-**8** with 40% *ee*. *Ent*-**2b** having *R,R,R*-configuration resulted in the formation of *(3S,4S)*-**8** with 38% *ee*. In both cases, the conversion was about 50% after 15 h.



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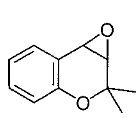

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One of the most attractive features of this new asymmetric oxidation is the use of simple 30% H_2O_2 as oxidant. It is a cheap, safe and readily available reagent which is characterized by a high active oxygen content.[4] Besides, the fact that its only by-product is water contributes to render any synthetic application of the reagent undoubtedly interesting.

This communication presents the first results demonstrating the general feasibility of asymmetric oxidations with chiral complexes bearing optically active 1,4,7-triazacyclononanes. Our current efforts are directed towards a refinement of the epoxidation protocol to improve catalyst activity and enantioselectivity.

Acknowledgment. This research was supported by the *Katalyse-Verbund NRW* and the *Fonds der Chemischen Industrie*.

References and Notes

(1) This paper is dedicated to Prof. Dr. F. Asinger on the occasion of his 90th birthday.
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(12) Typical experimental procedure: A mixture of $Mn(OAc)_2.4H_2O$ (15 μmmol) and ligand (22.5 μmmol) in 0.5 mL of MeOH was stirred for 15 min at 0 °C. The olefin (0.5 mmol) was then added followed by 30% aqueous H_2O_2 (**3**: 1 mmol; **5**: 1.5 mmol). After stirring at 0 °C for the time indicated the reaction mixture was diluted with diethyl ether and brine. The organic layer was separated and dried over Na_2SO_4. The conversions and *ee*-values were determined by GLC using Cyclodex-β-HP for styrene oxide (**4**), Lipodex-E for β-methylstyrene oxides (**6**) and Lipodex-B for chromene oxide **8**.

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