寄稿論文

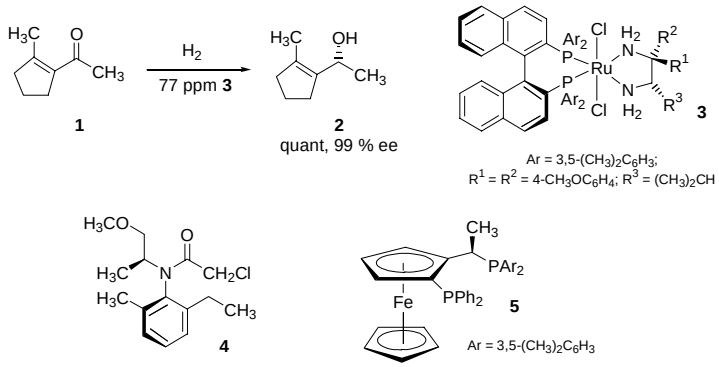
# Biomimetic Oxidation of Organic Substrates with Hydrogen Peroxide

Albrecht Berkessel
Prof. Dr.
Institut für Organische Chemie der Universität zu Köln
Greinstr. 4, D-50939 Köln, Germany

## I. Introduction: Catalytic organic synthesis and biomimetic oxidations: general considerations

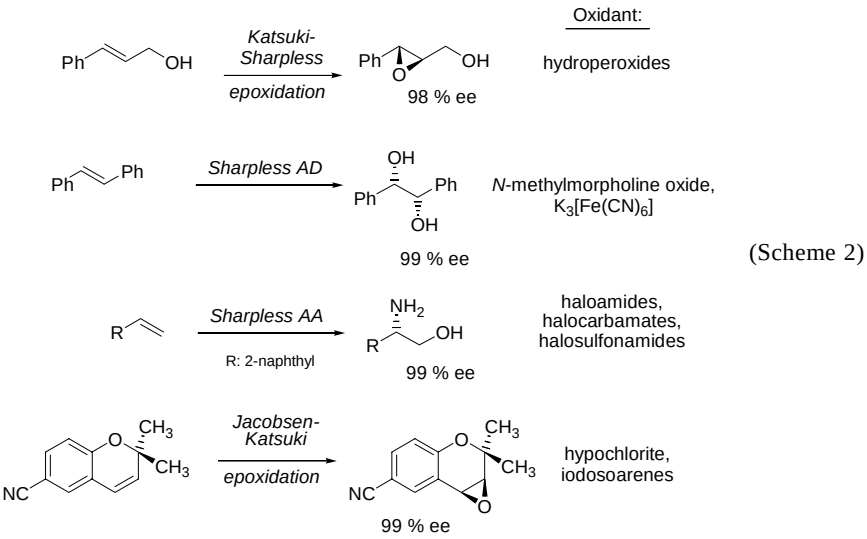
In recent years, the number of methods available for the high-yielding and selective transformation of organic compounds has increased tremendously, and further discoveries can be expected to be made at an even faster pace. Interestingly, most of the new reactions that are of practical importance, i.e. that are used routinely in the synthetic laboratory, are catalytic in nature. The reason for this is that the chemist aims at transformations that are as "atom-economic" as possible.[1] In other words, as many atoms as possible of the starting material should be present in the product, and the stoichiometric introduction and removal of auxiliary groups should be avoided. This does not only hold for the substrate in question, but also for the reagents used. Clearly, the incentive for performing transformations in an atom-economic fashion is not a purely academic one. For larger scale operations, financial and environmental aspects, such as the minimization of waste, become a serious driving force.

Let us deliberately pick some catalytic transformations that emerged in recent years. For example, a variety of palladium-catalyzed C-C- and C-N-bond formations have become standard operations in organic synthesis.[2,3] Furthermore, by careful optimization of chiral ligands, many catalytic reactions have been elaborated to a high level of enantioselectivity.[3] For example, the asymmetric hydrogenation of prochiral precursors ranges among the highly developed transformations for the production of enantiomerically pure products.[3] As an illustration, *Noyori* et al. recently reported that enones such as **1** can be quantitatively transformed to the allylic alcohol **2** with 99 % ee, employing just hydrogen and as little as 77 ppm of the ruthenium catalyst **3** (Scheme 1).[4] No reduction of the C=C-double bond occurs. Similarly, the industrial production of the herbizide (*S*)-Metolachlor **4** on a >10.000 t/a scale relies on an asymmetric imine hydrogenation (Scheme 1).[5] Also in this case, extremely high turnover numbers ( > $10^6$) of the Ir-catalyst derived from the ligand **5** could be achieved.[5]




(Scheme 1)

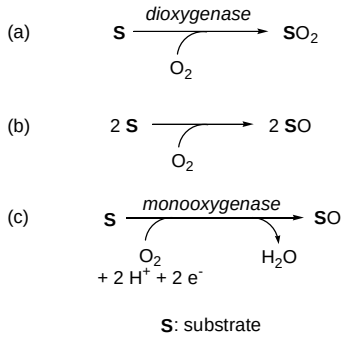
Please note that the catalytic transformations discussed so far were reductive in nature. When we turn to catalytic asymmetric oxidations, the three most prominent ones are the asymmetric epoxidation of allylic alcohols (*Katsuki-Sharpless* epoxidation),[6] the asymmetric dihydroxylation of olefins (*Sharpless AD*),[7] and the asymmetric aminohydroxylation of alkenes (*Sharpless AA*)[8] (Scheme 2). Furthermore, the *Jacobsen-Katsuk*i epoxidation of unfunctionalised olefins has become an important tool in organic synthesis (Scheme 2).[9]




(Scheme 2)

Compared to the hydrogenations shown in Scheme 1, the catalytic oxygenations shown in Scheme 2 achieve a comparable degree of enantioselectivity. However, with respect to atom-economy, even the highly elaborated oxygenations shown in Scheme 2 fall short of their reductive counterparts: All of the oxidants normally used give rise to by-products that must be either disposed of or recycled.

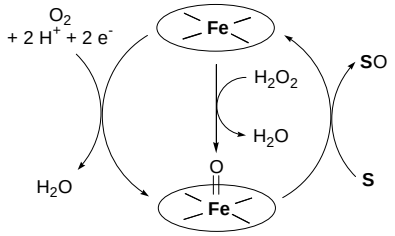
What is the ideal oxidant? Clearly, molecular oxygen itself would be the reagent of choice - provided that it was possible to transfer both oxygen atoms of the $O_2$-molecule to the substrate (Scheme 3). The first case (a) corresponds to the action of various dioxygenase enzymes (such as cyclooxygenase and catechol oxidase), as well as low-molecular weight models thereof.[10]




(Scheme 3)

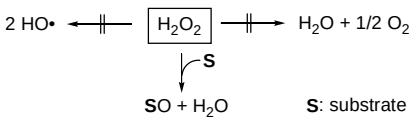
Products typically obtained from such dioxygenations are peroxides (from olefins) or carboxylic acids (from catechols). In the second case (b), the $O_2$-molecule is split, and one O-atom is transferred to one substrate molecule each. This most interesting transformation which corresponds e.g. to an epoxidation or sulfoxidation with air, is thermodynamically feasible. Unfortunately, up to now, it could only be realized in rare cases and at low catalyst turnovers using transition metal porphyrins[11] or phenanthroline complexes.[12] In nature, the monooxygenation of an organic substrate with molecular oxygen is usually performed by monooxygenases according to equation (c), Scheme 3. Here, only one of the oxygen atoms is transferred to the substrate and the other one is reduced to water by a co-reductant. Since the by-product water is low in energy, even the most demanding oxyfunctionalization, e.g. the hydroxylation of unactivated C-H-bonds are feasible.[13] Despite the enormous effort that has been spent over the years on the development of preparatively useful monooxygenase models, monooxygenases themselves (*in vivo* or *in vitro*) are still the only practical catalysts for the stereoselective hydroxylation of fully unactivated C-H-bonds, e.g. of a steroid nucleus.

The problems associated with the development of artificial monooxygenases are mainly due to the complexity of the mechanism, involving the reduction/protonation/fission of the $O_2$-molecule (Scheme 4, outer cycle). In the absence of spatial separation and exact timing (as in enzymes), common side reactions are the unproductive oxidation of the co-reductant or the self-destruction of the organic ligand. These problems can - at least partly - be avoided by using hydrogen peroxide as the oxidant: No co-reductant is required for the formation of the reactive oxene-species (Scheme 4, inner reaction), and water is the only by-product. Thus, oxidations with hydrogen peroxide are highly atom-economic. Furthermore, hydrogen peroxide is a safe, readily available and cheap reagent.




(Scheme 4)

All these properties make it an ideal oxidant for preparative organic chemistry. However, catalysts are needed that transfer oxygen from $H_2O_2$ to the substrate without effecting a disproportionation or a homolytic cleavage of the $H_2O_2$-molecule (Scheme 5). In nature, peroxidases perform this desired cleavage of the $H_2O_2$-molecule, and the X-ray crystal structures of peroxidases may thus serve as ÒblueprintsÓ for the construction of low-molecular weight analogues.[14] The following sections will describe our efforts in designing model compounds for heme peroxidases (chapter II.1), for vanadium peroxidases (chapter II.2), and the use of manganese 1,4,7-triazacyclononane (TACN) complexes for the epoxidation of olefins and the oxidation of alcohols with hydrogen peroxide (chapter III).

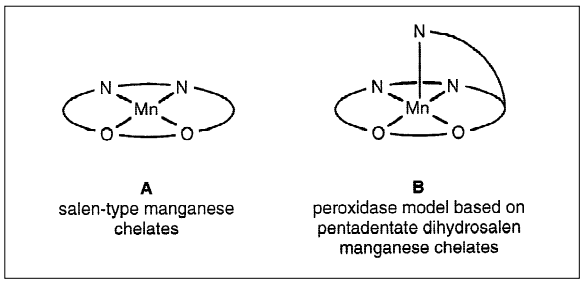



(Scheme 5)

## II. Peroxidase models as catalysts for oxidations with hydrogen peroxide

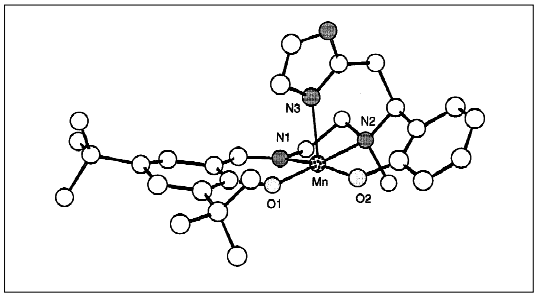
### II. 1 Models for heme peroxidases

In many peroxidases, the catalytically active iron center is coordinated by the four pyrrole nitrogen atoms of its heme ligand plus an axial imidazole donor.[14,15] This proximal donor is believed to facilitate O-O-heterolysis. Not surprisingly, imidazole, pyridine and derivatives thereof have proven beneficial as co-ligands for manganese-catalyzed epoxidations, especially with hydrogen peroxide as the source of oxygen.[16,17] For the efficient utilization of the latter oxidant in the enantioselective epoxidation of unfunctionalized olefins, the combination of the features of a peroxidase-like coordination sphere and a chiral manganese(III)-salen complex appeared especially promising. This reasoning is represented by the schematic structures **A** and **B** (Figure 1). In such an arrangement, a fifth, axial donor - preferably an imidazole group - is covalently attached to a salen-type complex. As it turned out, this approach indeed provided peroxidase models that are able to epoxidize olefins with hydrogen peroxide in the absence of co-ligands and with good yields and enantiomeric excesses.



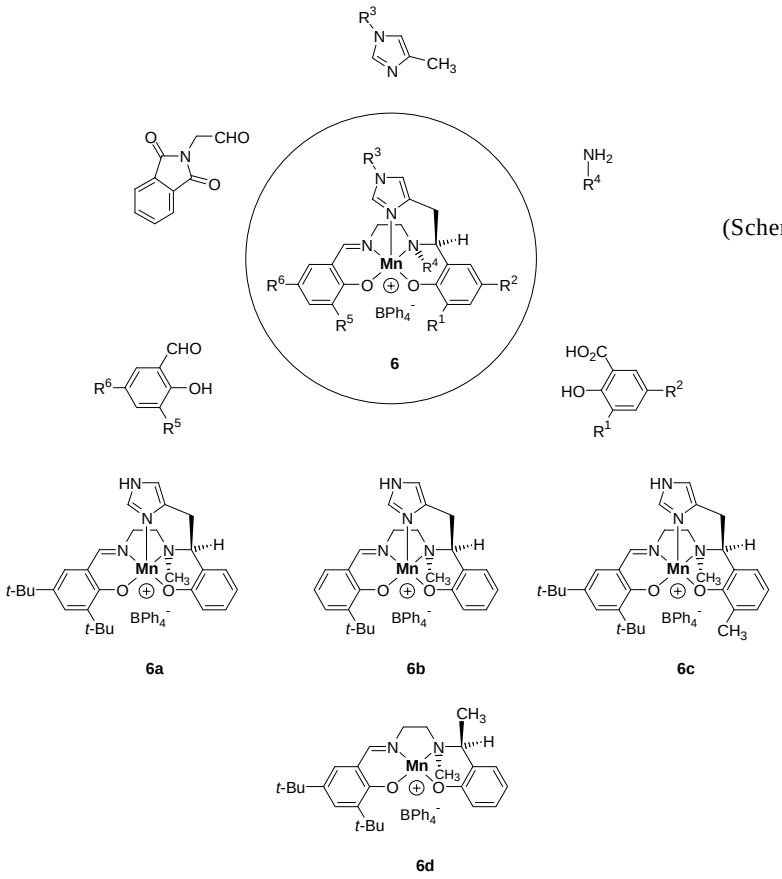

(Figure 1)

The schematic structure of our pentacoordinated peroxidase models **6** is shown in Scheme 6, together with the five building blocks that they are prepared from (a detailed account of the synthesis can be found in ref.18). From the large number of compounds prepared, the examples **6a-d** will be discussed in particular. First of all, the X-ray crystal structure of *rac*-**6a** proved that our ligand design actually afforded the desired pentacoordinated Mn-complexes (Figure 2).



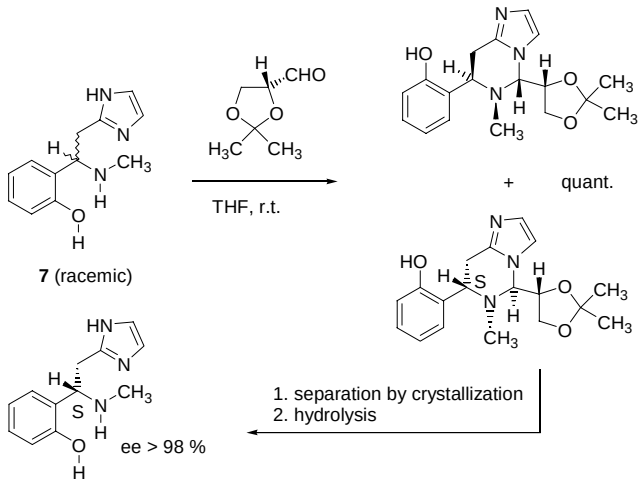

(Figure 2)

Furthermore, the sixth (axial) coordination site is vacant and may thus be expected to bind and activate a hydrogen peroxide molecule - just as in heme peroxidases. As could be expected, the dihydrosalen ligand is not planar. The planes of the two benzene rings of *rac*-**6a** intersect at an angle of ca. 45û. As shown, the (2-imidazolyl)methyl side chain and the methyl substituent at the amine nitrogen atom adopt a “transoid” orientation, with the *N*-substituent pointing “downward”, i.e. towards the face of the complex where the oxygen transfer is expected to take place.




(Scheme 6)

For the preparation of enantiomerically pure catalysts, a separation of enantiomers was performed on the stage of the intermediate secondary amine *rac*-**7**, as shown in Scheme 7.[19] Table 1 summarizes some results obtained with the peroxidase models **6a** and **6b** in the epoxidation of 1,2-dihydronaphthalene (DHN) and styrene with hydrogen peroxide.




(Scheme 7)

**Table 1**: Asymmetric epoxidation with hydrogen peroxide catalyzed by the enantiomerically pure manganese chelates **6a-c**.[a)]

| entry | catalyst[a)] | olefin | oxidant | reaction time [h] | olefin consumed [%] | epoxide formed[b,c)] [%] | ee[b)] [%] |
|---|---|---|---|---|---|---|---|
| **1** | **6a** | DHN | 1 % $H_2O_2$ | 1[d)] | 92 | 77 (84) | 59 |
| **2** | **6a** | DHN | 1 % $H_2O_2$ | 1 | 93 | 72 (77) | 66 |
| **3** | **6b** | DHN | 1 % $H_2O_2$ | 1 | 71 | 47 (66) | 66 |
| **4** | **6c** | DHN | 1 % $H_2O_2$ | 1 | 95 | 82 (86) | 65 |
| **5** | **6a** | styrene | 1 % $H_2O_2$ | 2 | 51 | 51 | 46 |
| **6** | **6b** | styrene | 1 % $H_2O_2$ | 2 | 67 | 67 | 52 |

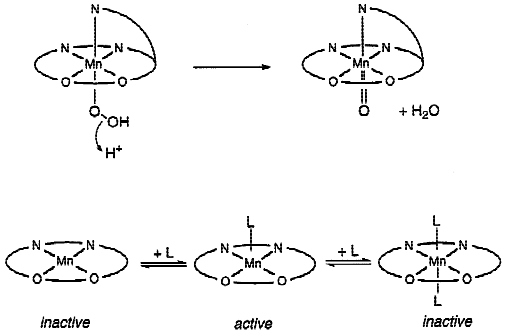
a) The reactions were carried out at 0 °C in a two-phase system consisting of methylene chloride and 1 % aqueous hydrogen peroxide; 10 eq. of hydrogen peroxide were used, and 10 mol-% of the catalyst (rel. to olefin).
b) Yield and ee determined by capillary GC [heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-*β*-cyclodextrin column], employing 1,2-dibromobenzene as internal standard. Absolute configurations of the major enantiomers were determined by comparison with authentic samples: epoxidation of DHN: (1*R*, 2*S*)-epoxide, epoxidation of styrene: (*R*)-epoxide.
c) Values in parentheses are corrected for incomplete conversion of the olefin (selectivity).
d) Epoxidation was carried out at ca. 20 °C.

As expected, the peroxidase models **6a-c** indeed catalyze the epoxidation of olefins with hydrogen peroxide. The reaction is normally carried out in a two-phase system, comprised of the olefin and the catalyst in dichloromethane, and aqueous hydrogen peroxide as the second phase - concentrations as low as 1 % $H_2O_2$ are suitable. With dihydronaphthalene as substrate, enantiomeric excesses up to 66 % were achieved (Table 1, entries 2,3). We soon realized that catalyst stability is a limiting factor in this system, and further efforts are directed towards the introduction of substituents into the "right" aromatic ring of the catalysts **6**. As a first example, the methylated material **6c** (Scheme 6) was prepared, and it indeed gives the best epoxide yields so far, at unchanged ee (Table 1, entry 4).

In Table 1, styrene is listed as a second substrate. In fact, also this terminal olefin can be epoxidized in reasonable yields and enantioselectivities (entries 5,6). As a general rule, our peroxidase models work best with electron rich olefins that are either terminal or 1,2-*cis*-disubstituted. In this respect, the reactivity pattern closely parallels that of the *Jacobsen-Katsuki*-catalysts.[9]

As mentioned in the beginning, the pentadentate character of our peroxidase models is intended to mimic the coordination of the iron atom in heme peroxidases. In order to prove whether this concept is indeed correct, we also synthesized the four-coordinate manganese dihydrosalen complex **6d** (Scheme 6), lacking the fifth axial donor. In fact, this material is catalytically inactive. This result proves that pentacoordination is indeed a prerequisite for the activation of hydrogen peroxide. It must be mentioned at this point that also the square-planar manganese salen complexes prepared by *Katsuki* and by *Jacobsen* can be used with hydrogen peroxide as terminal oxidant.[20,21]

However, to achieve catalytic activity, co-ligands such as alkylated imidazoles or pyridine derivatives must be added in considerable amounts. Why is this so? The mechanism of hydrogen peroxide activation most likely involves the binding of the hydroperoxide anion to the vacant sixth coordination site and subsequent heterolysis to the oxene species (Scheme 8). This heterolysis is facilitated by electron donation from the ligand trans to the hydroperoxide, i.e. the axial imidazole. In the case of the square-planar salen-systems, the pentacoordinated species is in equilibrium with both the (inactive) four-coordinate material and the (inactive) pseudo-octahedral complex (Scheme 8). Consequently, the positions of the equilibria determine whether a catalytically active five- coordinated species is formed at all, as opposed to the designed models **6**.

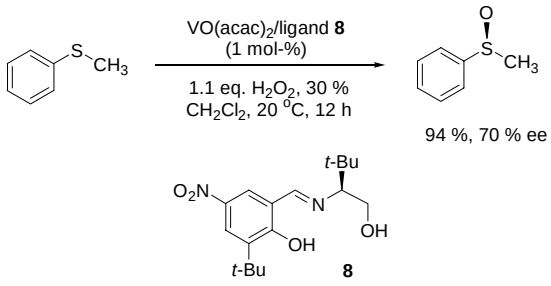



(Scheme 8)

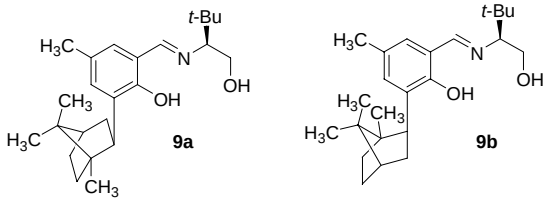
## II. 2 Models for vanadium peroxidases

A number of vanadium peroxidases have been characterized so far, the most well-known one being the bromoperoxidase from the sea weed *Ascophyllum nodosum*.[22] Unlike the heme peroxidases, the vanadium enzymes are normally not able to epoxidize olefins. However, their oxidative power is sufficient to smoothly transform thioethers to the corresponding sulfoxides. Furthermore, prochiral thioethers can afford chiral sulfoxides with enantioselectivities ranging up to ca. 99 %. With this in mind, it is not surprising that quite some effort has been expended on the development of low-molecular weight analogues for the asymmetric sulfoxidation with hydrogen peroxide as terminal oxidant.[24]

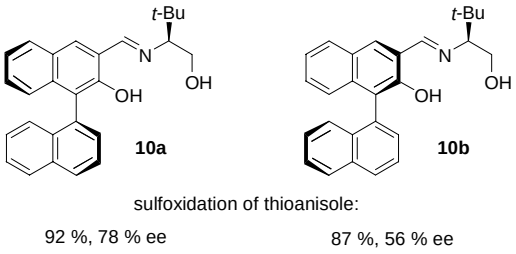
In 1995, a simple and efficient system for this purpose was presented by *Bolm* and *Bienewald*: In the presence of 1 mol-% of $VO(acac)_2$ and the ligand **8**, thioanisol and other prochiral thioethers can be oxidized with hydrogen peroxide in good yields and enantiomeric excesses (Scheme 9).[25] The Schiff-base ligand **8** harbors one center of chirality, it is derived from *tert*-leucinol and an achiral salicylic aldehyde. Due to the good performance of this catalyst system (low catalyst loading, low excess of oxidant, ambient temperature and no exclusion of air), we considered it worthwhile to further elaborate the ligand by employing chiral aldehydes. Clearly, with two centers of chirality in the molecule, one should expect matched/mismatched effects. The most important results of this study are summarized in Scheme 10.[26] The diastereomeric ligands **9a** and **9b** are derived from a salicylic aldehyde which carries a chiral camphane unit, whereas **10a** and **10b** contain additional axial chirality derived from a binaphthyl salicylic aldehyde.[27] In fact, a further increase in enantioselectivity was achieved with the "matched" ligands **9a** and **10a**, whereas the "mismatched" ligands **9b** and **10b** gave lower enantiomeric excesses. To the best of our knowledge, the enantioselectivity achieved with the ligand **9a** in the sulfoxidation of thioanisol is the highest one so far, using transition metal catalysts and hydrogen peroxide as terminal oxidant.




(Scheme 9)

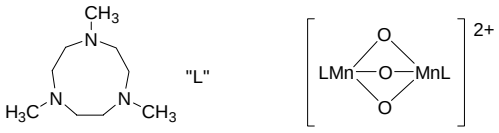



(Scheme 10)




## III. Oxidations catalyzed by the system Mn-TMTACN/ascorbic acid

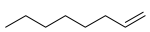
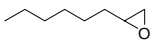
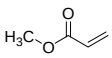
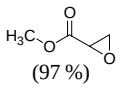
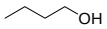
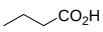
TMTACN stands for the tridentate ligand 1,4,7-trimethyltriazacyclononane (**11**, Scheme 11).[28] A huge number of metal complexes of this ligand has been prepared, including manganese.[28] In 1994, it was reported by researchers of Unilever that the dinuclear manganese (IV)-complex **12** of TMTACN is able to activate hydrogen peroxide for bleaching purposes in a catalytic manner.[29] In this publication, it was also reported that Mn-TMTACN catalyzes the epoxidation of olefins with hydrogen peroxide. However, under the conditions reported, this epoxidation method was seriously plagued by catalase activity, i.e. the catalytic disproportionation of hydrogen peroxide.




**11** **12** **13** (Scheme 11)

In the following years, the Mn-TMTACN sytem was improved continously, and a major breakthrough was achieved by *De Vos* et al.[30] The latter authors found that using oxalate as a co-ligand greatly enhances the activity of this catalyst, and turnover numbers up to ca. 700 were achieved, e.g. in the epoxidation of allyl acetate. In an attempt to extend this method to the *asymmetric* epoxidation of olefins, we screened a large number of potential chiral co-ligands. As it turned out, none of them induced significant enantiomeric excesses. Nevertheless, L-ascorbic acid **13**, a cheap and readily available bulk chemical, was identified as a co-ligand that renders extremely high catalytic activity to Mn-TMTACN.[31] Our results are summarized in Table 2. As shown in entry 1, less than 0.1 % of the manganese catalyst is required for full conversion of

**Table 2**: Mn-TMTACN-catalyzed epoxidation of olefins and oxidation of alcohols with hydrogen peroxide, ascorbic acid as co-ligand.

| entry | substrate | **stoichiometry** substrate:$H_2O_2$: Mn:TMTACN | **stoichiometry** Mn:ascorbic acid: sodium ascorbate | **product**[a] (yield)[b] |
|---|---|---|---|---|
| **1** |  | 1333:3500: 1:1.3 | 1:0.5: 2.1 |  (83 %) |
| **2** |  | 3333:6666: 1:1.3 | 1:0: 8 |  (97 %) |
| **3** |  | 3333:8000: 1:1.3 | 1:0: 6.7 |  (97 %) |
| **4** |  | 267:667: 1:1.3 | 1:0.5: 2 |  (90 %) |

a) In all cases, the products were isolated and identified by comparison of their spectroscopical data with those of authentic samples.
b) Determined by capillary GC.

1-octene to 1,2-epoxyoctane. Using *E*- and *Z*-1-deuterio-1-octene as substrate, the epoxidation of this terminal olefin was shown to be almost completely stereospecific (ca. 94 %). Even more striking, less than 0.03 % of catalyst is needed for the quantitative epoxidation of the electron-poor substrate methyl acrylate (Table 2, entry 2). The combination of Mn-TMTACN with ascorbic acid is also active in the oxidation of alcohols with hydrogen peroxide. As exemplified in entries 3 and 4 of Table 2, secondary alcohols are transformed to ketones in good yields, and primary

alcohols are directly converted to the corresponding carboxylic acid. In summary, the simple and readily available system Mn-TMTACN/ascorbic acid provides the highest turnover numbers achieved so far in Mn-catalyzed epoxidations with hydrogen peroxide, and it also shows quite remarkable turnover numbers in the oxidation of alcohols.[31]

## IV. Epilogue

What remains to be done? Quite a lot! As discussed in the beginning, hydrogen peroxide is an extremely advantageous source of oxygen. Unfortunately, only few catalysts have been discovered to date that allow for the selective oxygenation or fine chemicals with this oxidant. Significant challenges still remain, e.g. the selective hydroxylation of C-H-bonds for a broad substrate spectrum, or the efficient *Baeyer-Villiger*-oxidation of ketones using hydrogen peroxide. The former reaction has been achieved, e.g. with Mn-TMTACN as catalyst, but unfortunately with relatively low turnover numbers and selectivities.[32] The latter transformation is well known for strained ketones such as cyclobutanones.[33] However, the analogous transformation of e.g. cyclohexanone is much more demanding. It is hoped that also for this oxygenation, efficient low-molecular weight catalysts will be available in the future.

**Acknowledgements**

Throughout the years, our work has been supported financially by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and by the BASF AG, Ludwigshafen.

**References**

1. a) B. M. Trost, *Science* **1991**, *254*, 1471; b) B. M. Trost, *Angew. Chem.* **1995**, *107*, 285; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259.
2. a) J. Tsuji, *Palladium Reagents and Catalysts*, Wiley, Chichester (1995); b) for a recent issue of *Accounts of Chemical Research*, dedicated exclusively to Catalytic Asymmetric Synthesis, see *Acc. Chem. Res.* **2000**, *33* (6).
3. E. N. Jacobsen, A. Pfaltz, H. Yamamoto (eds.), *Comprehensive Asymmetric Catalysis*, Vols. I-III, Springer, Berlin-Heidelberg (1999).
4. T. Ohkuma, M. Koizumi, H. Doucet, T. Pham, M. Kozawa, K. Murata, E. Katayama, T. Yokozawa, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1998**, *120*, 13529; review: H. Ohkuma, R. Noyori in ref. 3, 199.
5. H.-U. Blaser, H.-P. Buser, K. Coers, R. Hanreich, H.-P. Jalett, E. Jelsch, B. Pugin, H.-D. Schneider, F. Spindler, A. Wegmann, *Chimia* **1999**, *53*, 275; review: H.-U. Blaser, F. Spindler in ref. 3, 247.
6. a) Discovery: T. Katsuki, K. B. Sharpless, *J. Am. Chem. Soc.* **1980**, *102*, 5976; b) reviews: T. Katsuki, V. S. Martin, *Org. React.* **1996**, *48*, 1; T. Katsuki in ref. 3, 621.
7. a) Discovery: S. G. Hentges, K. B. Sharpless, *J. Am. Chem. Soc.* **1980**, *102*, 4263; b) reviews: H. C. Kolb, M. S. Van Nieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483; I. E. Markö, J. S. Svendsen in ref. 3, 713.
8. a) Discovery: G. Li, H.-T. Chang, K. B. Sharpless, *Angew. Chem.* **1996**, *108*, 449; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 451; b) review: H. C. Kolb, K. B. Sharpless, *Asymmetric Aminohydroxylation*, in M. Beller, C. Bolm, (eds.) *Transition Metals for Organic Synthesis: Building Blocks and Fine Chemical*, Wiley-VCH, Weinheim (1998).
9. a) Discovery: R. Irie, K. Noda, Y. Ito, N. Matsumoto, T. Katsuki, *Tetrahedron Lett.* **1990**, *31*, 7345; W. Zhang, J. L. Loebach, S. R. Wilson, E. N. Jacobsen, *J. Am. Chem. Soc.* **1990**, *112*, 2801; b) review: E. N. Jacobsen, M. H. Wu in ref. 3, 649.

10. H. J. Krüger in B. Meunier (ed.), *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*, 363, Imperial College Press, London (2000).
11. J. T. Groves, R. Quinn, *J. Am. Chem. Soc.* **1985**, *107*, 5790.
12. A. S. Goldstein, R. H. Beer, R. S. Drago, *J. Am. Chem. Soc*. **1994**, *116*, 2424.
13. a) C.-H. Wong, G. M. Whitesides, *Enzymes in Organic Synthesis*, Elsevier, Oxford (1994); b) H. L. Holland, *Organic Synthesis with Oxidative Enzymes*, VCH, Weinheim (1992).
14. E. g. Cytochrome c peroxidase from Saccharomyces cerevisiae: D. B. Goodin, D. E. Mc Ree, *Biochemistry* **1993**, *32*, 3313.
15. a) B. Meunier in B. Meunier (ed.), *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*, 171, Imperial College Press, London (2000); b) A. Robert, B. Meunier, *ibid*. 543.
16. a) R. Irie, Y. Ito, T. Katsuki, *Synlett* **1991**, 265; b) E. N. Jacobsen, M. H. Wu in ref. 3, 649.
17. a) P. Battioni, J. P. Renaud, J. F. Bartoli, M. Reina-Artiles, M. Fort, D. Mansuy, *J. Am. Chem. Soc.* **1988**, *110*, 8462; b) P. L. Anelli, S. Banfi, F. Montanari, S. Quici, *J. Chem. Soc., Chem. Commun.* **1989**, 779.
18. A. Berkessel, M. Frauenkron, T. Schwenkreis, A. Steinmetz, G. Baum, D. Fenske, *J. Mol. Catal. A*, **1996**, *113*, 321.
19. A. Berkessel, M. Bolte, M. Frauenkron, T. Nowak, T. Schwenkreis, L. Seidel, A. Steinmetz, *Chem. Ber.* **1996**, *129*, 59.
20. R. Irie, N. Hosoya, T. Katsuki, *Synlett* **1994**, 255.
21. a) P. Pietikäinen, *Tetrahedron Lett*. **1994**, *35*, 941; b) oxidation of thioethers: M. Palucki, P. Hanson, E. N. Jacobsen, *Tetrahedron Lett.* **1992**, *33*, 7111.
22. R. Wever, *Nature* **1988**, *335*, 501.
23. H. B. ten Brink, A. Tuynman, H. L. Dekker, W. Hemrika, , Y. Izumi, T. Oshiro, H. E. Schoemaker, R. Wever, *Inorg. Chem.* **1998**, *37*, 6780.
24. C. Bolm, K. Muniz, J. P. Hildebrand in ref. 3, 697.
25. C. Bolm, F. Bienewald, *Angew. Chem.* **1995**, *107*, 2883; *Angew. Chem. Int. Ed. Engl*. **1995**, *34*, 2640.
26. A. H. Vetter, A. Berkessel, *Tetrahedron Lett.* **1998**, *39*, 1741.
27. H. Sasaki, R. Irie, T. Katsuki, *Synlett* **1993**, 300.
28. P. Chaudhuri, K. Wieghardt, *Progr. Inorg. Chem.* **1987**, *35*, 329.
29. R. Hage, J. E. Iburg, J. Kerschner, J. H. Koek, E. L. M. Lempers, R. J. Martens, U. S. Racherla, S. W. Russell, T. Swarthoff, M. R. P. van Vliet, J. B. Warnaar, L. van der Wolf, B. Krijnen, *Nature* **1994**, *369*, 637.
30. D. E. De Vos, B. F. Sels, M. Reynaers, Y. V. Subba Rao, P. A. Jacobs, *Tetrahedron Lett*. **1998**, *39*, 3221.
31. A. Berkessel, C. A. Sklorz, *Tetrahedron Lett.* **1999**, *40*, 7965.
32. J. R. Lindsay Smith, G. Shul'pin, *Tetrahedron Lett.* **1998**, *39*, 4909.
33. M. J. Bogdanowicz, T. Ambelang, B. M. Trost, *Tetrahedron Lett.* **1973**, 923.

## About the Author

***Prof. Dr. Albrecht Berkessel***

*Institut für Organische Chemie der Universität zu Köln*
*Greinstr. 4, D-50939 Köln, Germany*

Professor Berkessel was born in Saarlouis/Germany in 1955. He studied Chemistry in Saarbruecken and received his Ph.D. (mechanistic photochemistry) with Professor Waldemar Adam at the University of Wuerzburg in 1985. He then joined the research group of Professor Ronald Breslow at Columbia University, New York, to work on cyclodextrin-based enzyme-models and on the mechanism of action of the vitamin biotin. Back in Germany, he completed his habilitation on the mechanism of nickel-enzymes from methanogenic bacteria in 1990. This work was done at the University of Frankfurt (Professor Gerhard Quinkert). He was appointed Associate Professor at Heidelberg University in 1992 and Full Professor at the University of Cologne 1997.

His current research interests center around various aspects of catalysis in Organic Chemistry: biomimetic catalysis, combinatorial methods in catalysis, oxidation and asymmetric catalysis.