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Biomimetic Epoxidation of Olefins Catalyzed by Metalloporphyrins with Molecular Oxygen

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1. Introduction

The direct oxidation of hydrocarbon is a field of both academic and industrial importance and challenge.[1-3] Catalytic oxidation is a key technology for converting petroleum-based feedstock to useful chemicals of a high oxidation state such as alcohols, carbonyl compounds, and epoxides. Millions of tons of these compounds are annually produced worldwide and find applications in all areas of chemical industries.[4-6]

Epoxidation of olefins is an important reaction in organic synthesis because the formed epoxides are intermediates that can be converted to a variety of products.[7-10] Access to a variety of epoxides has largely been successful due to the remarkable catalytic activity of transition metal complexes, which have a unique ability to bring the alkene substrate and the oxygen source within the coordination sphere of the metal leaving to a facial transfer of oxygen atom to the carbon-carbon double bond.[11-15]

Cytochrome P-450 enzymes are heme-containing monooxygenases and play a key role in the oxidative transformation of endogeneous and exogeneous molecules.[16-20] They are virtually ubiquitous in nature and are present in all forms of life like plants and mammals, as well as in some prokaryotic organisms such as bacteria.[21-23] The active site of P-450s contains a highly conserved prosthetic heme IX complex coordinated by a thiolate ligand from a cysteine residue (Figure 1).

The primary function of cytochrome P-450 enzymes is the oxygenation of a wide variety of organic substrates by inserting one oxygen atom from O_2 to the substrate and reducing the other oxygen atom with reducing equivalents to a water molecule, utilizing two electrons that are provided by NAD(P)H via a reductase protein (***Scheme 1***).

$$R{-}H + O_2 + NAD(P)H + H^+ \xrightarrow{\text{cytochrome P-450}} R{-}OH + H_2O + NAD(P)^+$$

Scheme 1. Overall oxygenation reaction catalyzed by cytochrome P-450

Being a triplet (two unpaired electrons in ground state), molecular oxygen is unreactive toward organic molecules at low temperatures. The reaction of dioxygen with the single state of organic substrates is spin-forbidden.[24] Consequently, the oxygenation of organic molecules at physiological temperatures must involve the modification of the electronic structure of one of the partners. Living systems mainly use enzymes like cytochromes P-450 to modify the electronic structure of dioxygen to form which is adapted for the desired

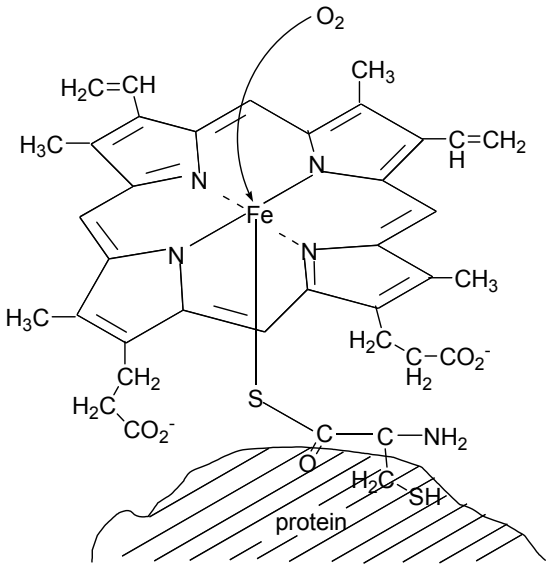


Fig. 1. Prosthetic of cysteinato-heme enzymes: an iron(III) protoporphyrin-IX covalently linked to the protein by the sulfur atom of a proximal cysteine ligand.

oxidation reaction. The mechanism of its catalytic activity and structural functions has been the subject of extensive investigation in the field of biomimetic chemistry. The high-valent iron(IV)-oxo intermediate, formed by the reductive activation of molecular oxygen via peroxo-iron(III) and hydroperoxy-iron(III) intermediates by cytochrome P-450, is responsible for the in vivo oxidation of drugs and xenobiotics. This high valent iron(IV)-oxo intermediate and probably other intermediates of the P450 catalytic cycle can be formed by the reaction of iron(III) porphyrins with different monooxygen donors.[25-27] Therefore, cytochrome P-450 enzymes are potent oxidants that are able to catalyze the hydroxylation of saturated carbon-hydrogen bonds, the epoxidation of double bonds, the oxidative dealkylation reactions of aminies, oxidations of aromatics, and the oxidation of heteroatoms. [28-30]

As the isolation of P-450 enzymes from plants is extremely difficult, the first reactions employing this hemoprotein's enzymes were carried out with bacterial and mammalian P-450. Only in recent years have genes of P-450 enzymes been isolated from plants, and the first reactions confirmed that these enzymes take an active part in herbicide detoxification. [31]

The use of chemical model systems mimicking P-450 might therefore be a very useful tool for overcoming the difficulty in working with enzymes in vivo and vitro.[32] The synthesis of cytochrome P-450 models is a formidable challenge for chemist to establish a system that is structurally equivalent to the enzymes. The synthetic mimic not only is a structural analogue exhibiting spectroscopic features close to the enzyme's cofactor but also displays a similar reactivity and catalysis.[33] In recent years, the development of efficient catalytic systems for oxidation reactions that mimic the action of cytochrome P-450 dependent momooxygenases has attracted much attention.[34-42] Synthetic metalloporphyrins have been used as cytochrome P-450 models and have been found to be highly efficient homogeneous or heterogeneous catalysts for oxidation reactions, especially for the alkane hydroxylation and alkene epoxidation.[43-45]

During the past two decades, the use of metalloporphyrins as catalysts for the epoxidation of olefins has received increasing attention since the leading works of Groves and co-workers by using iodosylbenzene (PhIO) as oxygen atom donor.[46] A variety of oxidants, such as hydrogen peroxides,[47-49] iodosylbenzene,[50-52] magnesium monoperoxyphthalate, [53-54] tetrabutylammonium monosulfate and eriodate,[55-56] in combination with a large variety of metalloporphyrin catalysts have been employed as oxygen atom donors.

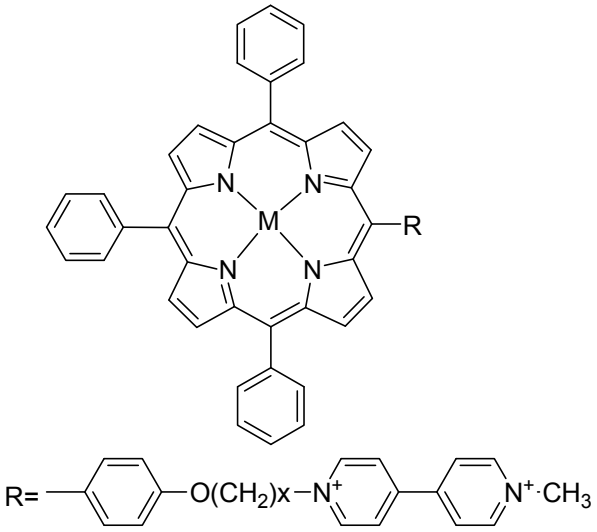
For economic and environmental viewpoints, the aerobic epoxidation of olefins catalyzed by metalloporphyrins is attracting more interests. The chapter will try to cover the biomimetic homogeneous and heterogeneous aerobic epoxidation of olefins catalyzed by metalloporphyrins in the recent years. It will focus on the modeling of the monooxygenase catalytic circle with synthetic metalloporphyrins. Since the stioichiometry of a monooxygenase-mediated oxygenation requires two electrons and two protons to reduce the second oxygen atom of dioxygen to water, most of works reported involve an electron source: borohydride, hydrogen and colloidal platinum, zinc powder, electrons from an electrode or aldehyde as reductant.[57-61] According to the sacrificial use of electrons, the recent advances in this section will focus on presenting the metalloporphyrin- mediated epoxidation in the presence of zinc powder, aldehyde as reductant or in absence of reductant. Both practical and mechanistic point of view for the epoxidation of olefins catalyzed by metalloporphyrins will be presented.

2. Zinc powder as reductant

A viologen-linked Mn(III) porphyrin complex ($MnPC_xMV$, ***Scheme*** **2**) with a short methylene-chain, in which a viologen is covalently linked by the methylene-chain into one phenyl group of 5,10,15,20- tetraphenylporphyrinatomanganese(III) chloride (MnTPPCl), was used as catalyst for a monooxygenase of cyclohexene in an air-equilibrated acetonitrile solution containing insoluble zinc powder as reductant, more cyclohexene oxide was obtained as a single product than when MnTPPCl was used as catalyst.[62] According to the reaction of an air-equilibrated acetonitrile suspension containing 1×10^{-4} M MnTPPCl, 1×10^{-4} M 1-MeIm (1-methylimidazole), 7.3×10^{-2} M zinc powder, 2×10^{-2} M benzoic acid (the cleaving reagent of dioxygen double-bond) and 0.47 M cyclohexene for 3 h at 30°C, about 1×10^{-3} M epoxide was obtained as the single oxidation product of cyclohexene. Since the turnover number of MnTPPCl was about 10, it was found that MnTPPCl acted as catalyst.

Further, when 1×10^{-4} M $MnPC_2MV$ or the mixture of 1×10^{-4} M MnTPPCl and 1×10^{-4} M MV^{2+} was used as the catalyst, the amount of the product epoxide remarkably increased and the turnover number reached about 40 for 3 h. The time-dependence of the amount of the product epoxide is shown in Figure 2. This suggests that viologen and the viologen moiety in $MnPC_2MV$ acted as the mediator for the electron transfer from zinc powder to Mn porphyin.

Enhancement of cyclohexene oxide was produced by adding an axial ligand for MnTPPCl such as Cl^-, Br^- in the catalytic system.[63] The Cl^- and Br^- promoted this epoxidation probably by assisting the oxygen transfer from Mn(V)-oxo complex, that is an intermediate in this reaction cycle, to cyclohexene, and HV^{2+} functioned as the mediator of electron transfer from zinc to Mn(II)TPP-dioxygen adduct, enhancing the production of epoxide. However, when a small amount of 1-MeIm ($< 10^{-2}$ M) was added in this system containing HV^{2+}, the epoxide was not produced and zinc was hardly consumed. Moreover, a larger amount of epoxide was obtained by adding 1-MeIm further ($> 10^{-2}$ M). A plausible mechanism was proposed as shown in Figure 3.



Scheme 2. Structure and abbreviation of covalently linked manganese(III) porphyrins-viologen

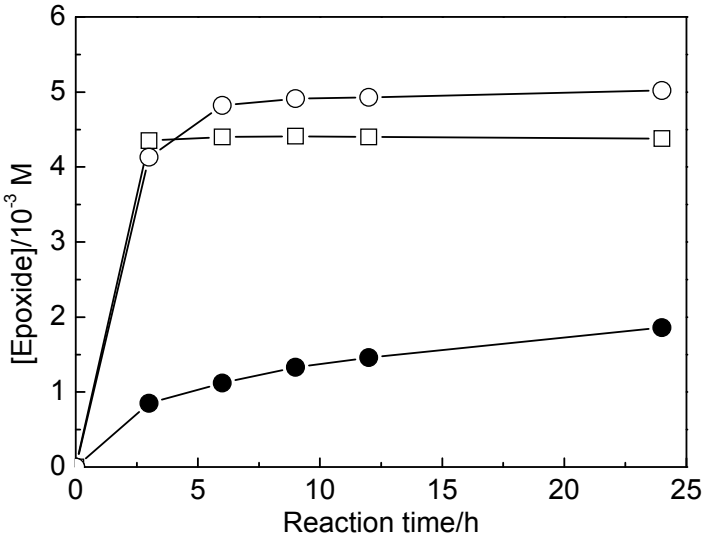


Fig. 2. Time-dependence of the amount of produced epoxide in air-equilibrated acetonitrile suspension containing 1×10^{-4} M Mn porphyrin, 5×10^{-3} M 1-MeIm, 7.3×10^{-2} M zinc powder, 2×10^{-2} M benzoic acid and 0.47 M cyclohexene at 30°C. Catalyst: MnTPPCl(●), $MnPC_2MV$(○) and MnTPPCl+1×10^{-4} M MV^{2+}(□)

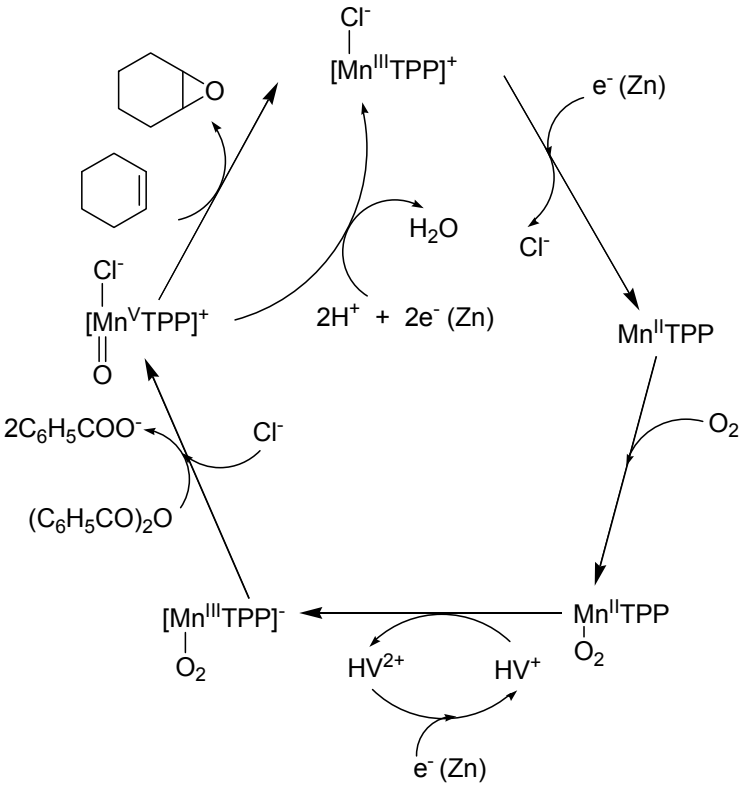


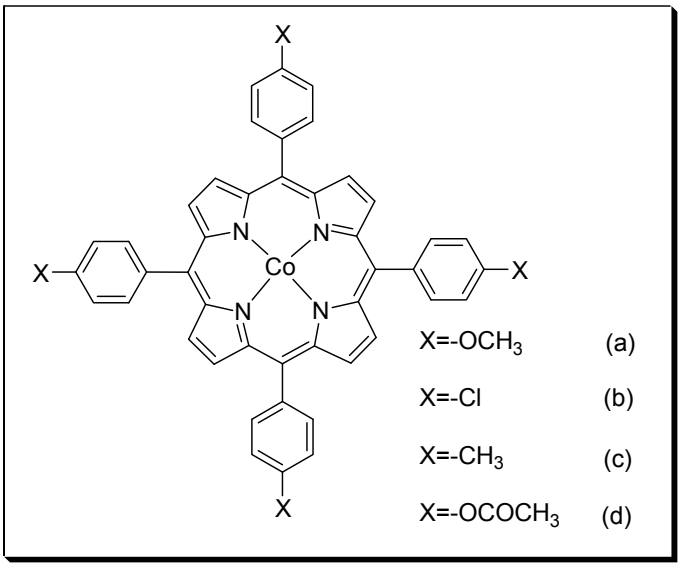
Fig. 3. Catalytic epoxidation cycle of cyclohexene using MnTPPCl as catalyst in the absence of 1-MeIm

The hexylviologen acted effectively as the mediator of electron transfer from zinc powder to Mn(II)TPP-O_2 adduct. Since the halogen ion can coordinate easily to the manganese ion in $[Mn(V)TPP=O]^+$ cation due to an additive electrostatic interaction, the oxygen transfer proceeded by the assistance of its coordinate bond. Thus, when HV^{2+} was added in the catalytic system using the Mn porphyrin catalyst with the Cl^- counter ion, the dioxygen-activated reductive epoxidation of cyclohexene occurred even in the absence of 1-MeIm.
According to the mechanism, the decrease of the epoxide production with increasing 1-MeIm ($<10^{-2}$ M) may be explained from the factor that the coordination of 1-MeIm to Mn(II)TPP depressed the formation of the Mn(II)TPP-O_2 adduct. Further, the epoxide was obtained by adding a large amount of 1-MeIm ($>10^{-2}$ M) because the reducing power of Zn may become strong by a complex formation between Zn^{2+} and 1-MeIm.

3. Aldehydes as reductant

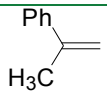
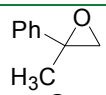
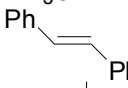
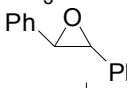
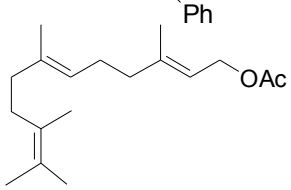
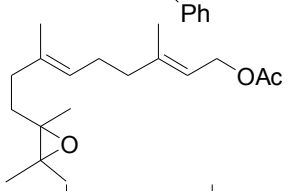
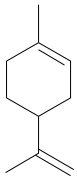
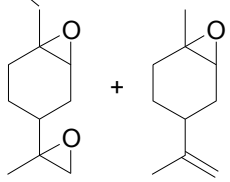
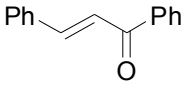
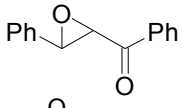
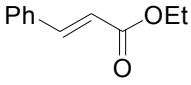
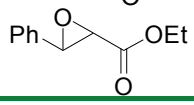
Aldehyde is another effective reducing agent for the epoxidation of olefins with dioxygen as oxidant. Mukaiyama reported an efficient approach for epoxidation of olefins using dioxygen as oxidant under ambient conditions. The process involved use of β-diketonate complexes of Ni^{2+}, Co^{2+}, and Fe^{3+} as catalysts and an aldehyde as oxygen acceptor.[64-66]

Subsequently, many metal catalysts e.g. manganese complex, cobalt-containing molecular sieves and metalloporphyrins demonstrated highly catalytic performance for the aerobic oxidation in the presence of aldehyde.[67-70]
Mandal and co-workers reported the epoxidation of various olefins using cobalt porphyrins (***Scheme 3***) in ambient molecular oxygen and 2-methylpropanal.[71]



Scheme 3. Structures of cobalt prophyrins used in the epoxidation of olefins

Methyl styrene, stilbene and farnesyl acetate were transformed to the corresponding epoxides in nearly quantitative yield (Table 1). It is noteworthy that *trans*-stilbene afforded the corresponding *trans*-epoxide (entry 2). While highly regioselective monoepoxidation of farnesyl acetate to give epoxide was observed under these conditions (entry 3). Similarly, limonene was readily transformed to a mixture of mono and diepoxide in 1:2.3 ratio in quantitative yield (entry 4). Interestingly, the α, β unsaturated carbonyl compounds i.e. chalcone (entry 5) and ethyl cinnamate (entry 6) were epoxidized in good yields to give stereochemically pure *trans* epoxides respectively.
In order to probe the substitute effect in the para position of aromatic ring of porphyrin, the catalytic activities of (a)-(c) were studied in the epoxidation of cyclohexene. Thus the oxidation of cyclohexene using (a) as catalyst afforded a mixture of corresponding epoxide, cyclohexenol, cyclohexenone in 1:3:1.2 ratio. On the other hand oxidation of cyclohexene in the presence of (b) yielded only a mixture of cyclohexenol and cyclohexenone whereas catalysis under (c) gave rise to a mixture of epoxide, cyclohexenol and cyclohexenone respectively. These results could be conceivable that the oxidation are proceeding via an analogous cobalt oxo species.
The simple structural metalloporphyrins has proven to be an excellent catalyst for the epoxidation of olefins in the presence of molecular oxygen and isobutylaldehyde. As a part of metalloporphyrins-catalyzed oxidations of our group works, the epoxidation of olefins catalyzed by very small amount of MnTPP (manganese *meso*-tetraphenyl porphyrin) was

Entry	Substrate	Product[b]	Yields (%)[a]
1			94
2			100
3			80
4		 2.3:1	100[c]
5			83
6			51

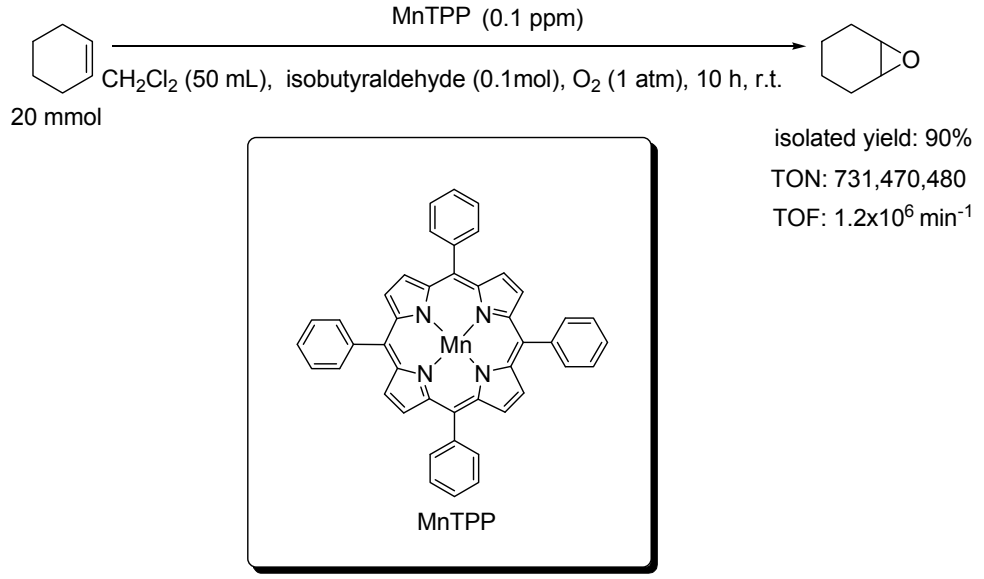
[a] Isolated yield. [b]Yield determined from ^{1}H-NMR of the crude reaction mixture.
[c]Obtained as a mixture of syn-anti diastereomers

Table 1. Co(II) porphyrin catalyzed oxidation of olefins using 2-methylpropanal and dioxygen

reported (***Scheme 4***), in which extremely high turnover number that could be comparable to most enzyme catalysis was obtained.[72] When the amount of manganese *meso*-tetraphenylporphyrin catalyst was 2.5×10^{-8} mmol, the cyclohexene oxide could be obtained with the isolated yield of 90%.

It should be mentioned that the turnover number of the present catalyst could reach 731,470,480. Since commonly, TOF is used to express the catalytic efficiency of enzyme with the definition as converted substrate (mol) per enzyme (mol) per minute. The TOF of most enzymes is about 1000 min^{-1} or more. For example, the TOF of catalase is 6×10^6 min^{-1}, and the TOF of β-galactosidase is 1.25×10^4 min^{-1}. In the present manganese *meso*-tetraphenylporphyrin catalyzed system, the TOF reaches up to 1.2×10^6 min^{-1}, which is the range for enzyme activity.

Also, various olefins could be smoothly converted to corresponding epoxides in the catalytic system under ambient conditions. As shown in Table 2, it seems that the efficiency of epoxidation in this catalytic system is very dependent on the steric structure of substrates. The influence of steric effects could further be found when styrene and its derivatives were oxidized, the conversion rates of styrene, *trans*-β-methylstyrene and *trans*-stilbene were 95%, 89% and 86% after reacting for 4.5, 7.0 and 8.0 h, again demonstrating a steric effect (entries 4-6).



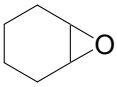
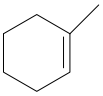
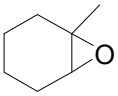
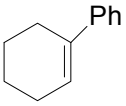
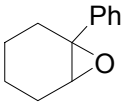
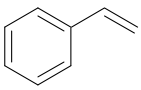
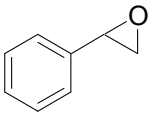
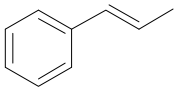
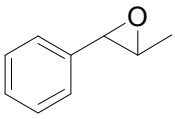
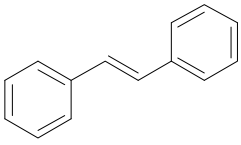
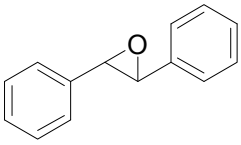
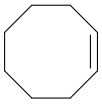
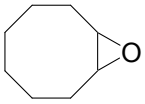
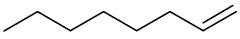
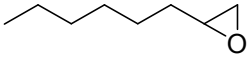
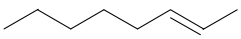
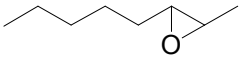
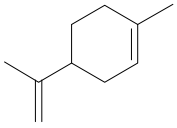
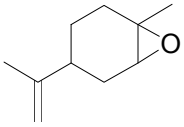
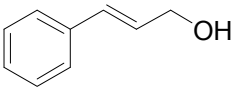
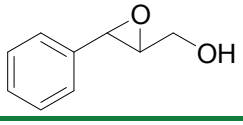
Scheme 4. Manganese *meso*-tetraphenylporphyrin catalyzed epoxidation of olefins

Similarly, in the epoxidation of other cycloolefin *e.g.* cyclooctene, the reaction system exhibits high catalytic performance with 93% yield of cyclooctene epoxide (entry 7). Epoxidation of linear chains *e.g.* 1-octene and *trans*-2-octene smoothly proceeded with high conversion and yield, and similar catalytic activities for the two substrates shows the located position of C=C bond on linear chain alkenes could hardly influence their catalytic performance (entries 8-9).

Despite of the high efficiency of the catalyst system, another salient feature of the present epoxidation is its high regioselectivity (entry 10). In addition, the catalyst system exhibits specific selective oxidation performance towards C=C bond and hydroxyl group activation. C=C bond was preferentially activated and the corresponding epoxide as the only product with 90% yield could be obtained for the cinnamyl alcohol oxidation, and no products from hydroxyl group oxidation could be detected (entry 11).

The extremely high catalytic performance (comparable to enzymes) exhibited by manganese *meso*-tetraphenylporphyrin is most interesting. In order to gain insight into the likely reasons, the epoxidation processes of cyclohexene in the presence of isobutyraldehyde and molecular oxygen with different amounts of catalyst of 10000, 100, 10, 1, 0.1 ppm (based on substrate) were tracked. The reaction profiles are shown in Figure 4.

Although the amount of the catalyst decreased exponentially, cyclohexene could be nearly stoichiometrically oxidized within the reaction times ranged from 2.0 to 5.0 h, as shown in Figure 1. When the amount of catalyst was 1 or 0.1 ppm, the reaction displays an induction period, then followed by a sharp acceleration until completion. When a radical scavenger such as tetrachloromethane was added to the reaction system, the conversion was stopped and no product could be detected after 5 h, even with 10000 ppm catalyst. Therefore, the epoxidation catalyzed by metalloporphyrin should involve radical species. The result is consistent with those of Qi, Nam, and Ravikumar using ruthenium complex, cyclam or manganese acetate dihydrate as catalysts.[73-76]

Entry	Substrate	Product	Reaction time (h)	Conv. (%)	Yield (%)
1			4.5	97	95
2			5.0	93	90
3			6.0	83	72
4			4.5	95	93
5			7.0	89	87
6			8.0	86	85
7			5.0	95	93
8			5.0	94	93
9			5.0	93	89
10			5.0	92	91
11			6.0	92	90

[a] substrate (2 mmol), isobutyraldehyde (0.01mol), CH_2Cl_2 (5 mL), O_2 bubbling, r.t.

Table 2. Epoxidation of alkenes catalyzed by manganese *meso*-tetraphenylporphyrin in the presence of molecular oxygen and isobutyraldehyde[a]

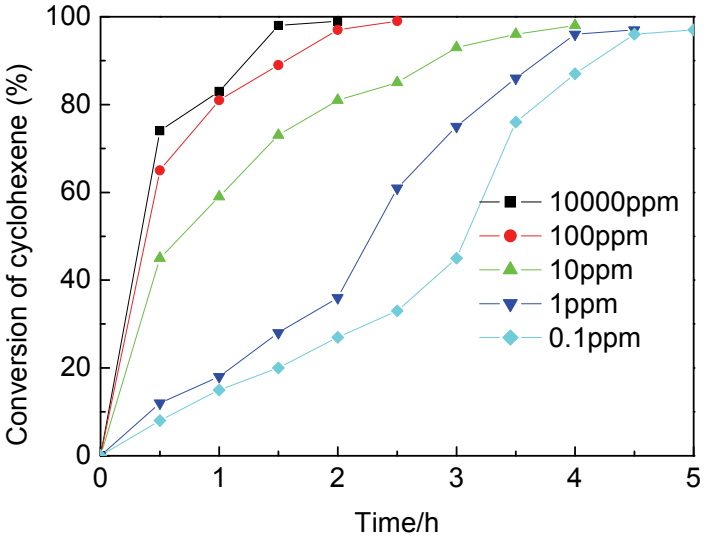


Fig. 4. Conversion rates profile of cyclohexene oxide with different amounts of Mn(TPP) [a]

[a] substrate (2 mmol), isobutyraldehyde (0.01mol), CH_2Cl_2 (5 mL), O_2 bubbling (1atm), r.t.

Iron, ruthenium and cobalt also showed excellent activity for cyclohexene epoxidation by molecular oxygen (Table 3). [77] Comparing the catalytic activities of different porphyrin catalysts, it was found that manganese porphyrin was the most effective since cyclohexene could be completely converted within 4.0 hours. The catalytic activity of different metalloporphyrins is probably influenced by their electric potential and the stability of different valences of metal atoms.

Entry	Catalyst	Conv. (%)	Yield (%)
1	Mn(TPP)Cl	>99	>99
2	Fe(TPP)Cl	93	92
3	Co(TPP)Cl	90	90
4	Ru(TPP)Cl	86	85
5	-	15	13

[a] Olefins (2 mmol), aldehyde (0.01mol), catalyst (2×10^{-6} mmol), CH_2Cl_2 (5 mL), O_2 bubbling, r.t., 4 h

Table 3. Epoxidation of cyclohexene by molecular oxygen in the presence of various metalloporphyrins and isobutyraldehyde[a]

The mechanisms of alkene epoxidation by molecular oxygen in the presence of metal complexes and aldehyde have been already investigated. For such oxidation system, all evidence indicates that the reaction proceeded *via* free radical process. Oxygenation of substrates is assumed to occur *via* reactive high-valent metal oxo intermediates that are produced by the reaction of peroxyacid with the metal catalysts from this mechanism.

In the system of olefin epoxidation by dioxygen, the process of epoxidation can follow different pathways depending on catalyst and reaction conditions. Nam and coauthors concluded that acylperoxy radicals from the autoxidation reaction or complexes of metal with the acylperoxy radicals were the active epoxidants, [74] and the metal complexes could accelerate the free radical autoxidation of aldehyde during the initiation step. Ravikumar reported that the epoxidation of olefin in perfluoro-2-butyltetrahydrofuran occurred either by the direct reaction of metal-peroxy species with olefins or through metal oxo species.[75] However, Kaneda *et al.* proposed that the key epoxidizing agent was not the metal oxo species, the peroxyacid was generated during the autoxidation of aldehyde, and the role of transition metal catalyst could be omitted.[78]

For the manganese porphyrin catalyzed epoxidaiton system, the typical product compositions of aerobic oxidation of cyclohexene are shown in Figure 5. Except the epoxide, isobutyric acid and perisobutyric acid generated from isobutyraldehyde could be detected in the reaction mixture. The formation of perisobutyric acid could be hardly detected within the first two-hour period. After reacting for 2 hours, the concentration of perisobutyric acid increased slightly while that of epoxidized cyclohexene increased sharply. It seems that the epoxidation occurred first with induction period, and then followed by sharp acceleration till completion, which agree with the feature of radical-involved reaction. In order to verify the free radical mechanism for the aerobic epoxidation of cyclohexene catalyzed by manganese porphyrins, a free radical inhibitor, 2,6-di-tert-butylphenol (2 mmol) was added to the oxidation system. It has been found that the running oxidation of cyclohexene could be subsequently quenched. In addition, epoxide, isobutyric acid or perisobutyric acid could not be found when the reaction was carried out under nitrogen atmosphere.

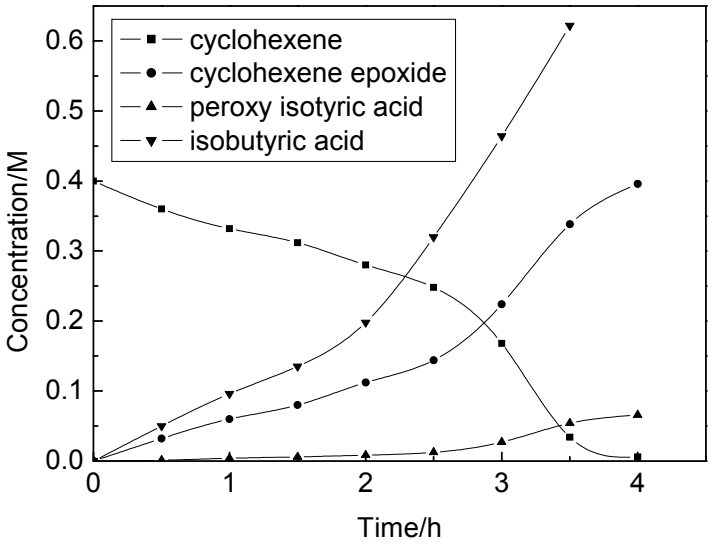


Fig. 5. Oxidation of cyclohexene by molecular oxygen in the presence of Mn(TPP)Cl and isobutyraldehyde: concentration of cyclohexene, 0.4 M; concentration of isobutyraldehyde, 2.0 M; concentration of catalyst, 4×10^{-5} M; O_2 bubbling; room temperature.

In contrary to Kaneda's results, the metalloporphyrins catalyst is absolutely necessary for the epoxidation of cyclohexene from the fact that only 13% yield of epoxide can be obtained in the blank experiment. Therefore, the mechanism of epoxides production *via* metallporphyrins-peroxy from the reaction of acylperoxy radical with metallporphyrins is impossible. The epoxide (yields up to 13%) in the absence of catalyst should be attributed to the reaction of acylperoxy radical with olefins directly. In the none-catalysis process, the acylperoxy radical was generated from acyl radical and dioxygen, and acyl radical was initiated from the auto-oxidation of aldehyde. A mechanism for the epoxidation of olefins by dioxygen in the presence of metalloporphyrins and isobutyraldehyde has been proposed from the experimental results, as shown in Figure 6.

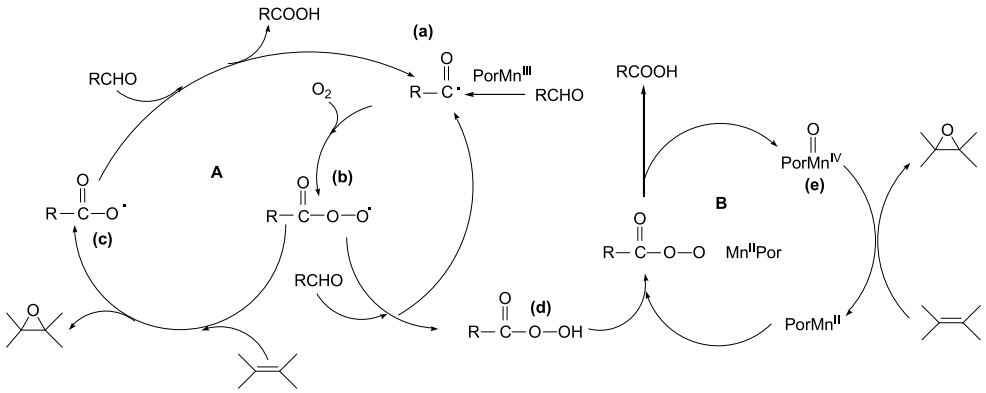


Fig. 6. Plausible mechanism of olefin epoxidation catalyzed by Mn(III) porphyrins in the presence of molecular oxygen and isobutyraldehyde

Based on the proposed mechanism, the manganese porphyrin reacts with the aldehyde to generate an acyl radical (a) at first. The acyl radical then reacts with dioxygen to give an acylperoxy radical (b). The acylperoxy radical is assumed to play two roles. Firstly, it reacts with olefins to yield epoxides directly accompanying the generation of carboxyl radical (c), which reacts with aldehyde to generate another acyl radical and carboxylic acid (pathway A). Secondly, in pathway B, the acylperoxy radical acts as a carrier by reacting with another aldehyde molecule to give peroxyacid (d), thereby generating another acyl radical. Formation of epoxide is assumed by active high-valent Mn porphyrin intermediates (e), which are formed by the reaction of the peroxyacid with the manganese porphyrin. The evidence described above suggests that pathway B is usually superior over pathway A.

In order to obtain further information on the role of the high-valent Mn porphyrin species for the present oxidation, in stiu EPR measurement was used for the aerobic oxidation of cyclohexene. The catalytic epoxidation in CH_3CN was carried out in a sealed Wilmad WG-810-A quartz-flat cell filled with dioxygen. EPR spectra were recorded with 20 min intervals. Figure 7 exemplifies the EPR results observed for Mn(III) porphyrin. Figure 7a shows the initial EPR spectrum of the Mn(TPP)Cl and the silent spectrum is characteristic of Mn(III) species from integer-spin (non-Kramers) Mn(III) S=2 porphyrin compound.[79-81] When isobutyraldehyde was added into Mn(TPP)Cl solution, a broad EPR signal of Mn(II) was observed (Figure 7b).[82] The change of EPR signal was attributed to the reaction of Mn (III) porphyrin with aldehyde, from which an acyl radical was generated and the Mn (III)

porphyrin was converted to Mn(II) species. This is in agreement with the first step of the proposed mechanism. The six lines shown in Figure 7c are a typical signal of Mn(IV) species, which indicates the catalytic process should involve high-valent oxo intermediate. [83-84]

As the reaction went on, it was interesting to find that the intensity of signal (g=2.02) increased, the peak became stronger and sharper, coupling with the decreasing intensity of adjacent signal (g=1.98). The EPR spectra are shown in Figure 7d-f. The fact demonstrated that Mn(II) porphyrins species might be there in the mixture, which are formed by the reduction of Mn(IV) intermediate.

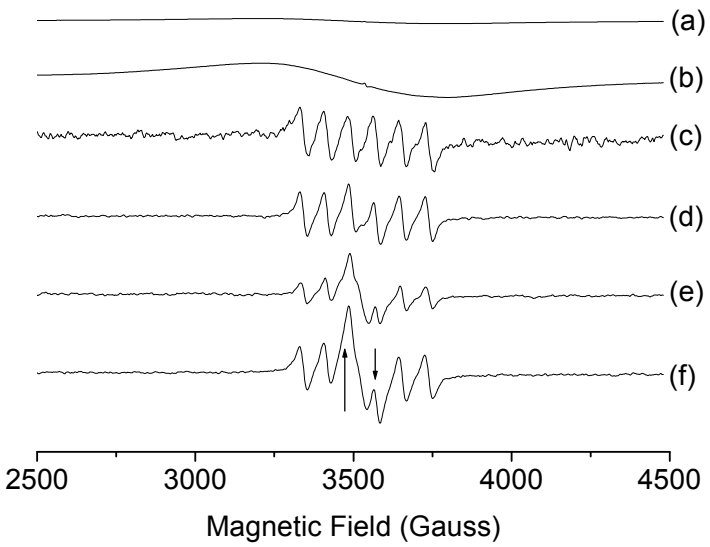


Fig. 7. In-situ EPR spectra of cyclohexene epoxidation catalyzed by Mn(TPP)Cl in the presence of dioxygen and isobutyraldehyde. (a) spectrum of Mn(TPP)Cl; (b) spectrum of Mn(TPP)Cl plus isobutyraldehyde; (c) initial spectrum of cyclohexene epoxidation; (d) epoxidation spectrum after 20 min; (e) epoxidation spectrum after 40 min; (f) epoxidation spectrum after 60 min.

The curves of UV-vis spectra for metalloporphyrins during the reaction process are shown in Figure 8. The spectrophotometer was programmed to acquire UV-vis spectrum every 10 minutes. As shown in Figure 8, a decrease in the Soret band at 445 nm was observed, with a concomitant slight increase in the typical Soret band at ~ 417 nm. The disappearance of the peak (445 nm) suggested that oxidant active species (Mn^{IV}=O) were consumed by substrate. [85-87] In addition, during the reaction, the color changes in the reaction mixture also indicate the presence of such high-valence species. GC analysis revealed the formation of the epoxide, which is indicative of the presence of an active oxidation species.

The epoxidation of cyclohexene in the presence of isobutyraldehyde and dioxygen to produce epoxidized cyclohexene with Mn(TPP)Cl as catalyst is a combination of oxidation of aldehyde and epoxidation of cyclohexene. Following the reaction mechanism given in Figure 6, the reaction equations can be listed as below:

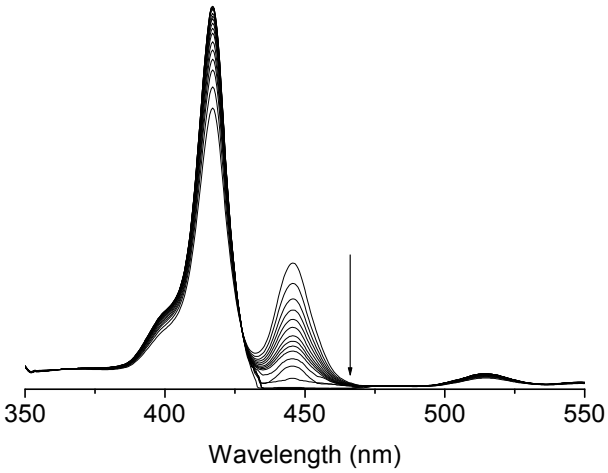


Fig. 8. In situ UV-vis spectra of the aerobic epoxidation of cyclohexene catalyzed by Mn(TPP)Cl (0.04 mM) in dichloromethane solution (time scan: 120 min, interval 10 min). Reaction conditions: cyclohexene (0.4 mol L^{-1}), catalyst (0.04 mM) and isobutyraldehyde (4 mol L^{-1})

Initiation: Equation 1 is the initiation step.

$$PorMn^{III} + RCHO \xrightarrow{k_0} PorMn^{II} + RC^{\cdot}O + H^{+} \quad (1)$$

Propagation:

$$RC^{\cdot}O + O_2 \xrightarrow{k_1} RCO_3^{\cdot} \quad (2)$$

$$RCO_3^{\cdot} + RCHO \xrightarrow{k_2} RCO_3H + RC^{\cdot}O \quad (3)$$

Termination: The main termination step is:

$$2RCO_3^{\cdot} \xrightarrow{k_3} \text{inactive} \quad (4)$$

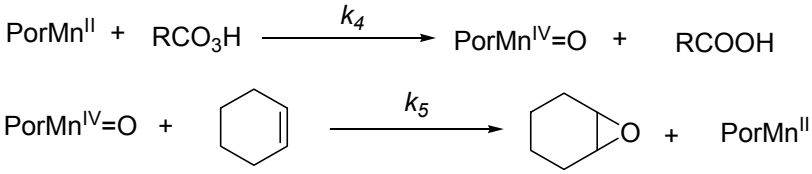
The other termination steps are:

$$2RC^{\cdot}O \longrightarrow \text{inactive} \quad (5)$$

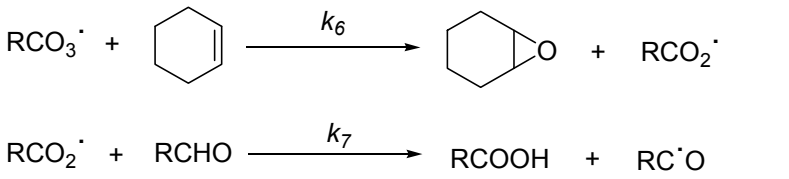
$$RCO_3^{\cdot} + RC^{\cdot}O \longrightarrow \text{inactive} \quad (6)$$

Epoxidation: The epoxidation steps include pathway A and B.

Pathway B:



Pathway A:



The molar balance equations for each component of the reactions are presented as follows: First, the changes of the free radicals concentrations are:

$$d[RC^{\cdot}O]/dt = k_0[RCHO][PorMn^{III}] - k_1[RC^{\cdot}O][O_2] + k_2[RCO_3^{\cdot}][RCHO] + k_7[RCO_2^{\cdot}][RCHO] \quad (11)$$

$$d[RCO_2^{\cdot}]/dt = k_6[RCO_3^{\cdot}][\text{cyclohexene}] - k_7[RCO_2^{\cdot}][RCHO] \quad (12)$$

$$d[RCO_3^{\cdot}]/dt = k_1[RC^{\cdot}O][O_2] - k_2[RCO_3^{\cdot}][RCHO] - 2k_3[RCO_3^{\cdot}]^2 - k_6[RCO_3^{\cdot}][\text{cyclohexene}] \quad (13)$$

Assuming that the system is in pseudo steady state, eqs 11-13 become

$$d[RC^{\cdot}O]/dt = d[RCO_2^{\cdot}]/dt = d[RCO_3^{\cdot}]/dt = 0 \quad (14)$$

Summing eqs. 11, 12 and 13,

$$k_0[RCHO][PorMn^{III}] = 2k_3[RCO_3^{\cdot}]^2 \quad (15)$$

In addition, eqs. 16 and 17 can be deduced from eqs. 7 and 8:

$$d[Mn^{IV}=O]/dt = k_4[PorMn^{II}][RCO_3H] - k_5[Mn^{IV}=O][\text{cyclohexene}] \quad (16)$$

$$d[RCO_3H]/dt = k_2[RCO_3^{\cdot}][RCHO] - k_4[PorMn^{II}][RCO_3H] \quad (17)$$

Based on pathways A and B, the total rate equation of epoxide (Re) can be expressed as:

$$Re = d[\text{epoxide}]/dt = k_5[Mn^{IV}=O][\text{cyclohexene}] + k_6[RCO_3^{\cdot}][\text{cyclohexene}] \quad (18)$$

Through the pseudo steady state hypothesis for the Mn(IV) high-valent intermediate and RCO_3H, eqs.16, 17 and 18 can be summarized to get the generating rate of epoxide as:

$$Re = k_2(k_6/2k_3)^{0.5}[RCHO]^{1.5}[PorMn^{III}]^{0.5} + k_6(k_6/2k_3)^{0.5}[RCHO]^{0.5}[PorMn^{III}]^{0.5}[cyclohexene] \quad (19)$$

Then, eqs. 19 can be simplified as:

$$Re = K_1[RCHO]^{1.5}[PorMn^{III}]^{0.5} + K_2[RCHO]^{0.5}[PorMn^{III}]^{0.5}[cyclohexene] \quad (20)$$

From equation 20, it can be seen that the rate of epoxidation is related with the concentration of cyclohexene, manganese porphyrins catalyst and isobutyraldehyde with 1, 0.5 and 1.5 power respectively. In order to verify the equation of the epoxidation rate further, the factors that influence epoxidation rate were investigated using cyclohexene as model substrate. The rate of epoxidation was obtained based on the following assumption: (1) There is very large excess of cyclohexene compared to catalyst (the [catalyst]/ [cyclohexene] ratio is $1/10^6$) in the catalytic system; (2) The conversion rate of cyclohexene should be controlled within 5%.

The catalytic epoxidation of cyclohexene in the presence of isobutyraldehyde and molecular oxygen was carried out with the range of cyclohexene concentration from 0.1 to 0.5 M. The results of epoxidation rate with different concentrations of cyclohexene are listed in Table 4. It indicated that increasing concentration of cyclohexene accelerated the epoxidation rate from 2.30×10^{-3} to 2.83×10^{-3} mol L^{-1} min^{-1}.

Entry	Concentration of cyclohexene (M)	$R\times10^3$ (mol L^{-1} min^{-1})
1	0.1	2.30
2	0.2	2.42
3	0.3	2.60
4	0.4	2.76
5	0.5	2.83

[a] Temperature: 308 K; Concentration of isobutyraldehyde: 2.0 M; Concentration of Mn(TPP)Cl, 0.4×10^{-6} M; O_2 bubbling.

Table 4. Effect of cyclohexene concentration on the aerobic epoxidation rate in the presence of isobutyraldehyde [a]

A plot of epoxidation rate against the concentration of cyclohexene yields a straight line, as shown in Figure 9.

As seen in Figure 9, linear correlation between epoxidation rate and [cyclohexene] was evident using Mn(TPP)Cl as catalyst, in which correlation coefficient was 0.992. Consequently, the catalytic reaction also exhibited first-order dependence in relation to the concentration of cyclohexene. Thus, the experimental results are in good agreement with the theoretical analysis as shown in equation 20.

The results indicated that increasing the concentration of catalyst results in an increase of the initial reaction rate. Increasing the concentration of catalyst from 0.8×10^{-4} to 4.0×10^{-4} M increases the epoxidation rate from 1.98×10^{-3} to 4.47×10^{-3} mol L^{-1} min^{-1} as shown in Table 5.

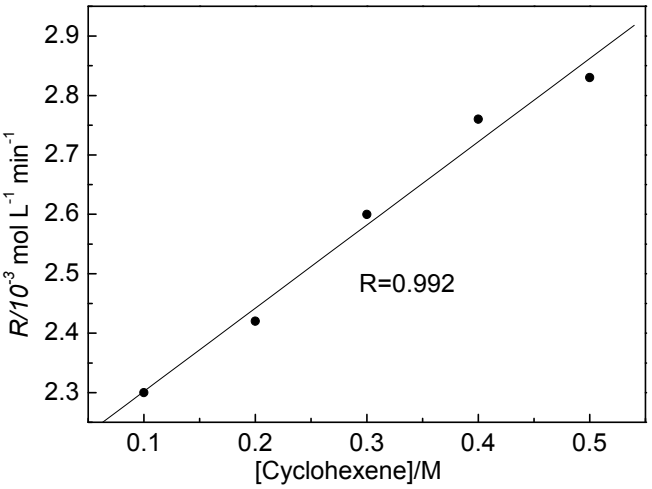


Fig. 9. Effect of cyclohexene concentration on the epoxidation rate in the presence of isobutyraldehyde and molecular oxygen: concentration of isobutyraldehyde, 2.0 M; concentration of Mn(TPP)Cl, 0.4×10^{-6} M; O_2 bubbling; room temperature.

Entry	[Mn(TPP)Cl], M	$[Mn(TPP)Cl]^{0.5}\times10^{2}$, $M^{0.5}$	$R\times10^{3}$, mol L^{-1} min^{-1}
1	0.8×10^{-4}	0.89	1.98
2	1.6×10^{-4}	1.26	2.94
3	2.4×10^{-4}	1.55	3.61
4	3.2×10^{-4}	1.79	4.01
5	4.0×10^{-4}	2.00	4.47

[a] Temperature: 308 K; Concentration of isobutyraldehyde: 2.0 M; Concentration of cyclohexene: 0.4 M; O_2 bubbling.

Table 5. Effect of concentration of Mn(TPP)Cl catalyst on the aerobic epoxidation rate in the presence of isobutyraldehyde [a]

Plot of the initial rate of epoxidized cyclohexene versus the concentration of $[Mn(TPP)Cl]^{0.5}$ yields a straight line as shown in Figure 10.

As can be observed in Figure 10, linear correlation between epoxidation rate and $[Mn(TPP)Cl]^{0.5}$ was evident, in which correlation coefficient was 0.997. The line can be expressed by:

$$Re=0.081\times 10^{-3} + 2.217 \times [Mn(TPP)Cl]^{0.5}$$

The results indicated that increasing of isobutyraldehyde concentration from 0.8 to 2.4 M resulted in an increase of the initial rate of epoxidized cyclohexene from 1.11×10^{-3} to 3.41×10^{-3} mol L^{-1} min^{-1} as shown in Table 6.

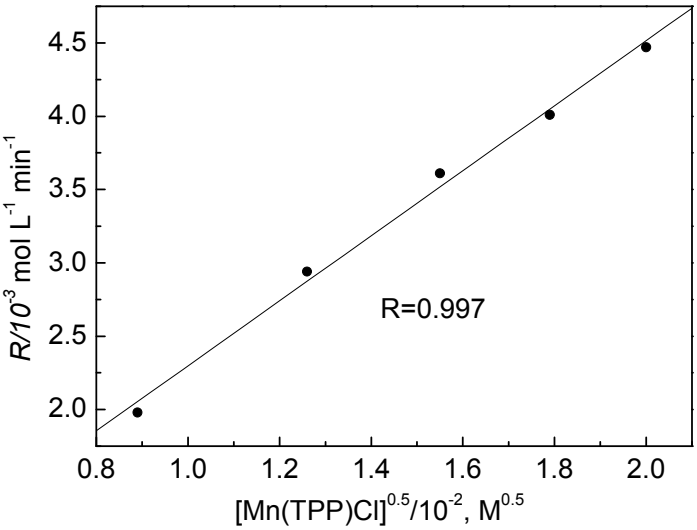


Fig. 10. Effect of the concentration of Mn(TPP)Cl catalyst on the epoxidation rate in the presence of isobutyraldehyde and molecular oxygen: concentration of isobutyraldehyde, 2.0M; concentration of cyclohexene, 0.4 M; O_2 bubbling; room temperature.

Entry	[aldehyde], M	[aldehyde]$^{1.5}$, M$^{1.5}$	[aldehyde]$^{0.5}$, M$^{0.5}$	R×10^3, mol L^{-1} min^{-1}
1	0.80	0.72	0.89	1.11
2	1.20	1.31	1.10	1.64
3	1.60	2.02	1.26	2.16
4	2.00	2.83	1.41	2.75
5	2.40	3.72	1.55	3.41

[a] Temperature: 308 K; Concentration of cyclohexene: 0.4 M; Concentration of Mn(TPP)Cl, 0.4×10^{-6} M; O_2 bubbling.

Table 6. Effect of isobutyraldehyde concentration on the aerobic epoxidation rate in the presence of molecular oxygen [a]

The plot of the epoxidation reaction rate versus [isobutyraldehyde]$^{0.5}$ is shown in Figure 11. The graph shown in Figure 11 illustrated clearly that the reaction rate versus [isobutyraldehyde]$^{0.5}$ yielded a cube curve, which was consistent with the analysis as shown in equation 20.

As shown above, the experimental results correlate the theoretical analysis well. The good agreement for kinetics could further explain that the metalloporphyrin-catalyzed epoxidaiton of cyclohexene is *via* a high-valent metal intermediate.

Bismetalloporphyrin dimers are composed of two covalently bound mono-metalloporphyrins molecules. Investigations over the past decades indicated that μ-oxo-bisiron porphyrins (***Scheme 5***) are inactive or have low activity for hydroxylation of alkanes. Recently, high catalytic activities of μ-oxo dimeric metalloporphyrins for the oxidation of cyclohexane, ethylbenzene and toluene have been reported.[88-90]

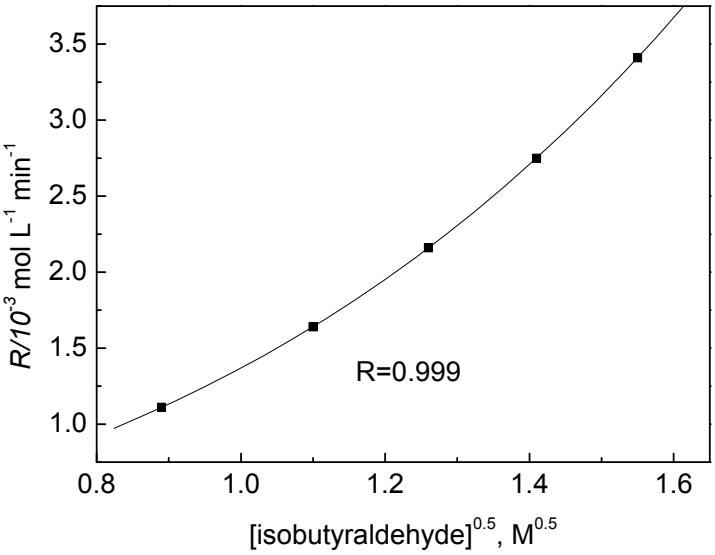
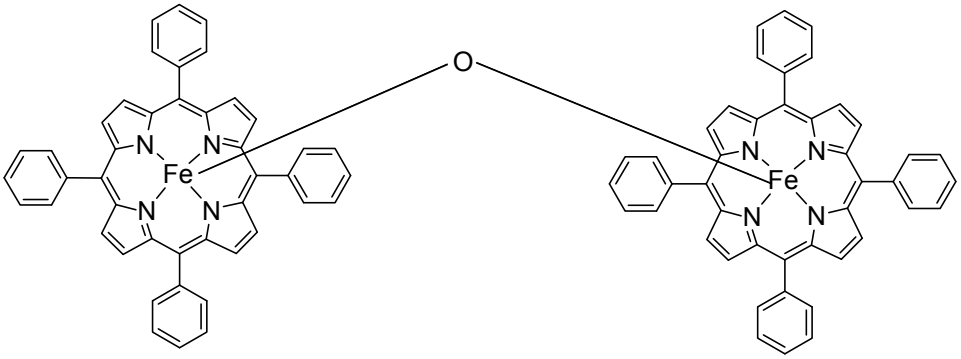


Fig. 11. Effect of isobutyraldehyde concentration on the epoxidation rate in the presence of molecular oxygen: concentration of cyclohexene, 0.4 M; concentration of Mn(TPP)Cl, 0.4×10^{-6} M; O_2 bubbling; room temperature.



Scheme 5. Structure of μ-oxo-bisiron(III) porphyrin

With cyclohexene as model compound, the effects of reaction conditions on the epoxidation in the presence of $(Fe^{III}TPP)_2O$ with molecular oxygen as oxidant have been investigated. Table 7 summarizes the main results obtained under different reaction conditions. It could be found from entry 1 of Table 7 that only 21% cyclohexene could be converted in the absence of catalyst, indicating that the $(Fe^{III}TPP)_2O$ catalyst is crucial for the epoxidation. As depicted in Table 7, it was observed that the yield is considerably enhanced when the catalyst was used. The conversion of cyclohexene could reach up to 96% even the amount of catalyst was only 0.01 ppm (entry 2). The optimal amount of catalyst for the epoxidation was 0.05ppm (entry 3). On the contrary, attempts for enhancing the yield by increasing the

amount of catalyst were unsuccessful. The yield decreased with the increase of catalyst amount (entries 4-6). This is the typical characteristics of metalloporphyrins-catalyzed oxidation, which caused by the shielding effect due to the more catalyst intermediates by increasing amount of metalloporphyrins.

Entry	Amount of catalyst/ppm	Conv.%	Yield/%
1	0	21	21
2	0.01	96	93
3	0.05	>99	96
4	0.1	90	88
5	1.0	81	80
6	10.0	84	81
7[b]	0.05	0	0
8[c]	0.05	92	90
9[d]	0.05	>99	96
10[e]	0.1	85	82

[a] Substrate (2 mmol), isobutylaldehyde (0.011 mol), acetonitrile (6 mL), O_2 bubbling, 4h, rt
[b] No isobutylaldehyde
[c] Substrate /isobutylaldehyde =1: 5
[d] Substrate /isobutylaldehyde =1: 6
[e] $Fe^{III}TPPCl$ as catalyst

Table 7. Aerobic epoxidation of cyclohexene catalyzed by $(Fe^{III}TPP)_2O$ in the presence of isobutyraldehyde[a]

The effects of isobutyraldehyde on the reaction were also investigated. As shown in Table 7, the reaction could not take place in the absence of isobutyraldehyde (entry 7), strongly implying that $(Fe^{III}TPP)_2O$ could not activate molecular oxygen without aldehyde as an oxygen acceptor under ambient conditions. The epoxidation with various molar ratio of substrate to isobutyraldehyde were examined. When the substrate/isobutyraldehyde molar ratio reached 1:5, 92% cyclohexene could be converted (entry 8). Increasing molar ratio gave higher conversion (entry 9). However, no significant difference was observed when the substrate/isobutyraldehyde molar ratio exceeds 1:5.5.

Compared with the aerobic epoxidation catalyzed by mono-metalloporphyrin, ($Fe^{III}TPPCl$, entry 10), it is clear that μ-oxo dimeric iron(III) porphyrin exhibited higher catalytic performance for the aerobic epoxidation of cyclohexene, probably because $(Fe^{III}TPP)_2O$ has superior stability for epoxidation than $Fe^{III}TPPCl$.

Solvent played an important role for the epoxidation by using μ-oxo-bisiron(III) porphyrin as the catalyst (Table 8).

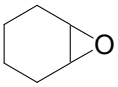
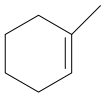
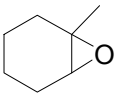
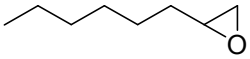
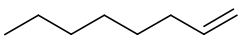
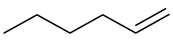
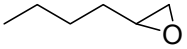
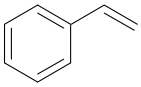
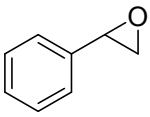
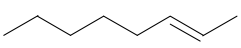
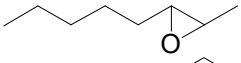
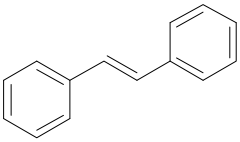
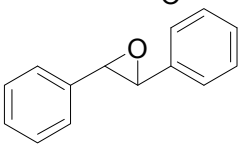
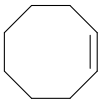
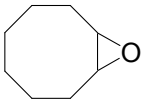
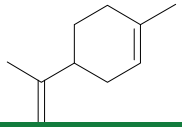
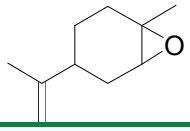
It has been observed that solvent played an important role for the oxidation reaction. Polar solvents e.g. acetonitrile and benzotrifluoride seemed to be more favorable for the epoxidation of cyclohexene. Dichloromethane was not suitable for this catalytic epoxidation, although it was commonly used in metalloporphyrins-catalyzed epoxidation systems. [91-93] It may be due to the instability of $(Fe^{III}TPP)_2O$ in dichloromethane, which could be partly converted to monometalloporphyrins.

Most olefins could be smoothly converted to corresponding epoxides with high conversion rate and excellent selectivity in the μ-oxo-bisiron(III) porphyrin catalyzed system (Table 9). It seems that the efficiency of the epoxidation in this catalytic system is not closely related

Entry	Solvent	Conv.%	Yield/%	Selectivity/%
1	acetonitrile	>99	96	96
2	benzotrifluoride	73	71	97
3	methanol	66	64	97
4	dichloromethane	60	57	95
5	toluene	61	59	96

[a] Substrate (2 mmol), substrate /isobutylaldehyde =1:5.5 (molar ratio), $(Fe^{III}TPP)_2O$ (0.05 ppm), acetonitrile (6mL), O_2 bubbling, 4h, rt

Table 8. Effect of solvent on the aerobic epoxidation of cyclohexene catalyzed by $(Fe^{III}TPP)_2O$[a]

Entry	Substrate	Product	Reaction Time/h	Conv./%	Yield/%
1			4	>99	96
2			5	>99	98
3			7	42	41
4[b]			7	73	72
5			7	36	34
6[b]			7	76	73
7			7	23	13
8[b]			7	70	64
9			4	>99	98
10			8	96	94
11			4	93	92
12			6	96	72

[a] Substrate (2 mmol), isobutylaldehyde (0.011mol), acetonitrile (6mL), O_2 bubbling, rt
[b] $(Fe^{III}TPP)_2O$ (1.0 ppm)

Table 9. Aerobic epoxidation of various alkenes catalyzed by $(Fe^{III}TPP)_2O$ [a]

with the steric conformation of substrates. For instance, slightly longer reaction time was required for 1-methylcyclohexene than cyclohexene (entries 1-2). However, slow oxidation occurred and an unsatisfactory conversion could be obtained for the simple α-olefins or terminal alkenes such as 1-octene, 1-hexene and styrene (entries 3, 5 and 7). When the amount of catalyst increased to 1.0 ppm, remarkable enhancement for conversion and yield was observed (entries 4, 6 and 8). While for the non-terminal linear olefin e.g. *trans*-2-octene, the catalytic system showed excellent catalytic performance, in which *trans*-2-octene was converted to the corresponding epoxide in 4 hours (entry 9). The catalytic system also seems favorable for the conversion of other cycloolefin *e.g.* cyclooctene, in which the reaction system exhibited highly catalytic performance with 92% yield of cyclooctene epoxide (entry 11).

Another salient feature of the present epoxidation is its high regioselectivity. When (+)-limonene was subjected to the epoxidation, the monoepoxide with the epoxide group on the ring was the main product and its selectivity was 72% (entry 12).

To further investigate the efficiency of the catalytic system, a large scale experiment for the aerobic epoxidation of cyclohexene was carried out. When the amount of $(Fe^{III}TPP)_2O$ catalyst used was 6.0×10^{-9} mmol, cyclohexene oxide could be obtained with the isolated yield of 87%. It should be mentioned that the turnover number of the μ-oxo dimeric porphyrin could reach 1,432,993,256, and its TOF was 2.4×10^{6} min^{-1}. Comparing with mono-metallporphyrins as catalyst, remarkable enhancement of reactivity was obtained for the present olefin epoxidation system, in which the turnover number (TON) of the catalyst has doubled from about 700 million to 1,400 million.

As reported previously, the oxygenation of organic substrates catalyzed by metalloporphyrin complexes plus aldehyde is usually considered to involve a radical and high-valent metal intermediate mechanism.[94-95] 2,6-Di-tert-butyl-4-methylphenol as a radical trap has been used in the epoxidation of cyclohexene, and it was found that the reaction was completely inhibited. Therefore, the aerobic epoxidation should involve radical species.

In order to obtain further information about the role of the high-valent iron porphyrin on the epoxidation, *in situ* UV-vis spectra was used. The catalytic epoxidation in CH_3CN was carried out in a quartz colorimetric cell with dioxygen bubbling. UV-vis spectra were recorded with 5 min intervals. Figure 12 exemplifies the UV-vis results observed for μ-oxo dimeric iron(III) porphyrins during the epoxidation process. The initial spectrum of $(Fe^{III}TPP)_2O$ catalyst with a characteristic of Soret band at 408 nm was shown in Figure 12a. When isobutyraldehyde was added into the mixture, a shift from 408 to 417 nm with loss in intensity was observed, as shown in Figure 12b. Besides, the disappearance of the two Q-band peaks at 570 and 610 nm was found with the addition of isobutyraldehyde. As the reaction continued, a decreasing in the Soret band at 417 nm was recorded. The changes of UV-vis spectra are indicative of the existence of an active species expected as the high-valent iron porphyrin.[96-98]

It is usually considered that μ-oxo dimeric metalloporphyrins could easily form monometalloporphyrins during the catalytic process. In fact, whether the dinuclear intermediate or the mononuclear intermediate is the active species remain controversial for the oxygenation of hydrocarbons catalyzed by μ-oxo dimeric metalloporphyrins. The possible mononuclear metalloporphyrins existed in the catalytic system are FeTPPCl or FeTPPOH. Attempts to obtain some useful information from UV-vis spectrum had been tried.

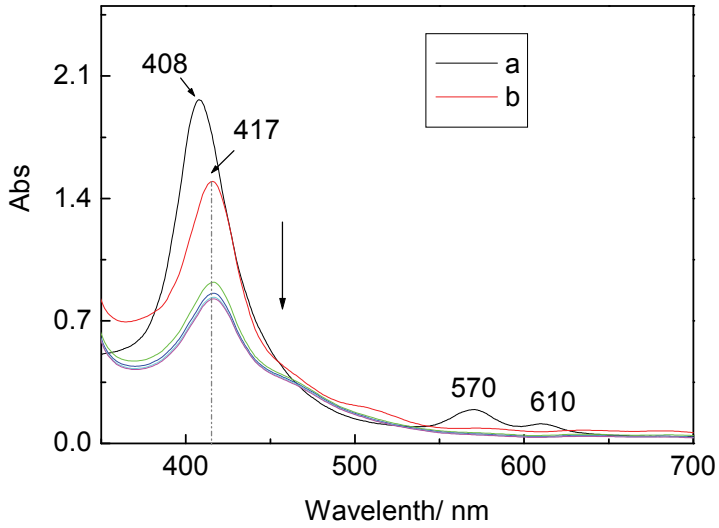


Fig. 12. *In situ* UV-vis spectra of cyclohexene epoxidation of catalyzed by $(Fe^{III}TPP)_2O$ in the presence of molecular oxygen and isobutyraldehyde (time scan with 5 min intervals) , cyclohexene (1mmol), acetonitrile (6mL), catalyst (1×10^{-8} mol/L), isobutyraldehyde (10mmol), rt, (a) $(Fe^{III}TPP)_2O$, (b) initial point of reaction in the presence of isobutyraldehyde

From the UV-vis spectra, FeTPPOH as the mononuclear intermediate in the process is impossible. The active intermediate of FeTPPOH would form a new peak at 461 nm, while no such peak was found from the *in situ* UV-vis spectra as shown in Figure 12. Figure 13a shows the UV-vis spectra of $(Fe^{III}TPP)_2O$ with isobutyraldehyde and cyclohexene after reacting for 20 min. Similar UV-vis curves could be obtained for FeTPPCl catalyst as shown in Figure 13b. If the high-valent intermediate was mononuclear iron porphyrin (FeTPPCl), the Soret peak at 416 nm would disappear as the reported previously. However, a certain degree loss of intensity for the Soret peak at 416 nm could be observed for the present system. As shown in Figure 13, the intensity of Soret peak at 416 remains unchanged after 20 min. The above results indicate that both the dinuclear and the mononuclear high-valent intermediate exist in the catalytic system. Probably two kinds of oxo-iron intermediates, that is $O={}^{V}Fe\text{-}O\text{-}Fe^{V}=O$ and $Fe^{V}=O$ were formed by series of free radical processes. Formation of epoxide is assumed by the reaction of oxo-iron intermediates with olefins.

In the biomimetic catalytic oxidation of olefins using metalloporphyrins, catalysts have been fixed on various supports in order to suppress the dimerization of oxo intermediates or inactivation due to the oxidation of the porphyrin ring to inhibit this reaction. However, in the oxidation using immobilized catalysts, the activity decreases due to suppression of the degree of freedom of the complexes or diffusion of reactants onto the catalytic sites. Aiming to develop a highly selective catalyst, composite materials were synthesized, in which porphyrin complexes with various substituents were intercalated between clay layers to maintain a space on the axis of the central metal of porphyrin as a reaction field.[99] Specifically, cationic porphyrinato cobalt complexes with the substituents of the quaternary ammonium salt of heterocyclic amine (***Scheme 6***) were synthesized, and these complexes were fixed between the montmorillonite layers. By using these pillared clay catalysts, the

epoxidation of cyclohexene with molecular oxygen in the presence of a reducing agent were examined for high activity and selectivity.

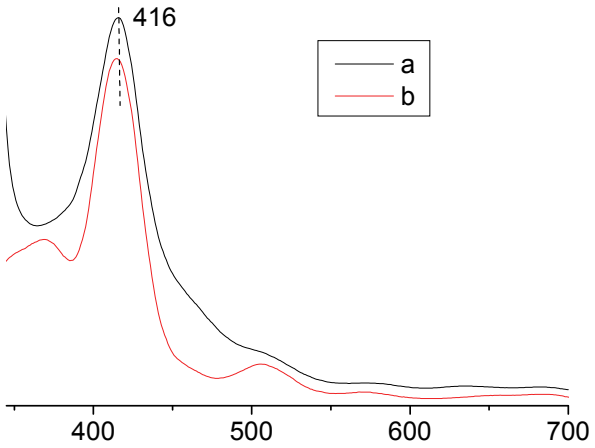
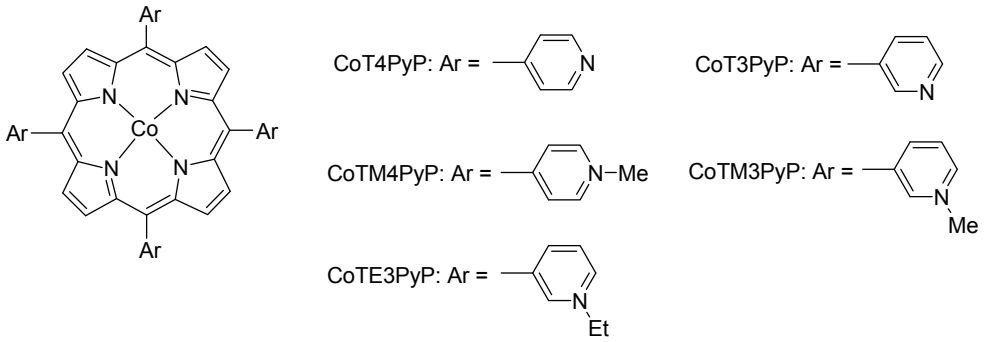


Fig. 13. The UV-vis spectra of $(Fe^{III}TPP)_2O$ with isobutyraldehyde and cyclohexene after 20 min of reaction time (a), FeTPPCl (b)



Scheme 6. Structure of cobalt porphyrin complexes

Figure 14 shows the relationship between the yield of epoxide and reaction time in the oxygen oxidation of cyclohexene in the presence of isobutyraldehyde using the CoTE3PyP/MT catalyst, in comparison with the cases of the reaction in a homogeneous system using the CoTE3PyP complex and the reaction of pure montmorillonite.

Although the homogeneous complex catalyst contained about 20 times as much CoTE3PyP as the interlayer-fixed catalyst, its activity for the oxidation was very low. Although a slight quantity of epoxide was generated in the presence of pure MT or T4PyP/MT free of a metal, the reaction stopped in about 5 h; the yield of 1,2-epoxycyclohexane was quite similar to that in the oxidation without catalyst. Therefore, it is suggested that peroxides contained in the substrate or reducing agent were involved in the reaction, and that neither MT nor T4PyP/MT was active for the oxygen oxidation. In the reaction using CoTE3PyP/MT as a catalyst, there

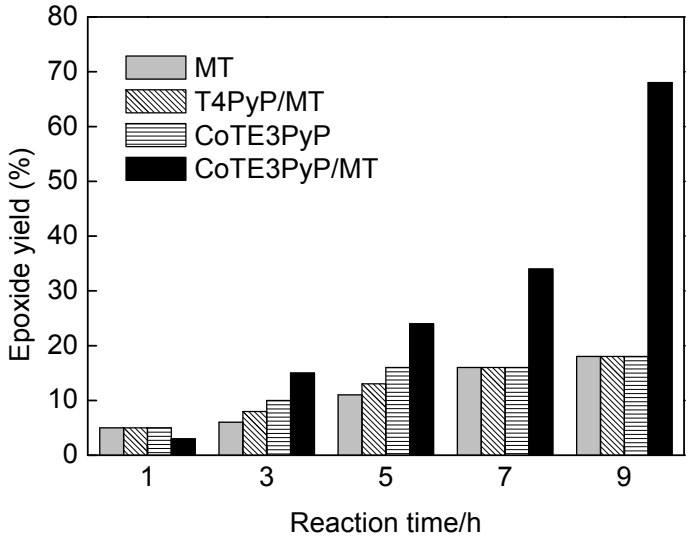


Fig. 14. Relationship between the yield of 1,2-epoxycyclohexane and reaction time. Conditions: cat., 20 mg (in case of T4PyP/MT and CoTE3PyP/MT, [porphyrin]: 6.4×10^{-5} mol/g); cyclohexene, 0.04 mol; isobutyraldehyde, 0.06 mol; acetonitrile, 10 mL.

was an induction period in the initial stage of the reaction and the yield of epoxide remarkably increased after 5 h. This result is attributed to the interlayer expansion by the swelling of montmorillonite to enhance the degree of freedom of catalytic sites and diffusion of reactants.

The results of the oxidation of cyclohexene by using various interlayer-fixed porphyrinato cobalt complexes, that is, the catalysts having the different clay basal spacing are shown in **Table 10.**

CoTE3PyP/MT, which has the largest interlayer spacing, gave the highest epoxide yield. Moreover, the oxygen oxidation of cyclohexene was carried out using CoTE3PyP/MT catalysts containing intercalated CoTE3PyP in the range of $(1.6\text{-}6.4)\times10^{-5}$ mol/g. The epoxide yield improved with the quantity of CoTE3PyP and by using CoTE3PyP/MT catalyst with a content of 6.4×10^{-5} mol/g the epoxide yield reached 65.9% in a reaction time of 9 h. On the other hand, the use of CoTM4PyP/MT and CoTM3PyP/MT, of which the interlayer spacing are 0.42 and 0.54 nm, respectively, as catalyst gave the low yield of epoxide. Their space on the central metal for the oxidation to occur must be restricted because of the thickness of the porphyrin molecule. Thus, it is difficult for cylcohexene of which the size is about 0.45 nm to pull in this space. By contrast, CoTE3PyP/MT having the interlayer spacing of 0.68 nm seems to provide sufficient space so that cyclohexene approaches the central metal of porphyrin. These results indicate that the formation of a reaction field can be controlled by a kind of meso-substitutent of the porphyrinato cobalt complex intercalated between montmorillonite layers and the oxidation can proceed selectively in the molecule size of the substrate by means of this reaction field.

Catalyst	Time (h)	Yield (%)		Turnover number
		1,2-Epoxycyclohexane	cyclohexanone	
CoTM4PyP/MT	9	17.6	2.6	25250
	24	36.6	7.7	55375
CoTM3PyP/MT	9	23.8	2.8	33250
	24	31.1	5.1	45250
CoTE3PyP/MT	9	41.5	4.9	58000
	24	56.1	9.8	82375
CoTE3PyP/MT[b]	9	48.8	7.3	23375
	24	56.1	12.2	28458
CoTE3PyP/MT[c]	9	65.9	9.8	23656
	24	61.0	12.2	22875
CoTE3PyP	9	31.7	4.9	580
	24	34.1	4.9	618
MT	9	17.1	2.4	-
	24	22.0	4.9	-

[a] Cat. 20 mg([porphyrin]: 1.6×10^{-5} mol/g); cyclohexene 0.04 mol; isobutyraldehyde 0.06 mol; acetonitrile 10 mL.
[b] Cat. 20 mg([porphyrin]: 4.8×10^{-5} mol/g)
[c] Cat. 20 mg([porphyrin]: 6.4×10^{-5} mol/g)

Table 10. Oxidation of cyclohexene by using various interlay-fixed porphyirnato cobalt complexes as catalyst[a]

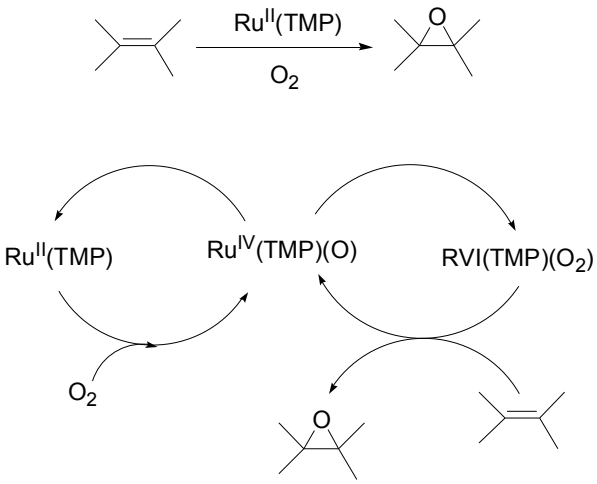
4. Epoxidation without reductant

The main goal in catalytic olefin epoxidations is to use both oxygen atoms of molecular oxygen to produce selectively epoxides without using reducing agents as co-factors. Such a reaction is particularly important for the large scale production of various epoxides. In the field of metalloporphyrin-catalyzed olefins epoxidation with molecular oxygen, the breakthrough was reported by Groves group. [100] $Ru^{VI}(TMP)(O)_2$ catalyzes the aerobic epoxidation of olefins at room temperature and normal pressure. Measurement of oxygen uptake during the oxidation of cyclooctene indicated that 2 mol of epoxide were produced per mole of molecular oxygen consumed. The proposed mechanism is shown in ***Scheme 7***. The active oxidant $Ru^{VI}(TMP)(O)_2$ reacts with an olefin to afford the epoxide and $Ru^{IV}(TMP)(O)$, and the disproportionation of the latter generates $Ru^{II}(TMP)$ and the active oxidant $Ru^{VI}(TMP)(O)_2$. The $Ru^{II}(TMP)$ re-enters the catalytic cycle after being oxidized by dioxygen to $Ru^{IV}(TMP)(O)$.

Since then, few examples on the metalloporphyrins-catalyzed epoxidation by dioxygen in the absence of a co-reductant could be found. Polymeric sheet porphyrin: polymeric *meso*-tetra-(1,5- naphthalene bisulfonyloxo) phenyl cobalt porphyrins (PTNBSOPPCo) showed good activity in the oxidation of styrene with dioxygen.[101]

Simple metalloporphyirns were employed as the catalyst for the aerobic oxidation of α-pinene in the absence of co-catalyst and solvent. Among various metalloporphyrins, MnTPPCl presented the best selectivity regarding the epoxide. When the reaction was carried out under 80°C for 5 h, the conversion of α-pinene was 23% and the selectivity for

the product of C=C bond was 60%. With increasing the electron- donating abilities of the peripheral substituents, the selectivity regarding the oxidation of C=C bond decreased. The mechanism involves a high-valence metal-oxygen positive radical, which plays an important role in the epoxidation of alkenes.[102]



Scheme 7. Ru(TMP)-catalyzed olefins epoxidation with dioxygen

5. Conclusion

From this chapter, it is convincing that metalloporphyrins are very versatile oxidation catalysts which can be used in epoxidation of olefins. It clearly demonstrated the impressive progress made in the area of metalloporphyrins-catalyzed aerobic epoxidation of olefins with different reductant, especially using aldehydes as reductant. Attempts have been made to avoid the sacrificial use electrons or reductant in the epoxidation of olefins with molecular oxygen. These methodologies described based on various epoxidation reactions have clearly opened new avenues for major growth in the area of epoxidation using molecular oxygen. The use of molecular oxygen as a source of oxygen atom and the formation of few neutral byproducts clearly make aerobic epoxidation a highly desirable, economically viable, and environmentally acceptable reaction.

Biomimetic catalysis of metalloporphyrins is now a meeting point for chemistry, chemical, catalysis and biology. Metalloporphyrins catalyzed aerobic epoxidation of olefins becoming an important and highly rewarding protocol for important feedstock for petrochemical and fine chemical industries. The aerobic epoxidation process of biomimetic catalysis will be performed at the industrial scale in the future due to the high efficiency and selectivity.

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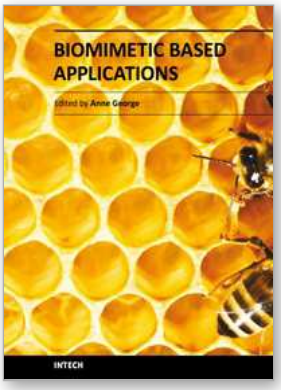
7. References

[1] Backvall, J. E. *Modern Oxidation Methods*; Wiley-VCH: Weinheim, 2004.
[2] Labinger, J. A.; Bercaw, J. E. *Nature* 2002, *417*, 507-514.
[3] Olah, G. A.; Molnar, A. *Hydrocarbon Chemistry*; John Wiley & Sons Inc.: Hoboken, 2003.
[4] Parshall, G. H. *Homogeneous Catalysis: The Application of Catalysis by Soluble Transition Metal Complexes*; Wiley: New York, 1980.
[5] Punniyamurthy, T.; Velusamy, S.; Iqbal, J. *Chem. Rev.* 2005, *105*, 2329-2363.
[6] Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidation of Organic Compounds*; Academic Press: New York, 1981.
[7] Burke, A. J. *Coordin. Chem. Rev.* 2008, *252*, 170-175.
[8] Xia, Q. H.; Ge, H. Q.; Ye, C. P.; Liu, Z. M.; Su, K. X. *Chem. Rev.* 2005, *105*, 1603-1662.
[9] Chatterjee, D. *Coordin .Chem. Rev.* 2008, *252*, 176-198.
[10] Wong, O. A.; Shi, Y. *Chem. Rev.* 2008, *108*, 3958-3987.
[11] Lane, B. S.; Burgess, K. *Chem. Rev.* 2003, *103*, 2457-2473.
[12] Luts, T.; Frank, R.; Suprun, W.; Fritzsche, S.; Hey-Hawkins, E.; Papp, H. *J. Mol. Catal. A* 2007, *273*, 250-258.
[13] Rubajlo, V. L.; Maslov, S. A.; Zaikov, G. E. *Liquid-Phase Oxidation of Unsaturated Compounds*; Nova Science Publishers, Inc.: Hauppauge, 1993.
[14] Castaman, S. T.; Nakagaki, S.; Ribeiro, R. R.; Ciuffi, K. J.; Drechsel, S. M. *J. Mol. Catal. A* 2009, *300*, 89-97.
[15] Serafimidou, A.; Stamatis, A.; Louloudi, M. *Catal. Commun.* 2008, *9*, 35-39.
[16] Loew, G. H.; Harris, D. L. *Chem. Rev.* 2000, *100*, 407-420.
[17] Sono, M.; Roach, M. P.; Coulter, E. D.; Dawson, J. H. *Chem. Rev.* 1996, *96*, 2841-2888.
[18] Gunsalus, I. C.; Pederson, T. C.; Sligar, S. G. *Annu. Rev. Biochem.* 1975, *44*, 377.
[19] Ortiz de Montellano, P. R.; De Voss, J. J. *Nat. Prod. Rep.* 2002, *19*, 477-493.
[20] Ortiz de Montellano, P. R. *Cytochrome P450: structure, mechanism and biochemistry*; Plenum: New York, 1996.
[21] Hayaishi, O. *Molecular mechanism of oxygen activation*; Academic Press: New York, 1974.
[22] Meunier, B.; Bernadou, J. *Top .Catal.* 2002, *21*, 47-54.
[23] Omura, T.; Ishimura, Y.; Fujii-Kuriyama, Y. *Cytochrome P450*; Kodansha: Tokyo, 1993.
[24] Filatov, M.; Reckien, W.; Peyerimhoff, S. D.; Shaik, S. *J. Phys. Chem. A* 2000, *104*, 12014-12020.
[25] Tshuva, E. Y.; Lippard, S. J. *Chem. Rev.* 2004, *104*, 987-1012.
[26] Meunier, B.; de Visser, S. P.; Shaik, S. *Chem. Rev.* 2004, *104*, 3947-3980.
[27] Costas, M.; Mehn, M. P.; Jensen, M. P.; Que, L., Jr. *Chem. Rev.* 2004, *104*, 939-986.
[28] Meunier, B. *Biomimetic Oxidations Mediated by Metal Complexes*; Imperial College Press: London, 2000.
[29] Meunier, B. *Chem. Rev.* 1992, *92*, 1411-1456.
[30] Meunier, B. *Metalloporphyrin Catalyzed Oxidation*; Kluwer Academic Publisher: 1994.
[31] Reichhart, D. W.; Hehn, A.; Didieriean, L. *Trends Plant Sci.* 2000, *5*, 116-123.
[32] Bernadou, J.; Meunier, B. *Adv. Synth. Catal.* 2004, *346*, 171-184.
[33] Woggon, W. D. *Acc.Chem. Res.* 2005, *38*, 127-136.
[34] Chen, H. Y.; Ji, H. B.; Zhou, X. T.; Xu, J. C.; Wang, L. F. *Catal. Commun.* 2009, *10*, 828-832.
[35] Zhou, X. T.; Ji, H. B.; Yuan, Q. L. *J. Porphyr. Phthalocya.* 2008, *12*, 94-100.
[36] Zhou, X. T.; Ji, H. B.; Yuan, Q. L.; Xu, J. C.; Pei, L. X.; Wang, L. F. *Chin. J. Chem.* 2008, *26*, 1114-1118.
[37] Ji, H. B.; Yuan, Q. L.; Zhou, X. T.; Pei, L. X.; Wang, L. F. *Bioorg. Med. Chem. Lett.* 2007, *17*, 6364-6368.

[38] Zhou, X. T.; Ji, H. B.; Cheng, Z.; Xu, J. C.; Pei, L. X.; Wang, L. F. *Bioorg. Med. Chem. Lett.* 2007, *17*, 4650-4653.
[39] Zhou, X. T.; Yuan, Q. L.; Ji, H. B. *Tetrahedron Lett.* 2010, *51*, 613-617.
[40] Turner, M.; Vaughan, O. P. H.; Kyriakou, G.; Watson, D. J.; Scherer, L. J.; Davidson, G. J. E.; Sanders, J. K. M.; Lambert, R. M. *J. Am. Chem. Soc.* 2009, *131*, 1910-1914.
[41] Alkordi, M. H.; Liu, Y. L.; Larsen, R. W.; Eubank, J. F.; Eddaoudi, M. *J. Am. Chem. Soc.* 2008, *130*, 12639-12641.
[42] Mirkhani, V.; Moghadam, M.; Tangestaninejad, S.; Kargar, H. *Appl. Catal. A* 2006, *303*, 221-229.
[43] Mansuy, D. *Coord. Chem. Rev.* 1993, *125*, 129-141.
[44] Ji H.B.; She Y.B. *Green Oxidation and Reduction*; China Petrochemical Press : Beijing, 2005.
[45] Zhou, X. T.; Ji, H. B.; Pei, L. X.; She, Y. B.; Xu, J. C.; Wang, L. F. *Chin. J. Org. Chem.* 2007, *27*, 1039-1049.
[46] Groves, J. T.; Nemo, T. E. *J. Am. Chem. Soc.* 1983, *105*, 5786-5791.
[47] Campestrini, S.; Tonellato, U. *J. Mol. Catal. A* 2001, *171*, 37-42.
[48] Nam, W.; Oh, S.-Y.; Sun, Y. J.; Kim, J.; Kim, W.-K.; Woo, S. K.; Shin, W. *J. Org. Chem.* 2003, *68*, 7903-7906.
[49] Stephenson, N. A.; Bell, A. T. *J. Mol. Catal. A* 2007, *275*, 54-62.
[50] Rahiman, A. K.; Bharathi, K. S.; Sreedaran, S.; Narayanan, V. *Catal. Lett.* 2009, *127*, 175-182.
[51] Castaman, S. T.; Nakagaki, S.; Ribeiro, R. R.; Ciuffi, K. J.; Drechsel, S. M. *J. Mol. Catal. A* 2009, *300*, 89-97.
[52] Li, Z.; Xia, C. G.; Ji, M. *Appl. Catal. A* 2003, *252*, 17-21.
[53] Haber, J.; Iwanejko, R.; Poltowicz, J.; Battioni, P.; Mansuy, D. *J. Mol. Catal. A* 2000, *152*, 111-115.
[54] Haber, J.; Iwanejko, R.; Poltowicz, J.; Battioni, P.; Mansuy, D. *J. Mol. Catal. A* 2000, *152*, 117-120.
[55] Mohajer, D.; Rezaeifard, A. *Tetrahedron Lett.* 2002, *43*, 1881-1884.
[56] Mohajer, D.; Karimipour, G.; Bagherzadeh, M. *New J. Chem.* 2004, *28*, 740-747.
[57] Tabushi, I.; Morimitsu, K. *Tetrahedron Lett.* 1986, *27*, 51-54.
[58] Tabushi, I.; Yazaki, A. *J. Am. Chem. Soc.* 1981, *103*, 7371-7373.
[59] Tabushi, I.; Kodera, M.; Yokoyama, M. *J. Am. Chem. Soc.* 1985, *107*, 4466-4473.
[60] Bedioui, F.; Devynck, J.; Bied-Charreton, C. *J. Mol. Catal. A* 1996, *113*, 3-11.
[61] Leduc, P.; Battioni, P.; Bartoli, J. F.; Mansuy, D. *Tetrahedron Lett.* 1988, *29*, 205-208.
[62] Tsuda, Y.; Takahashi, K.; Yamaguchi, T.; Matsui, S.; Komura, T. *J. Mol. Catal. A* 1998, *130*, 285-295.
[63] Tsuda, Y.; Takahashi, K.; Yamaguchi, T.; Matsui, S.; Komura, T.; Nishiguchi, I. *J. Mol. Catal. A* 1999, *138*, 145-153.
[64] Mukaiyama, T.; Yamada, T.; Nagata, T.; Imagawa, K. *Chem. Lett.* 1993, 327-330.
[65] Yamada, T.; Takai, T.; Rhode, O.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* 1991, *64*, 2109-2117.
[66] Nagata, T.; Imagawa, K.; Yamada, T.; Mukaiyama, T. *Chem. Lett.* 1994, 1259-1262.
[67] Qi, J. Y.; Li, Y. M.; Zhou, Z. Y.; Che, C. M.; Yeung, C. H.; Chan, A. S. C. *Adv. Synth. Catal.* 2005, *347*, 45-49.
[68] Ravikumar, K. S.; Barbier, F.; Begue, J. P.; Delpon, D. B. *Tetrahedron* 1998, *54*, 7457-7464.
[69] Raja, R.; Sankar, G.; Thomas, J. M. *Chem.Commun.* 2009, *9*, 829-830.
[70] Ellis, S.; Kozhevnikov, I. V. *J. Mol. Catal. A* 2002, *187*, 227-235.
[71] Mandal, A. K.; Iqbal, J. *Tetrahedron* 1997, *53*, 7641-7648.

[72] Zhou, X. T.; Ji, H. B.; Xu, H. C.; Pei, L. X.; Wang, L. F.; Yao, X. D. *Tetrahedron Lett.* 2007, *48*, 2691-2695.
[73] Qi, J. Y.; Qiu, L. Q.; Lam, K. H.; Yip, C. W.; Zhou, Z. Y.; Chan, A. S. C. *Chem.Commun.* 2003, 1058-1059.
[74] Nam, W.; Baek, S. J.; Lee, K. A.; Ahn, B. T.; Muller, J. G.; Burrows, C. J.; Valentine, J. S. *Inorg. Chem.* 1996, *35*, 6632-6633.
[75] Ravikumar, K. S.; Barbier, F.; Begue, J. P.; Delpon, D. B. *Tetrahedron* 1998, *54*, 7457-7464.
[76] Nam, W.; Kim, H. J.; Kim, S. H.; Ho, R. Y. N.; Valentine, J. S. *Inorg. Chem.* 1996, *35*, 1045-1049.
[77] Zhou, X. T.; Ji, H. B. *Chem. Eng. J.* 2010, *156*, 411-417.
[78] Kaneda, K.; Haruna, S.; Imanka, T.; Hamamoto, M.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* 1992, *33*, 6827-6830.
[79] Harvey, J. D.; Ziegler, C. J.; Telser, J.; Ozarowski, A.; Krzystek, J. *Inorg. Chem.* 2005, *44*, 4451-4453.
[80] Goldberg, D. P.; Telser, J.; Krzystek, J.; Montalban, A. G.; Brunel, L. C.; Barrett, A. G. M.; Hoffman, B. M. *J. Am. Chem. Soc.* 1997, *119*, 8722-8723.
[81] Lansky, D. E.; Mandimutsira, B.; Ramdhanie, B.; Clausen, M.; Penner-Hahn, J.; Zvyagin, S. A.; Telser, J.; Krzystek, J.; Zhan, R.; Ou, Z.; Kadish, K. M.; Zakharov, L.; Rheingold, A. L.; Goldberg, D. P. *Inorg. Chem.* 2005, *44*, 4485-4498.
[82] Caudle, M. T.; Mobley, C. K.; Bafaro, L. M.; Lobrutto, R.; Yee, G. T.; Groy, T. L. *Inorg. Chem.* 2004, *43*, 506-514.
[83] Friedermann, G. R.; Halma, M.; Dias de Freitas Castro, K.; Benedito, F. L.; Doro, F. G.; Drechsel, S. M.; Mangrich, A. S.; Assis, M. D.; Nakagaki, S. *Appl. Catal. A* 2006, *308*, 172-181.
[84] Konishi, S.; Hoshino, M.; Imamura, M. *J. Phys. Chem.* 1982, *86*, 4537-4539.
[85] Nunes, G. S.; Mayer, I.; Toma, H. E.; Araki, K. *J. Catal.* 2005, *236*, 55-61.
[86] Rebelo, S. L. H.; Pereira, M. M.; Simoes, M. M. Q.; Neves, M. G. P. M.; Cavaleiro, J. A. S. *J. Catal.* 2005, *234*, 76-87.
[87] Haber, J.; Mlodnicka, T.; Poltowicz, J. *J. Mol. Catal.* 1989, *54*, 451-461.
[88] Guo, C. C.; Liu, Q.; Wang, X. T.; Hu, H. Y. *Appl. Catal. A* 2005, *282*, 55-59.
[89] Guo, C. C.; Liu, X. Q.; Liu, Y.; Liu, Q.; Chu, M. F.; Zhang, X. B. *J. Mol. Catal. A* 2003, *192*, 289-294.
[90] Guo, C. C. *J. Catal.* 1998, *178*, 182-187.
[91] Reginato, G.; Di Bari, L.; Salvadori, P.; Guilard, R. *Eur. J. Org. Chem.* 2000, 1165-1171.
[92] Zhao, Y. C.; Xiang, Y. Z.; Pu, L.; Yang, M.; Yu, X. Q. *Appl. Catal. A* 2006, *301*, 176-181.
[93] Elemans, J. A. A. W.; Bijsterveld, E. J. A.; Rowan, A. E.; Nolte, R. J. M. *Eur. J. Org. Chem.* 2007, 751-757.
[94] Wentzel, B. B.; Alsters, P. L.; Feiters, M. C.; Nolte, R. J. M. *J. Org. Chem.* 2004, *69*, 3453-3464.
[95] Wentzel, B. B.; Gosling, P. A.; Feiters, M. C.; Nolte, R. J. M. *J. Chem. Soc., Dalton Trans* 1998, 2241-2246.
[96] Song, W. J.; Seo, M. S.; George, S. D.; Ohta, T.; Song, R.; Kang, M. J.; Kitagawa, T.; Solomon, E. I.; Nam, W. *J. Am. Chem. Soc.* 2007, *129*, 1268-1277.
[97] Nam, W.; Lim, M. H.; Moon, S. K.; Kim, C. *J. Am. Chem. Soc.* 2000, *122*, 10805-10809.
[98] Shimazaki, Y.; Nagano, T.; Takesue, H.; Ye, B. H.; Tani, F.; Naruta, Y. *Angew. Chem. Int. Ed.* 2004, *129*, 98-100.
[99] Kameyama, H.; Narumi, F.; Hattori, T.; Kameyama, H. *J. Mol. Catal. A* 2006, *258*, 172-177.
[100] Groves, J. T.; Quinn, R. *Inorg. Chem.* 1984, *23*, 3844-3846.
[101] He, Y. F.; Wang, R. M.; Wang, Y. P.; Xia, C. G. *Eur. Polym. J.* 2002, *38*, 2129-2132.
[102] Guo, C. C.; Yang, W. J.; Mao, Y. L. *J. Mol. Catal. A* 2005, *226*, 279-284.



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The interaction between cells, tissues and biomaterial surfaces are the highlights of the book "Biomimetic Based Applications". In this regard the effect of nanostructures and nanotopographies and their effect on the development of a new generation of biomaterials including advanced multifunctional scaffolds for tissue engineering are discussed. The 2 volumes contain articles that cover a wide spectrum of subject matter such as different aspects of the development of scaffolds and coatings with enhanced performance and bioactivity, including investigations of material surface-cell interactions.

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