Enzymatic-like mediated olefins epoxidation by molecular oxygen under mild conditions

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Abstract—Highly efficient epoxidation of olefins by molecular oxygen with catalytic amount of manganese *meso*-tetraphenylporphyrin (Mn(TPP)) at the ppm level were reported. The catalyst conferred high activity and selectivity for the olefins epoxidation under ambient temperature and atmospheric pressure. The turnover number (TON) of the catalyst could reach up to 700 million, which is comparable to enzyme catalysis.
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1. Introduction

Metalloporphyrins as model catalysts of cytochrome P-450 have been used to mimic various oxidation reactions, for example, hydroxylation of hydrocarbon, epoxidation of olefins under mild conditions.[1] During the past two decades, metalloporphyrins have been widely applied for epoxidation of olefins to give epoxides with high regio-, shape- and stereoselectivity since the leading works of Groves and co-workers.[2] A variety of oxidants, such as PhIO,[3] H_2O_2,[4] MMPP (magnesium monoperoxyphthalate),[5] TBAO (tetrabutylammonium monosulfate),[6] and *n*-Bu₄NIO₄ (tetrabutylammonium periodate),[7] in combination with different metalloporphyrin catalysts have been employed as oxygen atom donors.

The selective aerobic oxidation of hydrocarbons catalyzed by metalloporphyrins is attracting more interests because of its low cost and the environmentally friendly nature of the oxidant.[8] In metalloporphyrin catalyzed homogenous epoxidation of olefins, aldehyde is usually used as a reducing agent in the presence of molecular oxygen for the reductive activation of oxygen. Haber reported a successful aerobic epoxidation of propylene with Mn(TPP)Cl in the presence of propionaldehyde.[9] The TON of the catalyst was about 7 cycles per minute

for the epoxide products. Mandal and Iqbal used 0.125 mmol cobalt(II) porphyrin catalyst in the epoxidation of cyclohexene (5 mmol) with 2-methyl propanal and molecular oxygen, and obtained the cyclohexene epoxide in 16% yields.[10]

In our earlier studies on cyclohexane and nitrotoluene oxidation with dioxygen catalyzed by metalloporphyrins and metallophthalocyanines,[11] high product yields and TONs of catalysts with low dosages have been observed. As a part of our ongoing interest in metalloporphyrins-catalyzed oxidations, the epoxidation of alkenes catalyzed by very small amount of Mn(TPP) has presently been developed. This catalyst proved to be an effective catalyst in epoxidation systems with extremely high turnover number in the presence of molecular oxygen and isobutylaldehyde (Scheme 1), which is comparable to most enzyme catalysis.
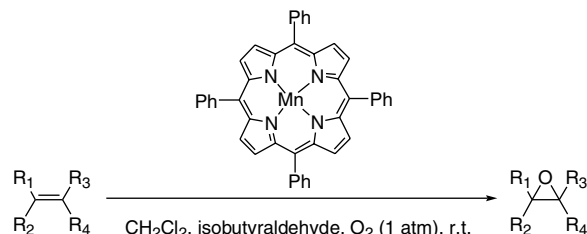
Scheme 1. Manganese *meso*-tetraphenylporphyrin catalyzed epoxidation of olefins.

2. Reaction conditions of cyclohexene epoxidation

Various amounts of Mn(TPP) catalyst,[12,13] that is, 10,000, 100, 10, 1 and 0.1 ppm (based on substrate), were used in the epoxidation of cyclohexene with molecular oxygen as oxidant in the presence of isobutyraldehyde.[14] All the reactions proceeded with high conversion and high selectivity for the desired cyclohexene epoxide by using a substrate-to-isobutraldehyde molar ratio of 1:5 (Table 1).

From Table 1, the simple structural manganese *meso*-tetraphenylporphyrin catalyst presented excellent catalytic performance for cyclohexene epoxidation under mild condition. As the amount of catalyst varied from 10,000 ppm to 0.1 ppm, more than 95% yields of cyclohexene oxide could be obtained within 2–5 h in the presence of molecular oxygen and isobutyraldehyde (entries 1–5). On the contrary, only 15% cyclohexene could be converted without the catalyst, indicating that the manganese *meso*-tetraphenylporphyrin catalyst is crucial for the epoxidation (entry 6). The importance of isobutyraldehyde in the epoxidation was also investigated. In the absence of isobutyraldehyde, neither cyclohexene epoxide nor 2-cyclohexen-1-ol and 2-cyclohexen-1-one could be obtained by conducting the reaction for 4.5 h (entry 7), strongly implying that the manganese *meso*-tetraphenylporphyrin catalyst could not realize the catalytic cycle without aldehyde as an oxygen acceptor. Thus the epoxidation with various molar ratios of substrate to isobutyraldehyde were examined. When the substrate/isobutyraldehyde molar ratio was increased to 1:4, 78% cyclohexene could be converted (entry 8), while higher molar ratio of the substrate to isobutyraldehyde gave higher conversion (entry 9). However, no significant difference was observed when the substrate/isobutyraldehyde molar ratio reached 1:5 for the present system. It should be noted that the catalytic efficiency of the metalloporphyrin was extremely high and the TON of 78,836,263 could be easily obtained (entry 5). Other solvent, such as toluene, could also be an alternative solvent for the epoxidation despite a little decrease of the catalytic activity (entry 10).

3. Epoxidation of various substrates catalyzed by manganese *meso*-tetraphenylporphyrin

Encouraged by the excellent catalytic performance for the cyclohexene epoxidation, various alkenes were subjected to the reaction system at room temperature in the presence of atmospheric oxygen using only 1 ppm of catalyst (Table 2).

As shown in Table 2, all substrates could be smoothly converted to epoxies with high conversion rates and excellent selectivities. It seems that the efficiency of epoxidation in this catalytic system is very dependent on the steric structure of substrates. For example, the conversion of cyclohexene was 97% (entry 1), other functional groups on the C=C bond, for example, 1-methylcyclohexene and 1-phenylcyclohexene, lowered the catalytic activities giving 93% and 83% conversion, respectively (entries 2–3). 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).

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

Despite the high efficiency of the catalyst system, 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 only product and its yield was 91% (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 10,000, 100, 10, 1, 0.1 ppm (based on substrate) were tracked. The reaction profiles are shown in Figure 1.

Table 1. Epoxidation of cyclohexene catalyzed by manganese *meso*-tetraphenylporphyrin in the presence of molecular oxygen[a]

Entry	Amount of catalyst (ppm)	Reaction Time (h)	Conv. (%)	Yield (%)	TON
1	10,000	2.0	>99	97	813
2	100	2.5	>99	98	81,274
3	10	4.0	98	95	796,490
4	1.0	4.5	97	95	7,883,626
5	0.1	5.0	97	96	78,836,263
6[b]	0	5.0	15	13	—
7[c]	1.0	4.5	0	0	0
8[d]	1.0	4.5	78	76	6,339,410
9[e]	1.0	4.5	>99	98	8,127,450
10[f]	1.0	4.5	85	82	6,908,332

[a] Substrate (2 mmol), isobutylaldehyde (0.01 mol), CH$_2$Cl$_2$ (5 mL), O$_2$ bubbling, rt.
[b] No catalyst.
[c] No aldehyde.
[d] Molar ratio of cyclohexene to isobutyraldehyde was 1:4.
[e] Molar ratio of cyclohexene to isobutyraldehyde was 1:6.
[f] Toluene as solvent.
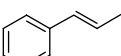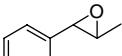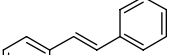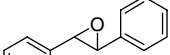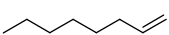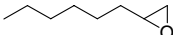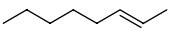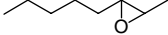
Table 2. Epoxidation of alkenes catalyzed by manganese *meso*-tetraphenylporphyrin in the presence of molecular oxygen and isobutyraldehyde[a]

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 (0.01 mol), CH_2Cl_2 (5 mL), O_2 bubbling, rt.

Although the amount of the catalyst decreased exponentially, cyclohexene could be nearly stoichiometrically
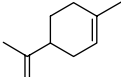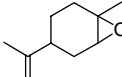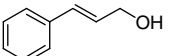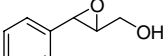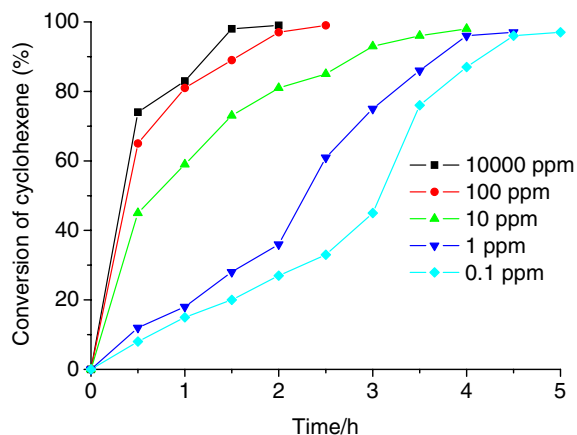

Figure 1. Profile of the conversion rates of cyclohexene oxide for different amounts of Mn(TPP): substrate (2 mmol), isobutyraldehyde (0.01 mol), CH_2Cl_2 (5 mL), O_2 bubbling (1 atm), rt.

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 10,000 ppm catalyst. Therefore, the epoxidation catalyzed by metalloporphyrin should involve radical species. The result is consistent with those of Qi,[15] Nam,[16] and Ravikumar[17] using ruthenium complex, cyclam or manganese acetate dihydrate as catalysts. Further studies on the mechanism of the epoxidation are in progress.

4. Large scale epoxidation of cyclohexene

A large scale of cyclohexene epoxidation experiment was carried out in the presence of molecular oxygen and isobutyraldehyde as shown in Scheme 2.[18]
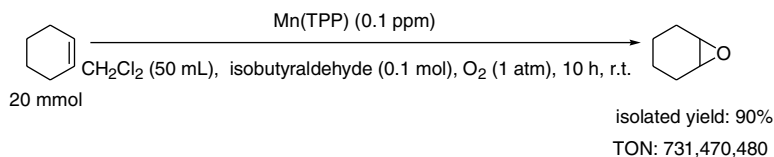
Scheme 2. Large scale epoxidation of cyclohexene.

When the amount of manganese *meso*-tetraphenyl-porphyrin 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.

5. Cyclohexene epoxidation catalyzed by Fe(III) and Co(II) porphyrins

Other simple structural metalloporphyrins, for example, iron and cobalt porphyrins, have similar catalytic performance for epoxidation of cyclohexene in the presence of molecular oxygen and isobutyraldehyde. When using 1 ppm loading of iron *meso*-tetraphenylporphyrin chloride (Fe(TPP)Cl) or cobalt *meso*-tetraphenylporphyrin Co(TPP)[13] as catalyst in the epoxidation of cyclohexene under the same reaction conditions, 95% and 89% yields of cyclohexene oxide were obtained, respectively. These results indicate that the metalloporphyrins are effective catalysts for epoxidation of cyclohexene with ppm level catalytic amount by using molecular oxygen as an oxidant.

It has been shown that the steric and electronic properties of substituent on the porphyrin rings or axial ligands could affect the catalytic performance of metalloporphyrins.[19] Further studies on substituent and axial ligands effects of catalytic activity for olefins epoxidation are in progress.

In conclusion, simple structural manganese *meso*-tetraphenyl porphyrin has proven to be an excellent catalyst for the epoxidation of olefins in the presence of molecular oxygen and isobutylaldehyde. Under ambient temperature and atmospheric pressure, the catalytic system displays high activity and selectivity for olefins epoxidation by using ppm level catalyst. The turnover number of catalyst could reach up to 731,470,480.

Acknowledgements

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12. *meso*-Tetraphenylporphyrin (TPP) was prepared according to the known procedure, see: Alder, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476.
13. Metalloporphyrins were prepared according to our previous works, see: Refs. 11a and 19a. The spectral and analysis data of Mn(TPP). FAB: *m/z* 667. Anal. Calcd for C$_{44}$H$_{28}$N$_4$Mn: C, 79.08; H, 4.19; N, 8.39. Found: C, 79.26; H, 4.05; N, 8.32. UV–vis (CH$_2$Cl$_2$) λ_{max}: 424 nm (Soret band), 545 nm (Q-band). IR: 1002 cm^{-1}. The spectral and analysis data of Fe(TPP)Cl. FAB: *m/z* 705. Anal. Calcd

for $C_{44}H_{28}N_4FeCl$: C, 74.98; H, 3.98; N, 7.95. Found: C, 75.12; H, 4.01; N, 7.89. UV–vis (CH_2Cl_2) λ_{max}: 418 nm (Soret band), 548 nm (Q-band). IR: 1006 cm^{-1}; 325 cm^{-1}. The spectral and analysis data of Co(TPP). FAB: *m/z* 671. Anal. Calcd for $C_{44}H_{28}N_4Co$: C, 78.61; H, 4.17; N, 8.34. Found: C, 78.32; H, 4.05; N, 8.19. UV–vis (CH_2Cl_2) λ_{max}: 425 nm (Soret band), 552 nm (Q-band). IR: 1004 cm^{-1}.

14. *General procedure for the catalytic epoxidation of alkenes to epoxides.* Dioxygen was bubbled through a solution of dichloromethane (5 mL), cyclohexene (2 mmol), isobutyl-aldehyde (10 mmol), manganese *meso*-tetraphenylporphy-rin (2.5×10^{-7} mmol) and 0.8 mmol naphthalene (inert internal standard) at room temperature. The consumption of the starting olefins and formation of oxidized products were monitored by GC (Shimadzu GC14C) and GC–MS (Shimadzu GCMS-QP5050A).

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18. *General procedure for the large scale cyclohexene catalytic epoxidation.* To a stirring solution of dichloromethane (50 mL), cyclohexene (20 mmol), isobutylaldehyde (0.1 mol) and manganese *meso*-tetraphenylporphyrin (2.5×10^{-8} mmol) were added in the presence of molecular oxygen at room temperature. The crude products were purified via column chromatography (silica gel, cyclohex-ane as eluting agent). After removing solvent under reduced pressure, the pure cyclohexene oxide (1.76 g) was obtained with the yield of 90%.

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