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# Epoxidation with an Electrocatalytic P-450 Model System in an Acidic Solution

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**An electrochemical P-450 model system using *meso*-tetraphenylporphyrinatomanganese(III) chloride (MnTPP), imidazole and acetic acid was tested in an acetonitrile solution, and epoxide was obtained with a good current efficiency. The results of cyclic voltammetry revealed that acid plays an important role in the second electron transfer.**

**Key words** electrolysis; oxidation; porphyrin; epoxide; epoxidation

The biomimetic chemistry of cytochrome P-450, which is an important drug-metabolizing enzyme, is of great interest because it catalyzes various types of oxygenation and has a unique catalytic cycle.[1)] In the generally accepted catalytic cycle for cytochrome P-450, a strong oxidant is produced by the transfer of two electrons and one dioxygen. In the electrochemical P-450 model system, metalloporphyrins are used as a model of the enzyme's active site, and the two-electron transfer is replaced by a cathodic reduction.[2)]

In the course of studies on the biomimetic oxidation of sulfides, we found that an electrochemical model system consisting of *meso*-tetraphenylporphyrinatomanganese(III) chloride (MnTPP), acetic acid (AcOH), 1-methylimidazole, and acetonitrile as a solvent gave a relatively good result.[3—6)] Thus, we attempted to apply this electrochemical model system to the epoxidation of alkenes. However, a similar model system had been reported.[2)] So, cyclic voltammetry was performed to elucidate the mechanism more clearly, and a better yield, based on consumed electrons, was obtained.

## Results

**Controlled Potential Electrolysis (CPE)** CPE was performed with a divided cell and reticulated vitreous carbon (RVC) electrode (glassy carbon with a porous structure having a free void volume of about 97% and surface area of about 65 $cm^2/cm^3$). A relatively small piece of RVC can provide an electrode with a substantial surface area owing to its low electrical resistance and physically continuous structure. The electrolytic solution was acetonitrile (40 ml) containing MnTPP (1 mM), cyclooctene (100 mM), acetic acid (200 mM), imidazole and $NaClO_4$ (100 mM) as a supporting electrolyte. At hourly intervals, 0.5 ml electrolytic solution was withdrawn and analyzed by gas chromatography. The electrolytic experiments were stopped after 4 h because of the durability of the methyl cellos plug that was the diaphragm of the divided cells. To find the optimal concentration of imidazole, CPE was performed using various concentrations. The results are summarized in Fig. 1.

When the concentration of imidazole was increased from 1 to 2 mM, the yield of the epoxide and the current efficiency were increased. On further increase of the concentration of imidazole, no drastic change was observed. However, the best current efficiency was obtained when 5 mM of imidazole was used.

Cyclooctene was replaced by other alkenes, and CPE was performed. The results are summarized in Table 1.

1-Octene and styrene gave the corresponding epoxide as a final product. Styrene also gave a good current efficiency. Cyclohexene gave cyclohexanol and cyclohexanone, as well as cyclohexene oxide.

Both imidazole and acetic acid are needed to realize epoxidation. Without imidazole, only background current was observed. In the absence of acetic acid, the current was very low and the color of the electrolyte was changed from dark green to brown over 1 h.

**Cyclic Voltammetry** Cyclic voltammetry of MnTPP (1 mM) was performed in dry acetonitrile containing $NaClO_4$ (0.1 M) in the presence and absence of imidazole (5 mM). A glassy carbon electrode, an Ag/AgCl electrode, a Pt wire, and dry acetonitrile were used as the working electrode, the reference electrode, the counter electrode, and the solvent, respectively. The potential sweep range was from 0.0 to $-0.9$ V. One cathodic peak ($-613$ mV *vs.* Ag/AgCl, 2.01 mA $(mV/s)^{-1/2}$) and a corresponding anodic peak ($-539$ mV *vs.* Ag/AgCl, 1.90 mA $(mV/s)^{-1/2}$) were observed

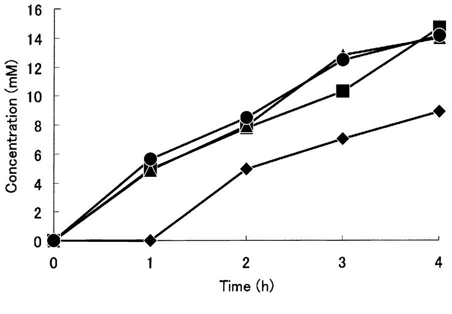

Fig. 1. Effect of the Concentration of Imidazole on the Yield of Cyclooctene Epoxide

1 mM (◆), 2 mM (■), 5 mM (▲), 10 mM (●).

Table 1. Results of Controlled Potential Electrolysis of MnTPP in the Presence of Alkenes

| Alkene | Product | Concentration (mM) | Current efficiency (%) |
|---|---|---|---|
| Styrene | Epoxystyrene | 5.4 | 89.5 |
| Cyclohexene | Epoxycyclohexene[a)] | 3.8 | 77.1 |
| 1-Octene | Epoxyoctene | 1.2 | 22.3 |

The electrolysis was performed for 4 h. *a*) 2-Cyclohexen-1-one (0.31 mM) and 2-cyclohexen-1-ol (0.17mM) were also found as byproduct.

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in the cyclic voltammogram obtained in dry acetonitrile containing MnTPP (1 mM), imidazole (5 mM) and $NaClO_4$ under $N_2$. The absolute values of the cathodic peak current and anodic peak current were about the same. The peak separation value ($\Delta Ep = Epa - Epc$) was 74 mV. The presence of a reversible one-electron transfer process is suggested by these results. Introducing air or additional acetic acid (0.2 M) into the solution did not affect the voltammogram. After acetic acid (0.2 M) was added to the solution, and it was stirred under an atmosphere for a while, the cyclic voltammograms were obtained. The anodic peak disappeared and the cathodic peak ($-654$ mV *vs.* Ag/AgCl, 12.1 mA $(mV/s)^{-1/2}$) increased a 6th time. This suggested that the electrochemical process was changed to an irreversible multi-electron transfer process.

## Discussion

The catalytic cycle of the electrochemical P450 model system must be essentially as discussed by Creager *et al.*[2] and they pointed out that the catalytic cycle has three major segments: (1) Initial reduction to Mn(II) followed by strong dioxygen binding promoting a second reduction step to an Mn(II) superoxo complex. (2) The latter complex has been shown to react with anhydrides, giving metallo acylperoxy complexes that undergo O–O bond heterolysis, yielding a high-valent manganese porphyrin complex. (3) This complex transfers one oxygen atom to a suitable substrate. We used acetic acid in the place of anhydride to cause O–O bond cleavage of the Mn(II) superoxo complex.

Cyclic voltammmetry in the absence of acetic acid showed that the electron transfer was reversible. However, addition of acetic acid made the electron transfer process irreversible, and the cathodic peak increased. The peak current in the reversible electrode process is calculated by the Randles–Sevcik equation: $ip = 2.69 \times 10^5 n^{3/2} A D^{1/2} C v^{1/2}$ at 25 °C, where $n$ is the number of electrons involved in the electrode reaction, $A$ the area of the electrode, $D$ the diffusion constant, $C$a bulk concentration of the electroactive species, and $v$ the scan rate. On the other hand, the peak current in the irreversible electrode process is calculated by the equation: $ip = 2.99 \times 10^5 n(\alpha n_a)^{1/2} A D^{1/2} C v^{1/2}$ at 25 °C, where $n_\alpha$ represents the number of electrons in the rate-controlling step and $\alpha$ is the transfer coefficient (normally with a value between 0.3 and 0.7).

Supposing that $n = na = 1$ and $a = 0.5$, the rate of the peak current of irreversible wave ($ip^{irrev}$) and the peak current of reversible wave ($ip^{rev}$): $ip^{irrev}/ip^{rev} = 2.99 \times 0.5^{1/2}/2.69 \fallingdotseq 0.79$. Therefore, when a reversible electrochemical reaction changes into an irreversible reaction, the ip must be reduced to 79%. However, the real rate ($ip^{irrev}/ip^{rev}$) is 6. This suggests that n is increased to more than 7 and the first electron transfer process does not need acid addition, but that acid plays an important role in the second electron transfer.

## Experimental

**Materials** Acetonitrile was purified as described previously.[8]

*Meso*-tetraphenylporphyrinatomanganese(III) chloride was prepared as described previously.[3]

Other chemicals were of reagent grade and used without further purification.

**Apparatus** A Hokuto Denko HF-102 coulometer and an HA-501 potentiostat were used for controlled potential electrolysis. Gas chromatography was carried out with a Shimadzu GC-14A equipped with a C-R6A Chromatopac. A BAS CV-50W electrochemical analyzer was used for cyclic voltammetry. Visible spectrometry was performed with a Hitachi U-3000 spectrometer.

**Controlled Potential Electrolysis (CPE)** A representative example of the procedure is given below. Acetonitrile (40 ml) containing MnTTP (282.2 mg), cyclooctene (0.52 ml), imidazole (136.1 ml), acetic acid (0.48 ml) and sodium perchlorate (0.5 g) as a supporting electrolyte was placed in a divided cell. CPE was performed at $-0.5$ V (*vs.* SCE) using an RVC electrode with $O_2$ gas bubbling through the solution, and 0.5-ml aliquots were diluted with acetonitrile containing diphenyl as an internal standard. Products were determined by GC (column, Silicon OV-101, Uniport HP).

## References and Notes

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