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Biomimetic Oxidation of Diphenyl Sulfide by Meso-Tetraphenyl-Porphyrinatochromium (3^+) Chloride as an Electrochemical P-450 Model Compound

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Abstract

Controlled potential electrolysis (CPE) of meso-tetraphenylporphyrinatochromium (3^+) chloride (CrTPP, 1 mM) at -1.23 V (*vs.* Ag-AgCl) in acetonitrile containing diphenyl sulfide (1 mM) and sodium perchlorate (0.1 mM) as the, supporting electrolyte with a glassy carbon cathode gave diphenyl sulfoxide. The addition of acetic acid to the electrolyte solution increased the yield of diphenyl sulfoxide, as did the addition of KO_2 to acetonitrile containing diphenyl sulfide. The catalytic cycle is thus similar to that of cytochrome P-450, an important drug-metabolizing enzyme.

Keywords: P-450 model; Meso-tetraphenylporphyrinatochromium (3^+) chloride; Sulfide oxidation

Introduction

The molecular mechanism of biological oxidation by cytochrome P-450 is of great interest because cytochrome P-450 is an important drug-metabolizing enzyme that catalyzes a wide variety of oxygenation reactions and has a unique catalytic cycle [1]. In the generally accepted model for the catalytic cycle of cytochrome P-450, an oxo-iron (5^+) species or oxo-iron (4^+) porphyrin π-cation radical is produced by the transfer of two electrons and one dioxygen. Metalloporphyrins are often used as model compounds for P-450 and several reductants, such as $NaBH_4$ or dihydrogen and colloidal platinum, are used as the electron source [2-13]. Metalloporphyrins are also effective in the oxidation of sulfides, the demethylation of dimethyl aniline, and the epoxidation of alkenes [14-21]. In the oxidation of sulfides, it is particularly important to choose the reductant carefully because the oxidation products of sulfides, sulfoxides, can be easily reduced to sulfides again. Since the applied potential can be changed freely, controlled potential electrolysis (CPE) is suitable for such studies. Other researchers,

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in particular Murry and co-workers, have used meso-tetraphenylporphyrinatochromium (3^+) chloride (CrTPP) to catalyze oxygen-atom transfer reactions or as P-450 model compounds [22].

In our previous paper we described the epoxidation of olefins by Cr (3^+) TPP, used as an electrochemical P-450 model compound [23]. The aim of this paper is to clarify the biomimetic oxidation of diphenyl sulfide using CrTPP as an electrochemical P450 model.

Materials and Methods

Materials acetonitrile was HPLC grade and the other chemicals were reagent grade. All reagents were purchased from Nacalai Tesque, Kyoto, Japan, and used without purification.

Apparatus A Hokutodenko (Tokyo, Japan) HF-102 coulometer and HA-501 potentiostat were used for controlled potential electrolysis. Gas chromatography was carried out with a Shimadzu (Kyoto, Japan) GC-14A equipped with a C-R6A Chromatopac.

Controlled potential electrolysis (CPE)

A representative procedure is as follows:

Acetonitrile (30 ml) containing CrTPP (21.33 mg), diphenyl sulfide (0.508 ml), imidazole (102 mg), acetic acid (0.3 ml) and $NaClO_4$ (0.37 g) used as the supporting electrolyte was placed in an undivided cell. A glassy carbon plate, a Pt plate, and an Ag/AgCl electrode were used as the working electrode, counter electrode, and reference electrode, respectively. CPE was carried out at -1.27 V for 4 h. Aliquots of the electrolyte (0.1 ml) were diluted with acetonitrile containing diphenyl as an internal standard to 0.2 ml and then analyzed. The products were determined by GC (capillary column, GL Sciences (Tokyo, Japan) Inert Cap (0.25 mm × 30 m, df 0.25 μm)).

Reaction with potassium superoxide acetonitrile (30 ml) containing CrTPP (21.48 mg), diphenyl sulfide (0.508 ml), $NaClO_4$ (0.37 g), imidazole (0.1 g) and acetic acid (0.3 ml) was placed in a flask and KO_2 (0.213 g) was added to the solution. The reaction was carried out for 1 h. Aliquots (0.1 ml) were diluted with acetonitrile containing diphenyl as an internal standard to 0.2 ml and then analyzed. The products were determined by GC as described above.

Results and Discussion

As noted earlier, the epoxidation of olefins by CrTPP in acetonitrile as an electrochemical P-450 model compound was previously reported. In the present study, similar solutions were tested for the biomimetic oxidation of diphenyl sulfide. Four electrolytic solutions were prepared: acetonitrile containing CrTPP (1 mM), diphenyl sulfide (100 mM) and $NaClO_4$ (0.1 M) (SA); acetonitrile containing CrTPP (1 mM), imidazole (5 mM), diphenyl sulfide (100 mM) and $NaClO_4$ (0.1 M) (SB);

acetonitrile containing CrTPP (1 mM), acetic acid (1%), diphenyl sulfide (100 mM) and $NaClO_4$ (0.1 M) (SC); and acetonitrile containing CrTPP (1 mM), imidazole (5 mM), acetic acid (1%), diphenyl sulfide (100 mM) and $NaClO_4$ (0.1 M) (SD).

The results of cyclic voltammetry of CrTPP (1 mM) in dry acetonitrile containing $NaClO_4$ have been reported [23]. The addition of acetic acid (1%) to the electrolyte resulted in fusion of the two cathodic waves in the potential range from 0 V to -1.6 V: the first cathodic wave shifted approximately 200 mV lower and the ip (peak current) of the cathodic wave increased more than sevenfold. The addition of imidazole (5 mM) to the electrolyte resulted in the cathodic wave shifting approximately 400 mV lower, in a manner similar to that observed following the addition of acetic acid.

When both acetic acid (1%) and imidazole (5 mM) were added to the electrolyte solution, a new oxidation wave appeared at -1.24 V and was a counterpart of the first cathodic wave.

CPE was performed in an undivided cell using a glassy carbon electrode and an Ag/AgCl electrode. The electrolytic solution was stirred during electrolysis under atmospheric conditions. At hourly intervals, 100 µl of electrolytic solution was withdrawn and analyzed by gas chromatography. The electrolytic experiments were stopped after 4 h and the results are summarized in FIG. 1.

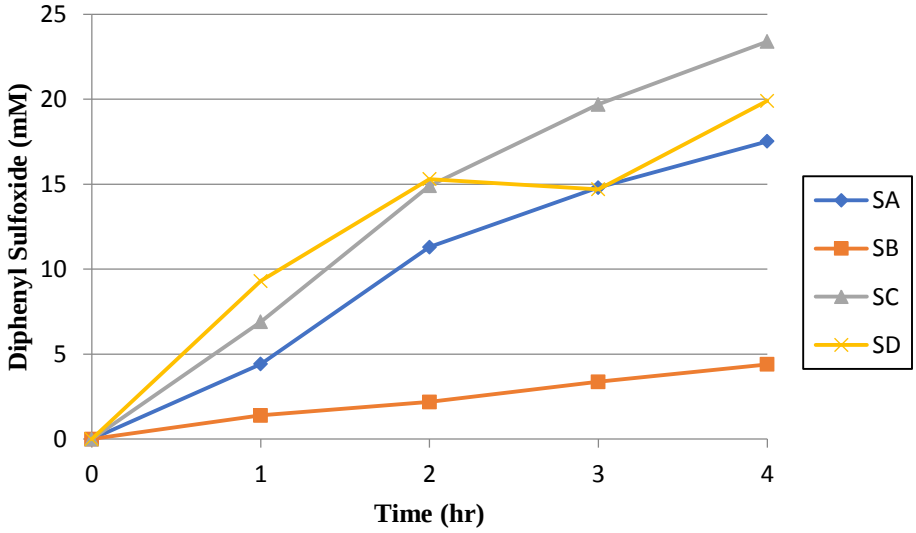

FIG. 1. **Concentration of diphenyl sulfoxide in the electrolyzed solutions.**

SA: Acetonitrile containing CrTPP (1 mM), diphenyl sulfide (100 mM) and $NaClO_4$ (0.1 M);

SB: Acetonitrile containing CrTPP (1 mM), imidazole (5 mM), diphenyl sulfide (100 mM) and $NaClO_4$ (0.1 M);

SC: Acetonitrile containing CrTPP (1 mM), acetic acid (1%), diphenyl sulfide (100 mM) and $NaClO_4$ (0.1 M);

SD: Acetonitrile containing CrTPP (1 mM), imidazole (5 mM), acetic acid (1%), diphenyl sulfide (100 mM) and $NaClO_4$ (0.1 M).

Diphenyl sulfoxide was detected in each electrolyzed solution. There were 17.5 catalytic cycle turnovers in SA over a 4 h period. The presence of acetic acid in the electrolyte solution (SC, SD) increased the turnover of the catalytic cycles, whereas the presence of imidazole (a base) reduced turnover.

In the catalytic cycle of cytochrome P-450, the iron peroxo species $Fe^{3+}O^{22-}$ is generated through two-electron reduction and dioxygen binding. Heterolysis of the O-O bond in the iron peroxo species, with concomitant generation of the reactive oxidant $[FeO]^{5+}$ and a molecule of water, requires two protons [1]. The addition of a large excess of imidazole to a solution of metalloporphyrin results in the exchange of the fifth ligand to imidazole. The fifth ligand of metalloporphyrins plays an important role in binding oxygen to the metalloporphyrin.

Our results suggest that the rate limiting step of the catalytic cycle is the heterolysis of the O-O bond in the chromium peroxo species.

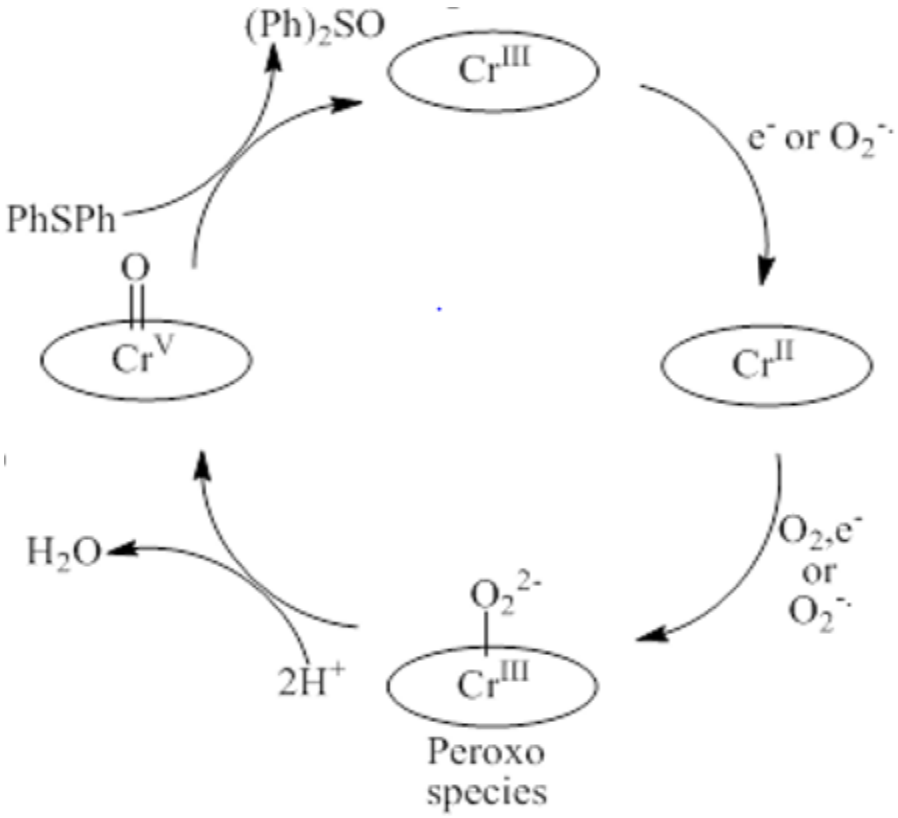

FIG. 2. **Biomimetic oxidation of diphenyl sulfide.**

The applied potential was -1.27 V and thus there was reduction of O_2 dissolved in the electrolyte solution. Potassium superoxide (0.213 g), a reduced product of dioxygen, was added to SD and the solution was stirred. The reaction was conducted for 1 h; GC analysis showed diphenyl sulfoxide (19.1%) and diphenyl sulfone (12.1%) (yields calculated based on the initial amount of diphenyl sulfide).

Shirazi pointed out that two moles of superoxide produce one mole of metallo peroxo species from metalloporphyrins [24]. The catalytic cycle may therefore include the generation of superoxide, and was proposed in FIG. 2. Details of this reaction are currently under study.

Conclusion

Electrochemical reduction of acetonitrile containing CrTPP (1 mM) and diphenyl sulfide (100 mM) in air selectively gave diphenyl sulfoxide. The rate limiting step of the catalytic cycle was the heterolysis of the O-O bond in the chromium peroxo species.

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