

A REACTION KINETIC STUDY ON THE GIF-TYPE BIOMIMETIC OXIDATION OF CYCLOHEXANE

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Abstract—Kinetics of the oxidation of cyclohexane under Gif type conditions have been studied. A kinetic model is proposed, which is in agreement with the experimental results obtained. The rate equation showed the first order with respect to cyclohexane. A temperature-dependence study of the reaction rate affords an activation energy of 14.3 kcal/mol.

Key words: Kinetic Study, Gif, Biomimetic, Oxidation, Cyclohexane

INTRODUCTION

The Cytochrome P-450 monooxygenase is a heme-containing porphyrin which is capable of oxygenating hydrocarbon readily in a catalytic way, yielding alcohols from alkanes and epoxides from alkenes at ambient conditions. Its physiological significance and unique mechanism have attracted much interest of many chemists and biochemists. The reaction systems using synthetic metalloporphyrins and several oxygen sources have served as models for Cytochrome P-450 monooxygenase enzymes. Groves et al. [1979] first found that (5,10,15,20-tetra phenyl porphinato) iron (III) chloride catalyzes the oxygen atom transfer from iodobenzene to olefin. Since then, many model systems have been proposed which could mimic the metalloporphyrin-catalyzed oxidations and their reaction mechanisms also have been discussed [Traylor, 1981; Sugimoto, 1988; Ojima, 1990; Archakov, 1990]. An important fraction of this work has focused on the study of the kinetics and mechanism of these oxygen-transfer reactions. Amongst several different models, Barton et al. developed a family of new biomimetic systems which allowed the oxidation and functionalization of saturated hydrocarbons under mild reaction conditions (ambient temperature, atmospheric pressure, nearly neutral pH) [Barton, 1983; About-Jaudet, 1990; Barton, 1992]. The systems are collectively called "Gif systems". All of them involve a pyridine, acetic acid (or other carboxylic acid), and a hydrocarbon. They are oxidized with an iron-based catalyst, an oxidant and an electron source. The two most practical members of the Gif family are Gif IV ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ as a catalyst, dioxygen from air as an oxidant and zinc powder as an electron source) and GoAgg II ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ as a catalyst, and hydrogen peroxide as a combined oxidant and electron source). Gif system was originally designed to emulate the non-heme enzymatic oxidation of alkanes.

According to a mechanism proposed by Barton [1992], the activation of saturated hydrocarbon by the Gif system can be represented by the following three steps.

(1) Activation of dioxygen molecule, formally as an $\text{Fe}=\text{O}$ spe-

cies,

(2) Activation of hydrocarbon through insertion of the $\text{Fe(V)}=\text{O}$ species into a carbon-hydrogen bond and

(3) Insertion of dioxygen into a carbon-iron bond, and formation of ketone or alcohol from the alkyl hydroperoxide intermediate.

Many reports have been published with respect to mechanism and rate determining step for epoxidation of alkenes with metalloporphyrins and various oxidants. Two main conflicting ideas exist regarding the rate determining step; the formation of metal oxo porphyrin complexes [Nolte, 1986; Dicken, 1986; Traylor, 1988] and the decomposition of metalloxetines [Collman, 1985; Amatsu, 1988].

However, there is no report on the kinetic study for Gif system. Thus, we carried out the reaction kinetic study to understand the rate determining step in this new biomimetic system and compared the reactivity of various cocatalysts. The activation energy was also obtained.

EXPERIMENTAL

The oxidation of cyclohexane under GoAgg II conditions was examined in a batch reactor. Experimental methods used throughout this work was as reported previously [Barton, 1990]. Quantitative analysis of reaction mixture was performed on a Shimadzu model 14A gas chromatograph equipped with a FID and using diisopropylbenzene as an internal standard.

1. General Procedure for GoAgg II Reaction

Cyclohexane, pyridine, acetic acid and the corresponding iron catalyst were placed in a 125 ml Erlenmeyer flask. These are presented in the corresponding Tables as footnotes. The reaction was initiated by addition of hydrogen peroxide (30% in water). The reaction mixture was stirred vigorously under air at room temperature for 16 hr.

2. General Work-up Procedure

Reaction mixture (2 ml) was chilled in an ice-salt mixture and H_2SO_4 [4 ml, 25% (v/v)] was slowly added with stirring. Then the mixture was extracted (3×2 ml) with ethylether and the acidic ethyl ether layer was washed successively with 10 ml of 5% (w/v) NaHCO_3 solution and brine. The dried (MgSO_4) ethylether

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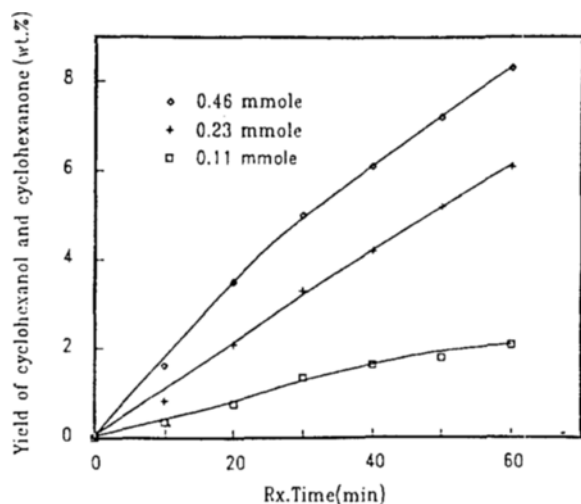


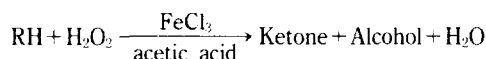
Fig. 1. Effect of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ concentrations in the GoAgg II reaction of cyclohexane.

(Rx. temp.: 15°C , cyclohexane: 9 mmole, H_2O_2 : 10 mmole, acetic acid: 35 mmole, pyridine: 30 ml)

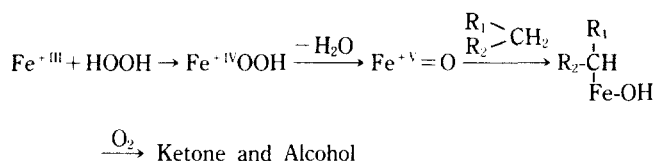
layer was mixed with a solution of an internal standard and analyzed by G.C.

RESULTS AND DISCUSSION

In GoAgg II oxidation system, reaction rate is affected by various factors such as concentrations of FeCl_3 , H_2O_2 and acetic acid from the following equation.



The mechanism of this reaction can be represented by the following equation



The effects of each factor were studied to investigate the rate determining step in this biomimetic system.

1. The Influence of Iron Catalyst

Lee et al. [1994] have studied the effect of the iron compounds on the activities and alcohol/ketone selectivity of the Gif system for biomimetic oxidation of cyclohexane. They have obtained the new experimental results for various iron compounds.

Reactivity was affected by various counter-ion Z group of iron compound Z-Fe. When Z group is the more electron withdrawing, the reactivity is increased in the GoAgg reaction. FeCl_3 , as a catalyst, showed good results.

Thus, FeCl_3 was selected as a catalyst in this study and the effect of the amounts of iron catalyst on the GoAgg II oxidation was investigated.

As shown in Fig. 1, the conversion of cyclohexane increased with the increase of iron catalyst.

2. Effect of the Concentration of Hydrogen Peroxide

The influence of hydrogen peroxide for the reaction rate in

Table 1. Effect of peroxide concentration on the conversion of cyclohexane in the GoAgg II system

Peroxide concentration (%)	Conversion (wt%)
30	12
15	11.5
6	10.4
1.8	3.2

*Reaction Condition: reaction temp. (15°C) cyclohexane (9.0 mmole), $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (1 mmole), picolinic acid (0.9 mmole), pyridine (30 mmole), acetic acid (35 mmole).

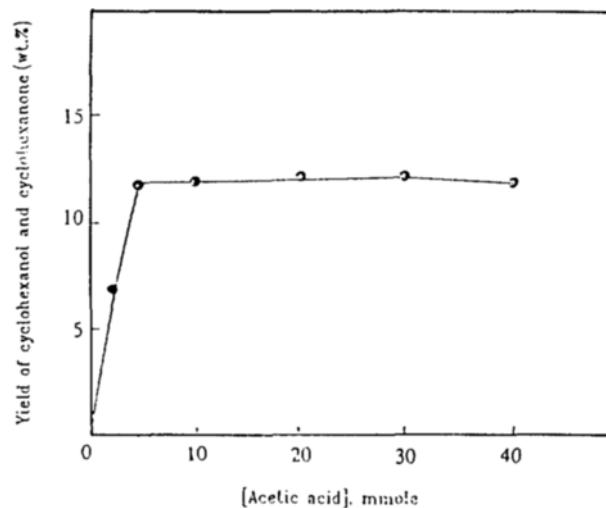


Fig. 2. Effect of amounts of acetic acid in the GoAgg II reaction of cyclohexane.

(Rx. temp.: 15°C , $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$: 1 mmole, cyclohexane: 9 mmole, H_2O_2 : 10 mmole, pyridine: 30 ml)

the GoAgg II reaction was shown in Table 1. There is no strong dependence of total cyclohexane conversion on the concentration of hydrogen peroxide. However, the reaction rate decreases remarkably when the concentration falls a certain limit.

The effect of the amounts of acetic acid on the GoAgg II oxidation was studied. As shown in Fig. 2, the conversion of cyclohexane remains constant as far as the amount of acetic acid is maintained above 5 mmole. The rapid decomposition of hydrogen peroxide seems to result when the concentration of acetic acid falls below 5 mmole.

3. Effect of Cocatalyst

Mansuy [1982] examined the effect of a cocatalyst by using imidazole in the hydroxylation of cyclohexane with porphyrin. They reported that imidazole gave good effects in the oxidation of hydrocarbons.

Barton also reported that picolinic acid derivatives increased reaction rates in the Gif oxidation of cyclododecane [12]. Thus, the effects of various cocatalysts containing imidazole were examined in the GoAgg II reaction. As shown in Fig. 3, picolinic acid showed the greatest reaction rate enhancement, followed by 4,5-imidazole dicarboxylic acid. But imidazole having the excellent results in the porphyrin system showed the lower yield than without cocatalyst. A similar trend was observed for the effect of the cocatalyst on the decomposition rate of hydrogen peroxide.

4. Effect of Reaction Temperature

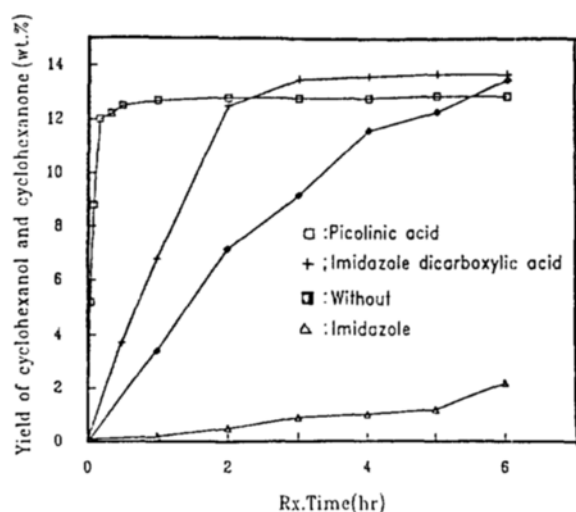


Fig. 3. Effect of various ligands in the GoAgg II reaction of cyclohexane.

(Rx. temp.: 15°C, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$: 1 mmole, ligand: 0.9 mmole, cyclohexane: 9 mmole, H_2O_2 : 10 mmole, AcOH: 35 mmole, pyridine: 30 ml)

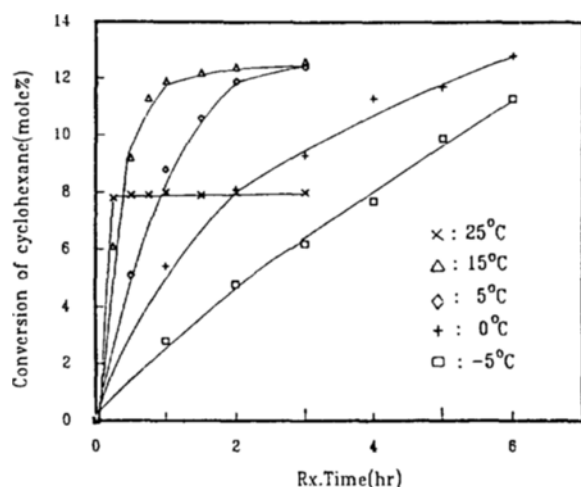


Fig. 4. Effect of reaction temperature in the GoAgg II reaction of cyclohexane.

($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$: 1 mmole, picolinic acid: 0.9 mmole, cyclohexane: 9 mmole, H_2O_2 : 10 mmole, AcOH: 35 mmole, pyridine: 30 ml)

In order to determine the optimum temperature for the oxidation of cyclohexane to cyclohexanone and cyclohexanol, series of tests were carried out at different temperatures ranging from -5°C to 25°C .

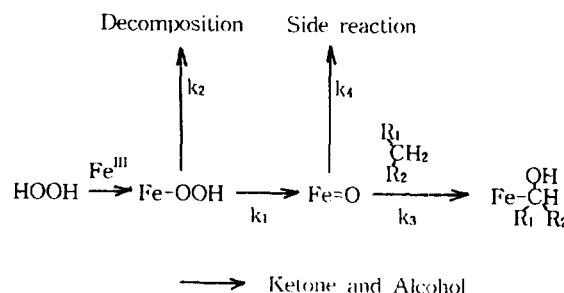
The rate of oxidation increased with reaction temperature in the range from -5°C to 25°C as shown in Fig. 4. However, the yield of ketone and alcohol was reduced considerably upon further increasing reaction temperature above 25°C as shown in Fig. 4.

The high reaction temperatures resulted in the increasing decomposition of hydrogen peroxide.

Hence, it can be deduced that the optimum reaction temperature for the formation of ketone and alcohol is about 15°C .

5. Reaction Kinetic Study

From these results, it was evident that the reaction rate was largely related to the consumption of hydrogen peroxide. Decom-



Scheme 1. Proposed reaction kinetic model of GoAgg II reaction.

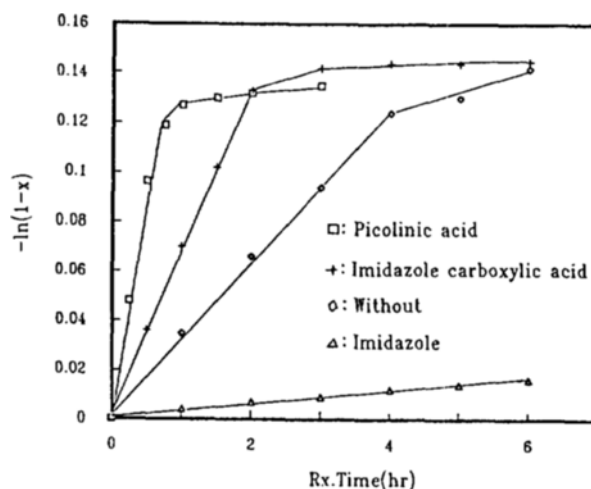


Fig. 5. Test of first order equation for GoAgg II system.

(Rx. temp.: 15°C , $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$: 1 mmole, ligand: 0.9 mmole, cyclohexane: 9 mmole, H_2O_2 : 10 mmole, AcOH: 35 mmole, pyridine: 30 ml).

position of peroxide can be divided into two competing paths. One is the self decomposition (k_2) to decrease the yield. The other step (k_1) is the decomposition of iron peroxide to the products via iron oxo species as shown in Scheme 1.

Reaction yield of cyclohexanone and cyclohexanol in the GoAgg II reaction using the hydrogen peroxide is determined by reaction rate constants k_1 and k_2 . k_2 can be neglected when enough amount of acetic acid is added. Life time of $\text{O}=\text{Fe}(\text{IV})$ and $\text{O}=\text{Fe}(\text{V})$ was reported to be smaller than 1 sec [Chin, 1980; Balch, 1985]. Bruce studied kinetics and mechanism of the epoxidation of alkene using manganese(II) porphyrin and proposed the rate determining step to be the oxygen transfer with formation of high valent manganese-oxo porphyrin species [Dicken, 1986]. Also, many researchers proved that rate determining step is the formation of metal oxo porphyrin complexes in the oxidation of hydrocarbons using porphyrin as a catalyst [Nolte, 1986; Dicken, 1986; Traylor, 1988]. Thus, we can suppose that k_1 step is rate determining step of the overall reaction. In order to increase the yield and reaction rate, values of rate constant k_1 and k_3 must be increased.

Hence, the primary role of cocatalyst in the reaction system appears to accelerate the step, k_1 to generate oxo-metal from intermediate Fe-OOH . The reaction rate showed the similar trend to that of decomposition rates of hydrogen peroxide under the same conditions.

If we assume a steady state concentration for the $\text{Fe}(\text{V})=\text{O}$

Table 2. Reaction rate constants for various ligands in the GoAgg II reaction of cyclohexane

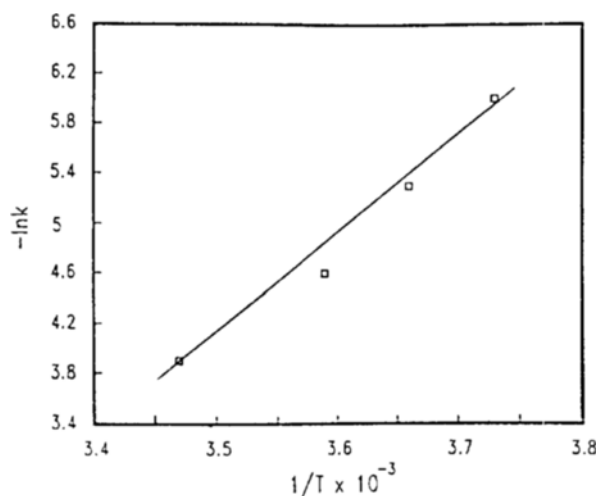
Ligand	k (hr ⁻¹)
Without	0.044
Picolinic acid	1.14
4,5-Imidazole dicarboxylic acid	0.37
Imidazole	0.0042

*Reaction condition: reaction temperature (15°C), cyclohexane (9 mmole), FeCl₃·6H₂O (1 mmole), acetic acid (35 mmole), ligand (0.9 mmole), pyridine (30 ml)

Table 3. The reaction rate constants at different reaction temperature in the GoAgg II reaction of cyclohexane

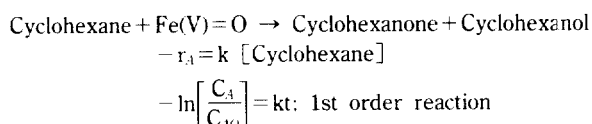
Rx. temp.	Reaction rate constants (hr ⁻¹)
-5	0.18
0	0.40
5	0.78
15	1.14

*Reaction condition: cyclohexane (9 mmole), FeCl₃·6H₂O (1 mmole), acetic acid (35 mmole), picolinic acid (0.9 mmole)

**Fig. 6. Temperature dependency of reaction rate for the conversion of cyclohexane in the GoAgg II reaction.**

(FeCl₃·6H₂O: 1 mmole, picolinic acid: 0.9 mmole, cyclohexane: 9 mmole, H₂O₂: 10 mmole, pyridine: 30 ml)

species, the rate equation can be expressed as first order with respect to the substrate (cyclohexane). Experimental results obtained from various catalysts satisfied with the first order equation as shown in Fig. 5.



In Table 2, reaction rate constants with the picolinic acid is 26 folds greater than the case without cocatalyst.

Also, reaction rate constants obtained from the Fig. 5 are shown in Table 3. The activation energy obtained from an Arrhenius plot in Fig. 6 was 14.3 kcal/mole.

CONCLUSIONS

Effects of varying concentrations of iron, hydrogen peroxide and cocatalyst on the rates of the GoAgg II reaction have been examined. From the experimental results, we propose a kinetic model for this reaction.

The cocatalyst may accelerate the step that generates the Fe(V)=O species from the precursor Fe-OOH, comparing with a reaction without cocatalyst.

The rate equation can be represented as a first order reaction with respect to cyclohexane. The activation energy value obtained is 14.3 kcal/mole.

REFERENCES

- About-Jaudet, E., Barton, D. H. R., Csuha, E. and Ozbalik, N., "The Effects of Ligand Variation on the Rate of Cyclododecane Oxidation under Modified GoAgg Conditions", *Tetrahedron Lett.*, **31**, 1657 (1990).
- Amatsu, H., Miyamoto, T. K. and Sasaki, Y., "Olefin Epoxidation Catalyzed by Sterically Bulky Metalloporphyrins by Use of Sodium Hypochlorite as an Oxygen Source", *Bull. Chem. Soc. Jpn.*, **31**, 3193 (1988).
- Archakov, A. I. and Bachmanopva, G. I., "Cytochrome P-450 and Active Oxygen", Taylor & Francis: London, 1990.
- Balch, A. L., La mar, G. N., Latos-Grazynski, L., Renner, M. W. and Thanabal, V., "Nuclear Magnetic Resonance Studies of Axial Aniline Coordination in Synthetic Ferryl, (Fe^{IV}O)²⁺, Porphyrin Complexes and in Ferryl Myoglobin", *J. Am. Chem. Soc.*, **107**, 3003 (1985).
- Barton, D. H. R., Biviere, S. D., Chavasiri, W., Csuha, E. and Doller, D., "The Functionalization of Saturated Hydrocarbons", *J. Am. Chem. Soc.*, **114**, 2147 (1992).
- Barton, D. H. R., Gastiger, M. J. and Motherwell, W. B., "A New Procedure for the Oxidation of Saturated Hydrocarbons", *J. Chem. Soc. Chem. Soc., Chem. Commun.*, **41**, 731 (1983).
- Barton, D. H. R., Lee, K. W., Mehr, W., Ozbalik, N. and Zhang, L., "Functionalization of Saturated Hydrocarbons", *Tetrahedron*, **46**, 3753 (1990).
- Chin, D. H., Balch, A. L. and La Mar, G. M., "Formation of Porphin Ferryl(FeO²⁺) Complexes through the Addition of Nitrogen Bases to Peroxo-bridged Iron(III) Porphyrins", *J. Am. Chem. Soc.*, **102**, 1446 (1980).
- Collman, J. P., Brauman, J. I., Meunier, B., Hayashi, T., Kodadek, T. and Raybuck, S. A., "Epoxidation of Olefins by Cytochrome P-450 Model Compounds", *J. Am. Chem. Soc.*, **107**, 2000 (1985).
- Dicken, C. M., Woon, T. C. and Bruce, T. C., "Kinetics and Mechanism of Oxygen Transfer in the Reaction of p-cyano-N,N-dimethyl Aniline N-oxide with Metalloporphyrin in Salts", *J. Am. Chem. Soc.*, **108**, 1636 (1986).
- Groves, J. T., Nemo, T. E. and Meyers, R. S., "Hydroxylation and Epoxidation Catalyzed by Iron-porphine Complexes", *J. Am. Chem. Soc.*, **101**, 1032 (1979).
- Lee, K. Y., Kim, S. B., Kim, Y. J. and Hong, S. I., "The Effect of Iron Catalysts on the Formation of Alcohol and Ketone in the Biomimetic Oxidation of Cyclohexane", *Bull. Korean Chem. Soc.*, **15**, 424 (1994).
- Mansuy, D., Bartoli, J. F. and Momenteau, M., "Alkane Hydroxylation Catalyzed by Metalloporphyrins", *Tetrahedron Lett.*, **23**, 2781 (1982).

- Nolte, R. J. M., Razenberg, J. A. S. J. and Schurman, R., "On the Rate-determining Step in the Epoxidation of Olefins by Monooxygenase", *J. Am. Chem. Soc.*, **108**, 2751 (1986).
- Ojima, R., Kobayashi, N. and Osa, T., "Catalytic Epoxidation of Cyclooctene with Oxygen Using Electrochemically Reduced Metalloporphyrins", *Bull. Chem. Soc. Jpn.*, **63**, 1374 (1990).
- Sugimoto, H., Tung, H. C. and Saywer, D. T., "Formation, Characterization and Reactivity of Oxene Adduct of [Tetrakis (2,6-dichlorophenyl) Porphinato]iron(III) Perchlorate in Acetonitrile", *J. Am. Chem. Soc.*, **110**, 2465 (1988).
- Traylor, T. G. and Miksatal, A. R., "Mechanism of Hemine-catalyzed Epoxidations", *J. Am. Chem. Soc.*, **109**, 2770 (1981).
- Traylor, T. G. and Xu, F., "Model Reactions Related to Cytochrome P-450", *J. Am. Chem. Soc.*, **10**, 1953 (1988).