Table I. Comparison of S–S Bond Lengths in Systems Containing S₄ Ligands

<table>
<thead>
<tr>
<th>S(1)–S(2)</th>
<th>S(2)–S(3)</th>
<th>S(3)–S(4)</th>
<th>ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.991 (13)</td>
<td>1.907 (19)</td>
<td>2.036 (14)</td>
<td>this work</td>
</tr>
<tr>
<td>2.014 (29)</td>
<td>2.017 (40)</td>
<td>2.041 (29)</td>
<td>this work</td>
</tr>
<tr>
<td>2.024 (8)</td>
<td>2.022 (10)</td>
<td>2.080 (10)</td>
<td>8</td>
</tr>
<tr>
<td>2.019 (5)</td>
<td>1.970 (6)</td>
<td>2.115 (5)</td>
<td>3</td>
</tr>
<tr>
<td>2.096 (16)</td>
<td>1.936 (19)</td>
<td>2.160 (19)</td>
<td>10</td>
</tr>
<tr>
<td>2.107 (1)</td>
<td>2.102 (1)</td>
<td>2.166 (1)</td>
<td>11</td>
</tr>
<tr>
<td>2.081 (8)</td>
<td>2.012 (1)</td>
<td>2.075 (1)</td>
<td>13</td>
</tr>
<tr>
<td>2.106 (16)</td>
<td>2.064 (14)</td>
<td>2.026 (9)</td>
<td>12</td>
</tr>
<tr>
<td>2.019 (3)</td>
<td>2.069 (19)</td>
<td>2.036 (19)</td>
<td>14</td>
</tr>
<tr>
<td>2.030 (3)</td>
<td>2.069 (19)</td>
<td>2.079 (3)</td>
<td>14</td>
</tr>
</tbody>
</table>

*Two or more crystallographically different S₄ groups per molecule.

On the Rate-Determining Step in the Epoxidation of Olefins by Monooxoxygenase Models

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Currently, synthetic metalloporphyrins are receiving considerable interest as models of the cytochrome P-450 class of enzymes. With single oxygen donors, e.g., iodosylbenzene, amine oxides, and hypochlorite, these compounds form high-valent oxometal complexes (e.g., 2), which, like the monooxoxygenases, are capable of oxygenating hydrocarbons. Recently, kinetic studies have appeared that deal with the mechanism of hydrocarbon oxidation by cytochrome P-450 models. In some of these studies it was proposed that the rate-limiting step in the reaction is the formation of the high-valent oxometal complex. In other studies, however, it was suggested that the rate-determining process is the transfer of oxygen from here to the substrate complex.

We wish to point out that (i), in certain cytochrome P-450 model systems, dimerization of the active metalloporphyrin may occur and (ii) that this dimerization reaction has consequences for the kinetic analysis of the systems. We will illustrate this point for the epoxidation of olefins by the monooxoxygenase model manganese(III) porphyrin with sodium hypochlorite as oxidant in the two-phase system water–dichloromethane (Meunier system). With regard to the rate-determining step in this model, conflicting opinions exist.

Previously, we reported that the epoxidation of cyclohexene by MnIII(TPP)OAc and NaOCl is zero order in substrate. Depending on the concentration of oxidant, the reaction order in hypochlorite varies between zero and one. We proposed that the rate-determining step in the catalytic process is the conversion of manganese(III) hypochlorite species I into the oxomanganese complex 2. This step is catalyzed by pyridine. Collman et al. recently measured the rate of epoxidation by MnIII(TPP)Cl and LiOCl for various olefins and likewise reported that the order in...
olefin is zero. Remarkably; however, they found that various olefins epoxidize at different rates. This result, which was confirmed by us, was taken by these authors as evidence for the involvement of olefin in the rate-determining step of the reaction. This step was proposed to be the decomposition of an intermediate metallooxetane \(^{(3)}\) formed from olefin and the active species 2 (Scheme I, step b). The above-mentioned kinetic results, however, can equally well be explained by a mechanism in which the formation of 2 is rate-determining (Scheme I, step a) and in which the decomposition of 2 goes via two routes: one with olefin to give epoxide and a second one with manganese(III) to form an unreactive dimer 4. Olefins with a higher reactivity will have a lower stationary-state concentration of 2 and, consequently, a smaller amount of manganese complex will be present in the equilibrium 2 =\(\rightleftharpoons\) 4. In this case, more manganese in the form of complex 1 will be available for further reaction. Hence, different olefins can display different rates in spite of the fact that they do not participate directly in the rate-determining step.\(^{(10)}\)

Figure 1. Rate of epoxidation of cyclohexene (●), 1-methylcyclohexene (O), and styrene (□) as a function of \(\text{Mnn(TPP)OAc}\) concentration.

Electronic - panchromatic (IV) porphyrin complexes have been isolated and characterized by Hill et al.: Smegal, J. A.; Schardt, B. C.; Hill, C. L. J. Am. Chem. Soc. 1983, 105, 3510-3515.

If we denote olefin by S, monomeric manganese porphyrin by Mn, dimeric manganese porphyrin by Dm, and the rate constants of the various steps in Scheme I as follows:

\[
\begin{align*}
1 & \rightarrow 2 \ (s=4) \\
& \rightarrow 3 \rightarrow \text{epoxide}
\end{align*}
\]

we can derive the following rate equation

\[
\gamma = \frac{(k_3 + k_2 \cdot [\text{Mn}]) \cdot [\text{S}]}{[\text{S} + (k_2 + k_3) \cdot k_1 \cdot [\text{Mn}]/k_2 \cdot k_3]}
\]

If we make the assumption \(k_2 \cdot [\text{Mn}] \ll k_1 \cdot [\text{Mn}]\) and \(k_2 \ll k_1 \cdot [\text{Mn}]\), (1) reduces to the more simple equation, (2). For reactive substrates or sterically hindered porphyrins, the kinetic analysis is now independent of manganese concentration and first order in substrate concentration. Experimentally, we found that for solutions containing, e.g., 0.8 M cyclohexene and 0.008 M \(\text{Mnn(TPP)OAc}\), deviation from zero-order behavior occurs after \(\approx 50\%\) of olefin had been converted. For lower catalyst concentrations (\(\text{Mnn(TPP)OAc} < 0.003 \text{ M}\) reactions remain zero order in substrate concentration up to 80\% conversion. A generalized kinetic analysis without the assumptions mentioned above will be given in a full paper. In the limiting cases, however, similar conclusions are reached.

Figure 2. Rate of epoxidation of cyclohexene as a function of catalyst concentration: \(\text{Mnn(TPP)OAc}\) (O), \(\text{Mnn(TMOPP)OAc}\) (●), \(\text{Mnn(TMOPP)OAc}\) (□), \(\text{Mnn(TMP)OAc}\) (△), \(\text{Mnn(TTMeOPP)OAc}\) (▲).

We have tested this hypothesis by measuring the rate of epoxidation as a function of manganese concentration for a number of olefins and manganese(III) porphyrins having different reactivities and steric requirements.\(^{(11)}\) Some data are given in Figures 1 and 2. For highly reactive substrates (e.g., styrene) the reaction order in manganese is one. The same result is obtained when porphyrins are used for which dimerization is not possible because of steric reasons (\(\text{Mnn(TPP)OAc}\) and \(\text{Mnn(TMOPP)OAc}\)). The remaining olefins and catalysts in Figures 1 and 2, however, display curves in which the rate levels off at high manganese concentrations, suggesting that active catalyst is taken away by the equilibrium 2 =\(\rightleftharpoons\) 4.

Further evidence which supports the dimerization of the active porphyrin in synthetic model systems comes from experiments with manganese porphyrins anchored to a rigid polymer support. These experiments reveal that on anchoring, which creates site isolation, the epoxidation rate is considerably enhanced.\(^{(18)}\)

Finally, we found that addition of methanol (25 vol \%), \(\text{MeOH}/\text{CH}_2\text{Cl}_2\) ratio in the organic phase 0.10 \(\rightarrow\) 0.05 to the reaction medium increases the rate by a factor of 3 and changes the reaction order in olefin from zero to one.\(^{(12)}\) We verified that addition of this reagent did not change the product distribution. In the presence of methanol, the conversion of unchanged 1 to charged 2 is probably facilitated due to the higher polarity of the medium. Step a is now accelerated to such an extent that the rate-determining step of the reaction changes to (b).\(^{(13)}\)

In conclusion, our experiments have revealed that dimerization of the metalloporphyrin may well be a complicating factor in the kinetic analysis of monooxygenase model systems.\(^{(14)}\) Our results for the manganese porphyrins can probably be transferred to other systems, e.g., the biologically more relevant iron porphyrins. Care should therefore be taken when drawing conclusions with regard to the rate-determining step in these systems.

Acknowledgment. We thank professor W. Drenth for stimulating discussions.

Registry No. \(\text{Mnn(TPP)OAc}\), 101565-34-8; \(\text{Mnn(TMOPP)OAc}\), 58356-65-3; \(\text{Mnn(TMOPP)OAc}\), 101565-35-9; \(\text{Mnn(TMP)OAc}\), 101565-36-0; \(\text{Mnn(TTMeOPP)OAc}\), 98827-71-5; \(\text{HClO}_2\), 7681-52-9; cyclohexene, 110-83-8; 1-methylocyclohexene, 591-49-1; styrene, 100-42-5; cytochrome P-450, 9035-51-2.

\(^{(11)}\) In a typical experiment, the following components were mixed: olefinic substrate (0.480 mmol), toluene (internal standard, 0.105 mmol), \(\text{Mnn(TPP)OAc}\) (1.72 \(\rightarrow\) 1.3 mmol), 4-methylpyridine (0.670 mmol), and benzyltriethylammonium chloride (2.8 \(\times\) 10\(^{-3}\) mmol) in \(\text{CH}_2\text{Cl}_2\) (0.5 mL). To this solution an aqueous solution of NaOCl (2 mL, 0.35 M, pH 13) was added. From time to time samples (1 mL) were taken which were analysed by GLC (carbowax 20 M on Chromosorb W-HP). We verified that under our conditions the catalyst was not starved of oxidant.


\(^{(13)}\) Kinetic data (details to be published in a full paper) suggest that complex 2 reacts with olefin to give an intermediate, whose structure is not fully understood yet. This intermediate could either be a metallooxetane (3), a carbocation \([\text{Mnn(O-C-C=C-C)}^+]\), or a radical \([\text{Mnn(O-C-C=C)}^+\].

\(^{(14)}\) The experiments in the literature (see ref 4) were conducted under somewhat different reaction conditions, i.e., using low catalyst concentration, LiOCl as oxidant, and an imidazole instead of pyridine. Under these conditions it could be possible that the rate-determining step is shifted to step b (Scheme I). Therefore, our results and those found in the literature may not be necessarily contradictory but can be interpreted to mean that the rate-determining step of the catalytic cycle depends on the reaction conditions employed.