Epoxidation Reaction Catalysed by Cyclodextrin Sandwiched Porphyrin in Aqueous Buffer Solution

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Cyclodextrin sandwiched porphyrin catalysed epoxidation of hydrophobic alkenes in an aqueous buffer solution.

Cytochrome P-450 is one of the most thoroughly investigated oxidases in biomimetic chemistry. Various types of porphyrins and redox systems have been successfully used to mimic the reactions of P-450.[1,2] However, the model system that uses a porphyrin derivative which has a hydrophobic binding site acting in an aqueous solution as in native P-450 is unknown.

Recently, we reported the synthesis of water soluble cyclodextrin sandwiched porphyrins, **1**, which have two binding pockets of cyclodextrin in its structure.[3] Since it is well established that the binding pocket of cyclodextrin can recognize various types of hydrophobic organic compounds in an aqueous solution,[4] these porphyrins are expected to show interesting behaviour as a P-450 model acting in an aqueous medium. We now report epoxidation of hydrophobic alkenes in an aqueous phosphate buffer using iodosobenzene as the oxygen source and **1** as the catalyst.

The Fe^{II} complex of cyclodextrin sandwiched porphyrin used here is the mixture of two types of diagonal isomer, **1a** and **1b** (Fig. 1). Tetrakis(*p*-sulphonatophenyl)porphyrin, **2**, was also used as the reference water soluble porphyrin catalyst, which has no hydrophobic binding site. The results of the present epoxidation reaction are summarized in Table 1 together with the experimental details. As one can easily see from Table 1, a reasonable amount of aliphatic and aromatic epoxide corresponding to the alkenes employed were obtained when **1** is used as the catalyst.

In contrast with these results, only a trace amount of cyclohexene oxide was observed for the **2**–cyclohexene–

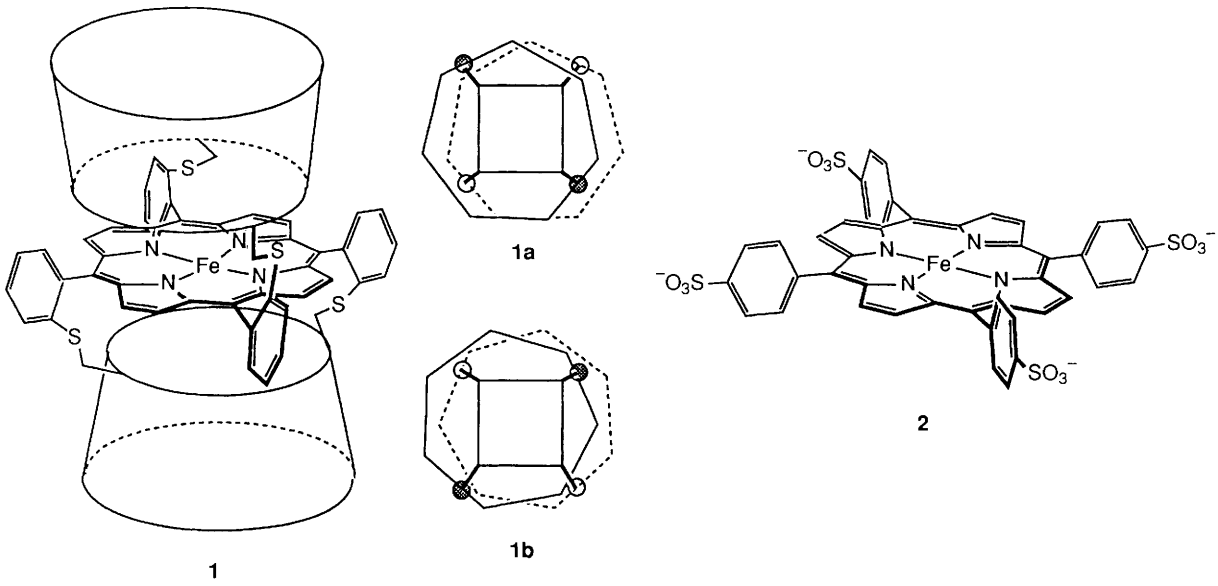

Fig. 1

Table 1 Epoxidation of alkane catalysed by **1** and **2** in aqueous phosphate buffer[a]

Run No.	Alkene	Catalyst	Yield (%)[b]
1	cyclohexene	**1**	55
2		**2**	<2
3	2,3-dimethylbut-2-ene	**1**	29
4		**2**	28
5	norbornene	**1**	14[c]
6	styrene	**1**	18
7	*p*-chlorostyrene	**1**	29

[a] Reaction conditions and procedures: To a phosphate buffer solution (250 μl, pH 7.4) of catalyst (3×10^{-4} mol dm^{-3}) and alkene (6×10^{-5} mol) was added the solution (50 μl) of iodosobenzene in methanol (5×10^{-2} mol dm^{-3}) for 2 h at 0 °C under Ar with vigorous stirring. The final mole ratio of components, alkene–iodosobenzene–catalyst, was 800 : 33 : 1. After extraction with ether, the product was analysed by GC. [b] Yields based on used iodosobenzene. [c] The product is the *exo*-isomer and, at the present time, no *endo*-isomer has been detected.

iodosobenzene system in the same buffer solution. Because the present reaction system is heterogeneous owing to the low solubilities of alkenes (also iodosobenzene) in the aqueous buffer solution, it is expected that the present marked difference between the catalytic abilities of **1** and **2** is due to the effective binding of hydrophobic alkenes and/or iodosobenzene in cyclodextrin cavities of **1**. In order to clarify which binding step is important for the present efficient catalytic effect of **1**, the epoxidation of 2,3-dimethylbut-2-ene which is more reactive than cyclohexene[5] has been investigated (see Table 1). The results clearly indicate that, even in the present aqueous media, the oxene of **2** is actually generated and trapped only by 2,3-dimethylbut-2-ene to afford the corresponding epoxide but not by less reactive cyclohexene. In the latter case, the oxene of **2** rather decomposes *via* reactions such as eqn. 1.[6]

$$\text{Fe}^{+}\text{=O} + \text{Fe–OH} \rightarrow 2\ \text{Fe=O} + \text{H}^{+} \qquad (1)$$

Thus, the present catalytic effect of **1** in the epoxidation of less reactive alkenes such as cyclohexene may be attributed to effective binding of alkenes in the cyclodextrin cavities of **1**.†

Interestingly, the cyclodextrin binding site of **1** also affects the substrate reactivities. The rate ratio of epoxidations determined by the competition of 2,3-dimethylbut-2-ene–cyclohexene is *ca.* 0.2 for **1**, while that for **2** is *ca.* 7 which is in good agreement with that reported for TPP–iodosobenzene system.[5] Thus, the present reaction catalysed by **1** seems to be dominated by steric factors rather than the usual electronic one.

The present results suggest that, in the reactions generating highly reactive intermediates in an aqueous solution such as that presently reported, the hydrophobic binding site on the porphyrin active site strongly affects not only the reactivities but also the reaction path.

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† Another possible explanation for the present results is that the oxene generated in the aqueous media is stablilized by the bulky and hydrophobic cyclodextrin groups of **1**.