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Porphinatoiron-Catalyzed Oxygenation of Styrene in Aqueous Solution

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A quantitative oxygenation of styrene to 1-phenylethanol is realized in a reaction catalyzed by an iron complex of 5,10,15,20-tetrakis(1-methyl-4-pyridinio)porphine tetrachloride (FeTMPyP) in water at pH 12 containing $NaBH_4$. A plausible mechanism involving a styrene carbanion stabilized by Fe(III)TMPyP as an intermediate is presented.

In spite of many attempts, no success has been achieved in wholly mimicking the enzyme reactions catalyzed by cytochrome P-450. In most model systems,1) alkenes are oxidized by iodosylbenzene or hydroperoxides to give epoxides in organic solvents containing metal complexes of 5,10,15,20-tetraphenylporphine (TPP) derivatives. Recently, sodium chlorite ($NaClO_2$) was found to oxidize saturated hydrocarbons in manganese porphyrin catalyst system.2) These model systems are quite useful to study the mechanisms for mono-oxygenation of alkenes or alkanes by metal oxo complexes. The biological system, however, uses molecular oxygen and water as an oxidizing agent and a solvent, respectively. As a preliminary step to overcome such difficulties, we tried to oxidize styrene by molecular oxygen which is activated by a water-soluble porphinatoiron in water.3) An iron complex of 5,10,15,20-tetrakis(1-methyl-4-pyridinio)porphine tetrachloride (Fe(III)TMPyP•Cl) was used as a catalyst. Sodium borohydride ($NaBH_4$) was essential for oxygenation of styrene. A tetrahydroborate anion (BH_4^-) has already been used in the cytochrome P-450 model reactions in organic solvents.4) We report herein a plausible mechanism involving a styrene carbanion stabilized by Fe(III)TMPyP as an intermediate.

A typical example of the reaction is as follows. Styrene (1 mmol) and Fe(III)TMPyP•Cl (5 μmol) was added into 5 ml of aqueous alkaline solution (pH 12, NaOH) in a flask and the reaction atmosphere was replaced by oxygen. Aliquots (0.5 ml) of an aqueous alkaline solution (pH 12) of $NaBH_4$ (1 mmol/2.5 ml) were added into the flask at intervals of 1 h. The mixture was stirred at room temperature during the reaction. The total reaction time was 5

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h. The reaction mixtures were analyzed by means of gas chromatography. The results are listed in Table 1.

Table 1. FeTMPyP-Catalyzed Oxygenation Reactions of Alkenes in Aqueous Alkaline Solution (pH 12) at Room Temperature[a)]

Catalyst	Substrate	Conversion/%	Product (yield/%)[b)]
FeTMPyP	styrene	100	1-phenylethanol (100)
FeTMPyP	*p*-chlorostyrene	73	1-(*p*-chlorophenyl)ethanol (39) *p*-chloroacetophenone (34)
FeTMPyP	*p*-methoxystyrene	82	1-(*p*-methoxyphenyl)ethanol (14) *p*-methoxyacetophenone (65)
FeTMPyP	*cis*-stilbene	39	no oxygenation product
FeTMPyP	cyclohexene	-	no oxygenation product
FeTMPyP	vinylcyclohexane	-	no oxygenation product
Hemin	styrene	98	no oxygenation product
Fe(III)EDTA	styrene	77	no oxygenation product
Vitamin B_{12}	styrene	100	1-phenylethanol (9)
Co(II)salen	styrene	100	1-phenylethanol (35)

a) The reactions were carried out under the same conditions as described in the text.

b) The yields were calculated on the basis of the initial concentration of the substrate.

FeTMPyP-catalyzed reaction of styrene affords 1-phenylethanol in a quantitative yield (turnover number = 200 molecules/mole of catalyst) whereas 1-phenylethanol (31%) and benzyl alcohol (1%) were the products in the FeTPP-catalyzed reaction of styrene in C_6H_6-C_2H_5OH (1:1).[5)] In the cases of *p*-chlorostyrene and *p*-methoxystyrene, the corresponding acetophenone derivatives were formed along with their reduced products. Although both *p*-chloroacetophenone and *p*-methoxyacetophenone are easily reduced with $NaBH_4$ in homogeneous solution, the reduction is suppressed in aqueous medium because of the poor solubilities of these ketones in water. On the basis of these findings, it may be quite reasonable that the acetophenones are selectively produced as the intermediates in the FeTMPyP-catalyzed oxygenation of the styrenes. Another characteristic of the reactions in aqueous solutions is substrate selectivity. No oxygenation proceeds for *cis*-stilbene, cyclohexene, and vinylcyclohexane in the aqueous FeTMPyP system. FeTMPyP was the best catalyst amongst the metal complexes used in this work.

Deuterium incorporation during the course of the reaction of styrene was studied by using $NaBD_4$ and D_2O. The results are summarized in Table 2. The results can be explained in terms of a rapid H-D exchange of methyl protons of acetophenone in the presence of NaOH (Scheme 1) and suggest that acetophenone is the only precursor of 1-phenylethanol. The problem is the origin of a proton of a methyl group of acetophenone. We believe that a proton of the methyl group comes from $NaBH_4$. In a previous paper, we reported a hemin-catalyzed Markovnikov-type addition of thiophenol to styrene in C_6H_6-C_2H_5OH where a methyl proton

Table 2. Deuterium Incorporation during FeTMPyP-Catalyzed Reaction of Styrene in Aqueous Alkaline Solution (pH 12)

Solvent	Reducing agent	Product[a)]
H_2O	$NaBD_4$	$C_6H_5CD(OH)CH_3$
D_2O	$NaBH_4$	$C_6H_5CH(OD)CD_3$
D_2O	$NaBD_4$	$C_6H_5CD(OD)CD_3$

a) The products were isolated by silica gel column chromatography and analyzed by means of ^1H NMR and mass spectroscopy.

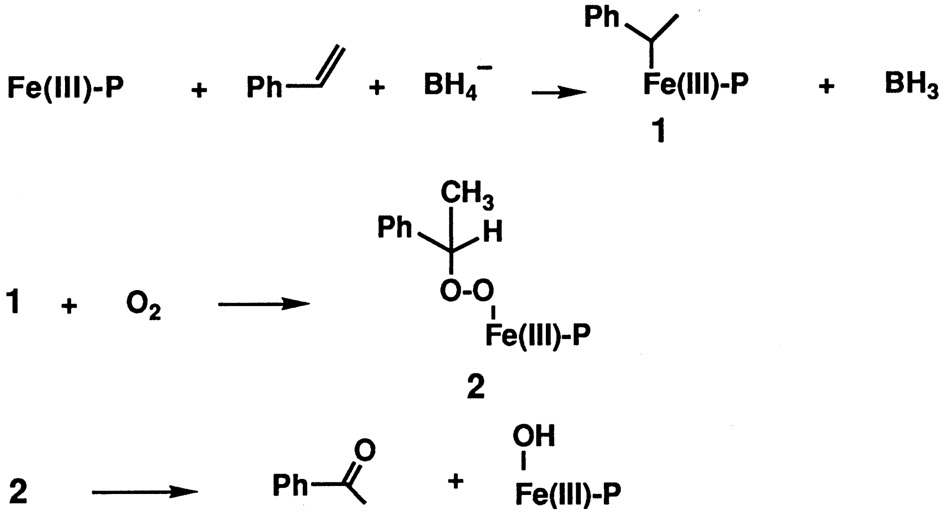
$$C_6H_5\text{-}CH{=}CH_2 \xrightarrow{\text{FeTMPyP/NaBH}_4} C_6H_5COCH_3 \xrightarrow{D_2O/OH^-}$$

$$C_6H_5COCD_3 \xrightarrow{NaBH_4/D_2O} C_6H_5CH(OD)CD_3$$

Scheme 1.

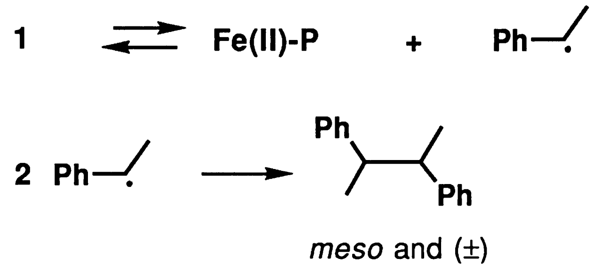
of the adduct (phenyl 1-phenylethyl sulfide) has been proved to be provided by $NaBH_4$.[6)]

On the basis of these results, we assumed the following mechanism for the oxygenation of styrene in the water-soluble porphinatoiron catalyst system:



Scheme 2.

Since styrene oxide is hardly reduced by BH_4^-, the oxirane may not be produced as a reaction intermediate. It may be reasonable to consider, therefore, that an iron oxo porphyrin complex is not an active species of the monooxygenation reaction. Then we assumed a styrene carbanion stabilized by Fe(III)TMPyP (**1**) as an intermediate, which has also been postulated for the hemin-catalyzed addition reactions of thiols to styrene.[6)] Quite recently, Setsune and Ishimaru[7)] have detected the similar σ-alkyl complexes of Fe(III)TPP, which are formed by the reactions of alkenes with Fe(III)TPP in an organic solvent containing $NaBH_4$, by means of ^1H NMR. The formation of 1,4-dideuterio-2,3-diphenylbutanes (*meso* and (±), ca. 2 % yield) was detected by means of GC-MS spectroscopy when the reaction was carried out using $NaBD_4$ under a nitrogen atmosphere, and can be explained in terms of an equilibrium between **1** and a styrene radical and Fe(II)TMPyP (Scheme 3). This strongly supports the intermediate **1** formed by the reaction of styrene, $NaBH_4$, and Fe(III)TMPyP. Intermediate **1** may easily react with oxygen to give acetophenone.[8]



Scheme 3.

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