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DEOXYGENATION OF TERTIARY AMINE N-OXIDES AND ARENE OXIDES BY IRON(II) PORPHYRIN AS A MODEL OF CYTOCHROME P-450 DEPENDENT REDUCTION[1]

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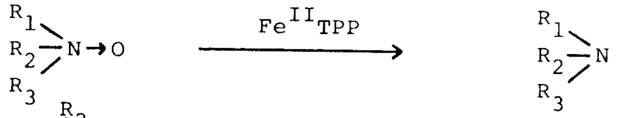
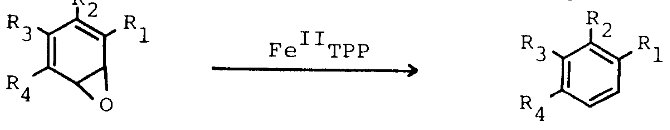
Tetraphenylporphinatoiron(II), a model complex of reduced cytochrome P-450, reduces several substrates such as tertiary amine N-oxides and arene oxides at room temperature in anaerobic conditions. A process for the direct oxene transfer from oxide to reduced iron porphyrin is suggested.

KEYWORDS——cytochrome P-450; reduction; deoxygenation; tertiary amine N-oxide; tetraphenylporphinatoiron(II); oxene transfer; arene oxide; ferryl oxide

Cytochrome P-450 catalyzes wide varieties of oxidation by the reductive activation of molecular oxygen at its iron porphyrin site. Besides this major role, much evidence for the involvement of cytochrome P-450 in microsomal reduction has been reported in recent years.[3] This cytochrome P-450 dependent reduction can be divided into two groups. One is the reductive deoxygenation of several oxides such as amine oxides[3a] and arene oxides,[3b] and the other is one electron reduction of nitro compounds,[3c] and alkyl halides.[3d] The active species in these reductions is presumed to be a reduced state of cytochrome P-450, containing an iron(II) porphyrin complex, which is formed in a catalytic cycle of the oxidation of substrates.[4] In fact, the one electron reduction activity of iron(II) porphyrin complex has been well studied[5] but the reductive deoxygenation activity has hardly been reported. In this paper, we wish to report the deoxygenation of amine oxides (eq. 1) and arene oxides (eq. 2) by tetraphenylporphinatoiron(II) ($Fe^{II}TPP$),[6] a model complex of the reduced cytochrome P-450.



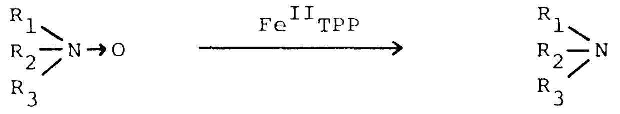
(eq. 1)



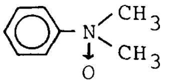
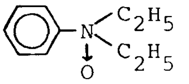
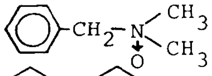
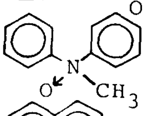
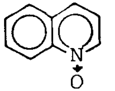
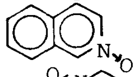
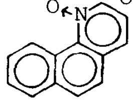
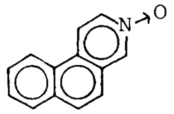
(eq. 2)

In a typical experiment, tertiary amine N-oxide (0.01 mmol) was treated with $Fe^{II}TPP$ (0.02 mmol) in methylene chloride (10 ml) under strictly anaerobic conditions. Deoxygenation took place smoothly and the absorption spectrum of $Fe^{II}TPP$ changed to that of μ-oxo dimer ($(FeTPP)_2O$). The yields of the corresponding tertiary amine are summarized in Table I. No appreciable deoxy-

Table I. Reductive Deoxygenation of Amine N-Oxides by $Fe^{II}TPP$



$$R_1R_2R_3N\rightarrow O \xrightarrow{Fe^{II}TPP} R_1R_2R_3N$$

Substrate	Reaction time	Yield (%)[a]
	5 min	88
	5 min	88
	5 min	87
	5 min	66
	15 h	83
	18 h	50
	45 h	66
	45 h	63

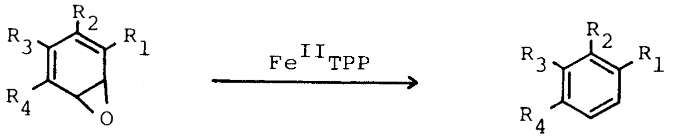
a) Yields were determined by HPLC analysis.

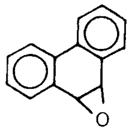
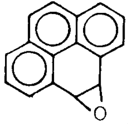
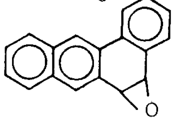
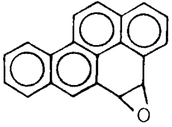
genation occurred with $Fe^{III}TPPCl$, the μ-oxo dimer or $FeCl_2$. Heteroaromatic amine oxides, listed in Table I, were also reduced to the corresponding amines, but longer reaction times were required.

Deoxygenation of several arene oxides to the parent hydrocarbons also proceeded, as summarized in Table II. When the deoxygenation of phenanthrene-9,10-oxide was run by the use of a large excess amount of epoxide (30-fold mol) to $Fe^{II}TPP$, the reaction proceeded more smoothly and the yield of phenanthrene went up over 70% based on $Fe^{II}TPP$. This indicates that the reduction activity of $Fe^{II}TPP$ was effectively used in this reaction system. Styrene oxide, *cis*- and *trans*-stilbene oxides, and cyclohexene oxide were scarcely reduced to the parent hydrocarbons. The fact that only the arene oxides, among several epoxides, are reduced agrees with the reduction properties of cytochrome P-450 reported by Sims and coworkers.[7)]

To elucidate the reductive deoxygenation mechanism, the reduction of quinoline N-oxide by $Fe^{II}TPP$ was carried out under the pseudo-first-order conditions [quinoline N-oxide] $\gg$ [$Fe^{II}TPP$]. The kinetics for the reduction of quinoline N-oxide, monitored by the change of the absorption spectrum of $Fe^{II}TPP$, was found to be of the first order in $Fe^{II}TPP$. Additionally, by using stoichiometric amounts

Table II. Reductive Deoxygenation of Arene Oxides by $Fe^{II}TPP$



Substrate	Reaction time	Yield (%)[a]
	2.5 h	21
	30 h	12
	60 h	8
	60 h	8

a) Yields were determined by HPLC analysis.

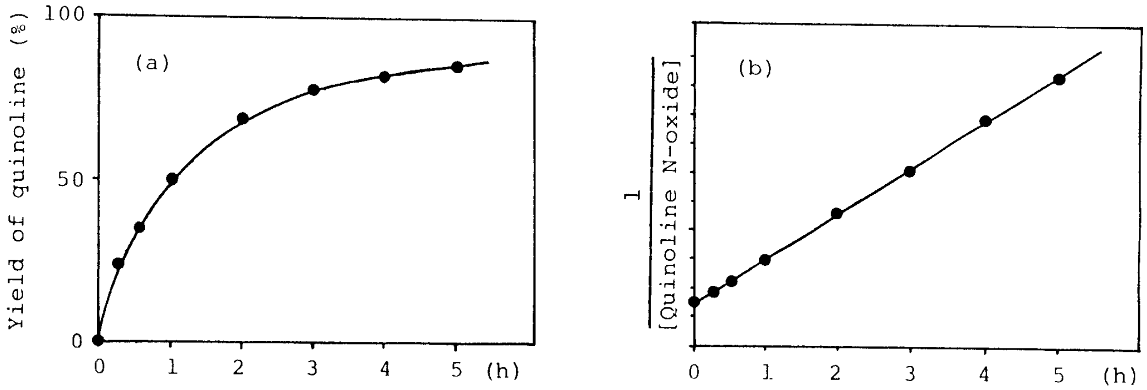


Fig. 1. The Time Course of the Yield of Quinoline (a), and 1/[Quinoline N-oxide] *vs.* Time (b), in the Reaction of Quinoline N-Oxide (0.01 mmol) with $Fe^{II}TPP$ (0.02 mmol)

of quinoline N-oxide and $Fe^{II}TPP$, the formation rate of quinoline was examined by HPLC (Fig. 1a). Since a plot of the reciprocal of the remaining quinoline N-oxide *vs.* time gave a straight line as shown in Fig. 1b, this reaction was found to be of the second order. Accordingly, it was ascertained that the deoxygenation is of the first order in both $Fe^{II}TPP$ and quinoline N-oxide.

On the basis of these results, it appears that $Fe^{II}TPP$ directly abstracts an oxygen atom from the oxide to form ferryl oxide (Fe^{IV}=OTPP) species as a reaction intermediate. However, ferryl oxide could not be detected in this reaction system. So we tried to prove the intermediary formation of ferryl oxide by using triphenylphosphine as an oxene acceptor from ferryl oxide.[8] That is, in the presence of an excess amount of triphenylphosphine (0.5 mmol), N,N-dimethylaniline N-oxide (0.13 mmol) in CH_2Cl_2 (10 ml) was treated with a catalytic amount of Fe^{II}TPP (0.01 mmol) under argon atmospher. Fe^{II}TPP was immediately oxidized in this system and 0.115 mmol of N,N-dimethylaniline was formed with the corresponding amount of triphenylphosphine oxide (the turn over number of Fe^{II}TPP was 11.5). As triphenylphosphine itself scarcely reduced amine oxides, it is concluded that Fe^{II}TPP is effectively reproduced by triphenylphosphine as summarized in Chart 1.

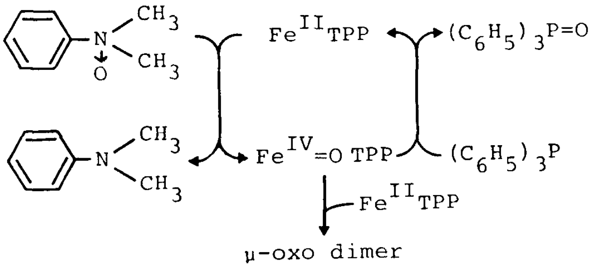


Chart 1

The results reported here clearly demonstrate that the reduced iron porphyrin has an ability to reduce amine oxides and arene oxides, and that ferryl oxide plays a key role in an oxygen atom transfer reaction.

REFERENCES AND NOTES

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