Alkene Epoxidation by Iodosylbenzene Catalysed by Porphyrin and Non-porphyrin Iron Complexes: the Importance of the Porphyrin Ligand in Cytochrome P-450 and Heme Model Reactions

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$FeCl_3$ and $Fe(acac)_3$ (acac = acetylacetonato), like Fe(TPP)(Cl) (TPP = tetraphenylporphyrinato), catalyse the epoxidation of styrene and stilbenes and the oxidation of non-1-ene by PhIO; however, several characteristics of the oxidations catalysed by non-porphyrin iron complexes, such as stereospecificity and sensitivity to dioxygen, are very different from those of the corresponding reactions catalysed by Fe(TPP)(Cl).

Cytochrome P-450-dependent mono-oxygenases catalyse alkane hydroxylation and alkene epoxidation not only by dioxygen in the presence of NADPH but also by oxygen-atom donors such as alkyl hydroperoxides or iodosylbenzene.[1] Simple Fe-,[2] Mn-,[3] and Cr-porphyrins,[4] as well as Cr(salen)-$(H_2O)PF_6$[5] [salen = *N*,*N*′-ethylenebis(salicylideneaminato)] or $Cu(NO_3)_2$[6], have also been found to catalyse alkene epoxidation by PhIO. As models for cytochrome P-450, simple iron-porphyrins, such as Fe(TPP)(Cl) (TPP = tetraphenylporphyrinato), are of special interest since several characteristics of the PhIO-dependent alkene oxidations that they catalyse, such as the total stereospecificity of epoxidation

of stilbenes[2a] and 1,2-dialkylethylenes[2b] and the secondary formation of allylic alcohols[2] and aldehydes (in the case of monoalkylethylenes[7]), are very similar to those of the corresponding enzymatic oxidations. This suggests that the thiolate ligand which is present in cytochrome P-450 is not necessary for the catalysis of oxygen atom transfer from PhIO to substrates. In order to determine the role of the porphyrin ligand, we have compared the PhIO-dependent oxidations of alkenes catalysed by porphyrin and non-porphyrin iron complexes and report here preliminary results showing that although the porphyrin ligand is not necessary for iron(III) catalysis of alkene epoxidation, it plays an important role in the control of the regioselectivity and stereospecificity of the reactions.

Under anaerobic conditions, $FeCl_3$ (5mM in MeCN) and $Fe(acac)_3$ (acac = acetylacetonato) (5mM in C_6H_6) catalyse the oxidation of styrene by PhIO (alkene : catalyst : PhIO 50 : 1 : 5) leading exclusively to styrene oxide (30 and 38% yield, based on PhIO, respectively). Under identical conditions Fe(TPP)(Cl) (5mM in C_6H_6) gives styrene oxide (50%) and minor amounts of phenylacetaldehyde (2%). However, although the Fe(TPP)(Cl)-catalysed reactions give almost identical yields and rates (Figure 1) under either anaerobic or aerobic conditions, the reactions catalysed by $FeCl_3$ or $Fe(acac)_3$ are greatly affected by the presence of O_2. Under aerobic conditions, the yield of styrene oxide decreases to about 10% and a new product, benzaldehyde, appears, its yield based on PhIO being as high as 350 and 210% after 50 h for $Fe(acac)_3$ and $FeCl_3$, respectively (Figure 1). On the other hand, the Fe(TPP)(Cl)-catalysed oxidation of styrene leads only to traces of PhCHO (5% after 50 h). Neither styrene oxide nor benzaldehyde are formed if either PhIO or the iron catalyst is omitted from the mixture. Moreover, PhCHO is not formed by oxidation of styrene oxide under the reaction conditions since treatment of the latter by the complete system (containing the iron catalyst, PhIO, and O_2) fails to give PhCHO and leaves styrene oxide unchanged.

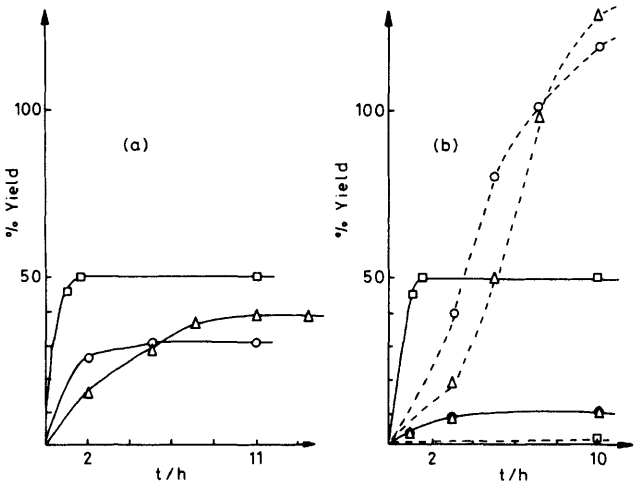

Figure 1. Formation of styrene-oxide (—) and benzaldehyde (- - -) *vs.* time in the oxidation of styrene by iodosylbenzene catalysed by Fe(TPP)(Cl) (□), $FeCl_3$(○), or $Fe(acac)_3$(△), under (a) an argon atmosphere and (b) aerobic conditions. Conditions indicated in the text. Under aerobic conditions, PhCHO formation ceased after 50 h, its yield being 350, 210, and 5% for $Fe(acac)_3$, $FeCl_3$, and Fe(TPP)(Cl), respectively.

As previously reported,[2a] Fe(TPP)(Cl) catalyses the stereospecific epoxidation of stilbenes by PhIO (Table 1). $Fe(acac)_3$ and $FeCl_3$ also catalyse the epoxidation of *cis*- and *trans*-stilbene but with lower yields and in a non-stereospecific manner (Table 1). It is now generally thought that Fe^{III}-porphyrin(P)-catalysed epoxidation of alkenes by PhIO involves the addition of a Fe^{IV}–O· species to the double bond and the efficient control of the radical so formed by the Fe^{IV} intermediate[2,7] [equation (1)], explaining the observed stereospecificity and the lack of influence of O_2 on the reaction because of the very short half-life of the intermediate radical.

If one considers a similar mechanism for epoxidations catalysed by non-porphyrin iron complexes, the above results, *i.e.* the lack of stereospecificity on epoxidation of stilbene and

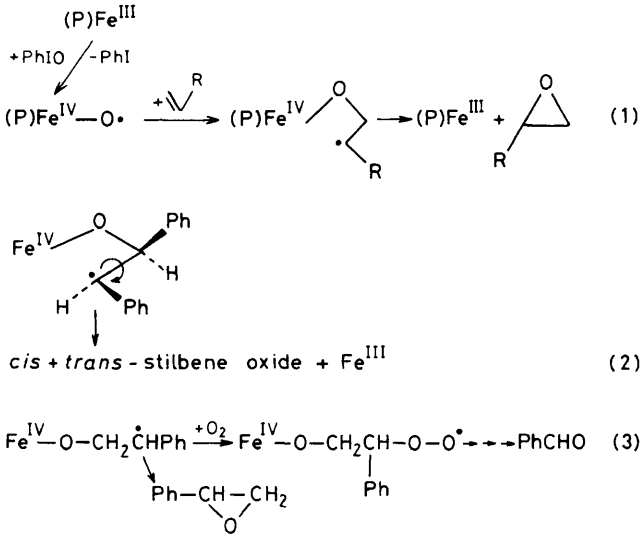

Table 1. Oxidation of alkenes by iodosylbenzene catalysed by iron complexes under anaerobic conditions.

Alkene	Products	Yield (%)[a] Fe(TPP)(Cl)	$Fe(acac)_3$	$FeCl_3$
Styrene	Styrene oxide	50	38	30
	Phenylacetaldehyde	2	0	0
cis-Stilbene	*cis*-Stilbene oxide	42	13	1
	trans-Stilbene oxide	0	4	3
trans-Stilbene	*cis*-Stilbene oxide	0	0	2
	trans-Stilbene oxide	8	8	7
Non-1-ene	Non-1-ene oxide	20	1	3
	Non-1-en-3-ol	5	1	2
	Non-2-en-1-ol[b]	1	0	5
	Nonanal	1	0	0

[a] Yields based on the initial amount of iodosylbenzene. Conditions indicated in the text. [b] The *cis* and *trans* isomers were not separated under our g.l.c. conditions.

the considerable influence of O_2 on styrene oxidation, could be explained by less efficient control of the intermediate alkene-derived free radical by the non-porphyrin than by the porphyrin iron catalysts [equations (2) and (3)]. However, at present a mechanism involving reactive species different from the proposed Fe^{IV}–O· species for oxidations catalysed by non-porphyrin iron complexes cannot be excluded.

Table 1 also illustrates the very different behaviour of the iron catalysts towards PhIO-dependent oxidation of a less reactive alkene, non-1-ene, under anaerobic conditions. With Fe(TPP)(Cl), the epoxide is the main product[2] and allylic alcohols and nonanal are formed as minor products.[7] With $FeCl_3$, the regioselectivity of non-1-ene oxidation is very different and the allylic alcohols are formed predominantly, indicating that the active species is more likely to abstract allylic hydrogen atoms than to add to the double bond.[2b] Furthermore, with $FeCl_3$, the primary alcohol becomes the major allylic alcohol product suggesting that the intermediate allylic radical derived from allylic hydrogen abstraction is less efficiently controlled by the iron catalyst.[8] $Fe(acac)_3$ has only a very slight catalytic effect on non-1-ene oxidation by PhIO.

These results show that non-porphyrin iron complexes can catalyse alkene epoxidation by PhIO, and suggest that the porphyrin ligand could play two important roles in cytochrome P-450- or iron-porphyrin-catalysed oxidations: to control efficiently the intermediate free radical formed upon oxidation of the substrate, which is the origin of the generally observed stereospecificity, and to modulate the intrinsic reactivity of the active oxygen–iron complex, which is at the origin of the regioselectivity observed in alkene oxidation.

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