

# Hydrogen Atom Transfer vs. Electron Transfer in Iron(III) Porphyrin catalysed Benzylic Oxidations

Enrico Baciocchi,<sup>a</sup> Manuela Crescenzi,<sup>b</sup> and Osvaldo Lanzalunga<sup>a</sup>

<sup>a</sup> Dipartimento di Chimica, Università 'La Sapienza,' 00185 Roma, Italy

<sup>b</sup> Centro CNR di Studio sui Meccanismi di Reazione, Roma, Italy

The scope of hydrogen atom transfer and electron transfer mechanisms has been established for the benzylic oxidations of alkylaromatic compounds and benzyltrimethylsilanes induced by an iron(III) porphyrin complex.

The study of oxidation reactions catalysed by iron-porphyrin complexes, which mimic the activity of the cytochrome P-450 family of enzymes, is attracting continuing interest.<sup>1</sup> Among these reactions the hydroxylation of saturated carbon atoms is one of the most important, being intensively investigated from both the mechanistic and the synthetic point of view.

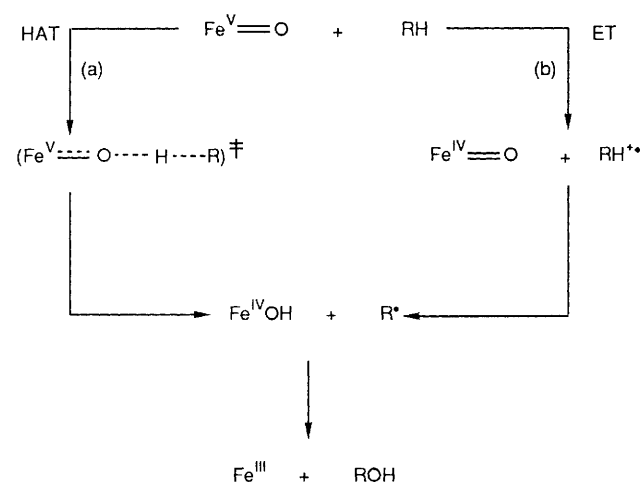
Generally, this process is discussed in terms of a critical step involving hydrogen atom transfer (HAT) from the substrate to the perferryl oxygen atom (formally indicated as Fe<sup>V</sup>=O), formed by interaction of the iron(III)-porphyrin complex with a suitable oxygen donor (iodosylbenzenes, peroxy acids, etc.) (Scheme 1, path a).

However, evidence in this respect has mainly been based on studies of unactivated alkanes<sup>2</sup> and it is therefore possible that an electron transfer (ET) mechanism takes over when more electron-rich substrates are used. A radical cation is produced (Scheme 1, path b), which is then deprotonated to give the

same radical pair formed in the HAT mechanism. In both cases collapse of this pair leads to the hydroxylated product. Indeed, an ET mechanism seems to occur in some reactions of cytochrome P-450 involving easily oxidizable compounds.<sup>3-5</sup>

We have felt that relevant information with respect to the scope of the two competing mechanisms could be obtained by the application of the criteria which our group has shown to be very suitable for distinguishing ET from HAT pathways in the side-chain oxidation of alkylaromatic compounds.<sup>6-8</sup> Thus, we report in this paper on the oxidation of the substituted benzenes (1) and (2) and silanes (3) and (4) promoted by iodosylbenzene in the presence of iron(III) tetrakis(pentafluorophenyl)porphyrin chloride [Fe(tfpp)Cl], an iron porphyrin which mimics quite well the properties of cytochrome P-450.<sup>9</sup> Reactions have been run in CH<sub>2</sub>Cl<sub>2</sub> and in CH<sub>2</sub>Cl<sub>2</sub>-MeOH-H<sub>2</sub>O (80:18:2).

The distribution of the isomeric alcohols (5) and (6) (Z = Bu<sup>t</sup> or Cl), *i.e.* the intramolecular selectivity, obtained in the

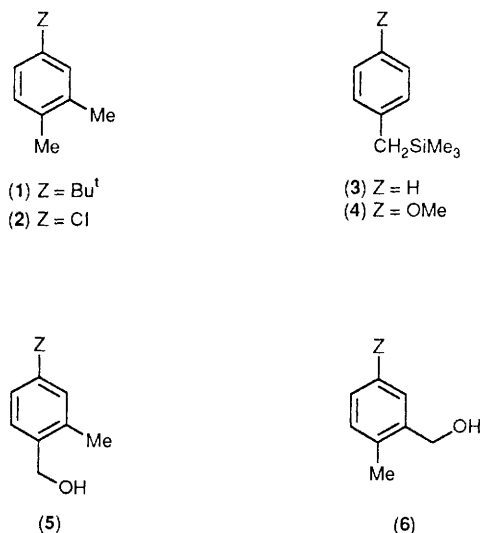


Scheme 1

**Table 1.** Ratios of products (5) and (6) in some side-chain oxidations of 4(Z)-substituted 1,2-dimethylbenzenes (1) and (2).

Z	Ratios of (5) to (6)			
	Fe(tfpp)Cl <sup>a</sup>			
	CH <sub>2</sub> Cl <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub> -MeOH-H <sub>2</sub> O <sup>d</sup>	NBS <sup>b</sup>	CAN <sup>c</sup>
Bu <sup>t</sup>	1.9:1 (23.6%)	2.0:1 (12.0%)	1.6:1	6.0:1
Cl	2.2:1 (43.8%)	2.2:1 (11.3%)	3.0:1	13.0:1

<sup>a</sup> Reactions carried out at room temperature for 30 min under dry argon. Molar ratio of substrate, PhIO, and catalyst, 100:10:1. The overall yields of alcohols referred to iodosylbenzene are in parentheses. <sup>b</sup> In CCl<sub>4</sub> at 80 °C, (5) and (6) were obtained by hydrolysis of the corresponding bromides. <sup>c</sup> In AcOH, (5) and (6) were obtained by hydrolysis of the corresponding acetates. <sup>d</sup> 80:18:2.



**Table 2.** Side-chain reaction products in the oxidation of some 4(Z)-benzyltrimethylsilanes (3) and (4) catalysed by Fe(tfpp)Cl.<sup>a</sup>

Z	Products (% yield) <sup>b</sup>	
	CH <sub>2</sub> Cl <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub> -MeOH-H <sub>2</sub> O
H	PhCHO (1.8)	PhCHO (3.2)
OMe	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> CHO (12.5)	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> CHO (21.3)
		<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OMe (5.1)
		<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH (14.2)

<sup>a</sup> For conditions see footnote a, Table 1. <sup>b</sup> Yields referred to iodosylbenzene.

Fe(tfpp)Cl-induced oxidation of (1) and (2) is reported in Table 1, together with the corresponding data<sup>7</sup> for the reaction of the same substrates with ammonium cerium(IV) nitrate (CAN), a *bona fide* one-electron transfer oxidant, and with Br<sup>•</sup> (*N*-bromosuccinimide), a species which certainly reacts by a HAT mechanism.

The intramolecular selectivity of the Fe(tfpp)Cl-catalysed reactions is close to that observed in the free-radical bromination, but significantly different from that found in the ET reactions with CAN. Thus, most probably these oxidations take place by a HAT mechanism.

The results for the oxidation of benzyltrimethylsilanes are displayed in Table 2. In both solvents the reaction of Fe(tfpp)Cl with (3) leads to benzaldehyde, a result not compatible with an ET mechanism. Fast desilylation to give a benzyl radical is the preferred reaction pathway for a benzyltrimethylsilane radical cation.<sup>8,10</sup> Thus, an ET mechanism would have led to benzylic derivatives (*i.e.* benzyl alcohol), which was not observed.† The formation of benzaldehyde can instead be rationalized by the HAT mechanism:  $\alpha$ -hydroxybenzyl-trimethylsilane is first produced which is then readily oxidised to benzaldehyde under the reaction conditions.‡

The oxidation of the more electron-rich silane (4) takes a different course.§ In this case the reactions in the two solvents lead to a different product mixture. Whereas in CH<sub>2</sub>Cl<sub>2</sub> only 4-methoxybenzaldehyde is formed (HAT mechanism), in CH<sub>2</sub>Cl<sub>2</sub>-MeOH-H<sub>2</sub>O substantial formation of benzylic derivatives (4-methoxybenzyl alcohol and 4-methoxybenzyl methyl ether) is observed. Thus it seems that under the latter conditions an ET mechanism begins to operate, probably favoured by the greater polarity of the medium, which allows a better stabilization of the intermediate radical ions,<sup>11</sup> and by the high energy of the Si-O bond formed by nucleophilic attack of H<sub>2</sub>O and MeOH at the silicon atom of (4)<sup>++</sup>. The latter factor would make the breaking of the C-Si bond compete successfully with back electron transfer.

† Benzyl alcohol, if formed, would have survived under the reaction conditions.

‡  $\alpha$ -Hydroxybenzyltrimethylsilane is completely converted to benzaldehyde under our reaction conditions. See also: J. Yoshida, T. Murata, and S. Isoe, *J. Organomet. Chem.*, 1988, **C23-C24**, 345.

§ An  $E_p$  value of 1.84 V *vs.* standard calomel electrode (SCE) for (3) has been measured in MeCN.<sup>8</sup> A 4-methoxy substituent should decrease this value by 0.6–0.7 V. Compare the  $E_p$  values for toluene and *p*-methoxytoluene: S. Fukuzumi and J. K. Kochi, *J. Am. Chem. Soc.*, 1981, **103**, 7240.

In conclusion, these results indicate that in a solvent of low polarity, like CH<sub>2</sub>Cl<sub>2</sub>, the HAT mechanism is the preferred one for benzylic oxidations catalysed by iron porphyrins.¶ It is also interesting that the scope of the HAT mechanism extends to include substrates with an oxidation potential as low as 1.4–1.2 V. In more polar solvents there is evidence for a changeover to an ET mechanism, which should occur at values of substrate oxidation potential of *ca.* 1.8–1.2 V. However, in view of the possible specific solvent effect discussed above, it is not yet certain whether the latter conclusion can also be applied to substrates not containing a  $\beta$ -silicon atom in the side chain.

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¶ According to preliminary experiments the same conclusions hold for reactions induced by iron(III) tetrakis(2,6-dichlorophenyl)porphyrin chloride.