Intermediate Formation of a σ-Alkyl Iron(III) Complex in the Reduction of 4-Nitrobenzyl Chloride catalysed by Iron(II)-porphyrins

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Formation of the σ-alkyl Fe^{III} (TPP)($CH_2C_6H_4NO_2$-4) complex (TPP = tetraphenylporphyrin) during reduction of 4-nitrobenzyl chloride (**1**) by sodium ascorbate catalysed by Fe(TPP)(Cl) was detected by visible spectroscopy, and its involvement as an intermediate in the reduction of (**1**) to 4-nitrotoluene was deduced from a study of the characteristics of this reaction.

Several compounds containing a carbon–halogen bond are reduced by iron(II)-porphyrins and hemoproteins, the first step of the reaction being the formation of the free radical derived from a one-electron reduction of the carbon–halogen bond.[1] Reduction of polyhalogenated compounds such as CCl_4 by iron-porphyrins[2] and cytochrome P450,[3] in the presence of an excess of reducing agent, leads to stable iron(II)-carbene complexes according to equation (1). The reaction steps leading from the free radical to the carbene complex are not yet well known. However, the intermediate formation of σ-alkyl-iron complexes in the reduction of halogenated compounds by iron(II)-porphyrins has been

$$\begin{array}{l} \overset{-X^-}{\longrightarrow} \\ RR'CX_2 + Fe^{II} \longrightarrow Fe^{III} + RR'\dot{C}X \\ \qquad\qquad\qquad\qquad \downarrow +2e^-,\ -X^- \\ \qquad\qquad\qquad\qquad [Fe^{II} \leftarrow CRR'] \end{array} \qquad (1)$$

postulated,[1] and, recently, complexes formed by reaction between Fe^{II}(deuteroporphyrin) and chloromethyl and methyl radicals have been detected, using pulse radiolysis techniques.[4] It is noteworthy that σ-alkyl iron complexes were prepared by other techniques such as reactions of an iron(III)-porphyrin with a Grignard reagent[5] and of an iron(I)-porphyrin with an alkyl halide.[6]

In this paper, a detailed study of the reduction of 4-nitrobenzyl chloride, (**1**), to 4-nitrotoluene, catalysed by an iron-porphyrin, is reported. Evidence is presented for the intermediate formation of a σ-alkyl Fe^{III}–$CH_2C_6H_4NO_2$-4 complex in this reaction.

A biphasic system with sodium ascorbate as a reducing agent in water (phosphate buffer pH 7.4) and Fe^{III}(TPP)(Cl) (TPP = tetraphenylporphyrin) in catalytic amounts in toluene, in the presence of trioctylmethylammonium chloride as a phase transfer agent, is able to perform most of the microsomal NADPH- and cytochrome P450-dependent reductions of organic substrates.[7,8] Reduction of (**1**) by this system was followed by gas chromatography–mass spectrometry and visible spectroscopy. The only reaction product was found to be 4-nitrotoluene, its formation being quantitative after 7 h reaction under argon at 20 °C with the following molar ratio of the reactants: Fe(TPP)(Cl) 2.5×10^{-3} M: (**1**): ascorbic acid = 1:10:100. The phase transfer and electron transfer [Fe(TPP)(Cl)] catalysts are absolutely necessary for this reduction to take place. In the aforementioned conditions, 0.2 mol of 4-nitrotoluene are formed per mol of Fe(TPP)(Cl) and per min (initial rate). The initial rate of the reaction is a decreasing function of the pH of the aqueous phase (Table 1) and is significantly reduced in the presence of dioxygen.

When the reaction is followed by visible spectroscopy, it is observed that two iron-porphyrin complexes exist simultaneously in steady state concentrations: Fe^{II}(TPP) and a new complex (**2**), characterized by two peaks at 412 and 523 nm. The proportion of complex (**2**) considerably decreases when the pH is lowered (Table 1). Accordingly, when (**1**) is reduced by Fe^{II}(TPP) in the presence of iron powder in a less acidic medium (CH_2Cl_2:MeOH = 20:1), complex (**2**) is almost quantitatively formed and is the only iron-porphyrin complex present in a steady state concentration during the reaction. Its visible spectrum (Figure 1), λ(ε) 412 (110 000) and 523 (10 500 $dm^3\ mol^{-1}\ cm^{-1}$) nm in toluene, is nearly superimposable on those of the σ-vinyl[9]- or σ-alkyl-iron(III)-(TPP)[6] complexes recently reported. Moreover, as has also been found for these complexes, complex (**2**) is very sensitive to dioxygen† and HCl, leading respectively to $[Fe(TPP)]_2O$ and Fe(TPP)(Cl) within a few seconds. It is noteworthy that reaction of complex (**2**) with HCl also leads quantitatively to 4-nitrotoluene.

Table 1. Reduction of 4-nitrobenzyl chloride by an iron-porphyrin system: influence of pH on the initial reaction rate and on the intermediate formation of complex (**2**).

pH	2.5	4	7.4	9
V_0[a]	0.70 ± 0.02	0.45 ± 0.02	0.20 ± 0.01	0.10 ± 0.01
% (**2**)[b]	0	5	8	10

[a] Initial rates in mol of 4-nitrotoluene formed per mol of Fe(TPP)(Cl) and per min, at 20 °C (conditions indicated in the text). [b] The proportions of complex (**2**) [(**2**)]/[(**2**)] + [Fe^{II}-(TPP)] were measured on samples of the reaction mixtures after dilution in toluene. Because of the sensitivity of (**2**) to dioxygen, they were probably underestimated. During the reduction (between t = 15 min and *ca.* 4 h), they were found to be almost constant.

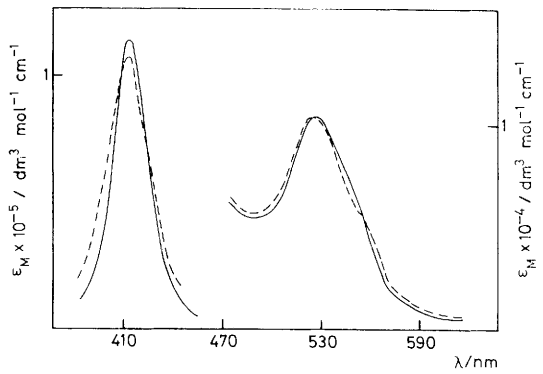

Figure 1. Comparison of the electronic spectra of complex (**2**) (——) and of the σ-vinyl complex [Fe^{III}(TPP)(CH=CPh_2)] (ref. 9) (– – – –) in toluene, at 25 °C.

The mechanism shown in equations (2)—(5) for the reduction of (**1**) to 4-nitrotoluene by the ascorbic acid-dependent system takes into account the reported data.

$$4\text{-}NO_2C_6H_4CH_2Cl + (TPP)Fe^{II} \rightarrow (TPP)Fe^{III}\text{–}Cl + 4\text{-}NO_2C_6H_4CH_2^{\bullet} \quad (2)$$
(**1**)

$$4\text{-}NO_2C_6H_4CH_2^{\bullet} + (TPP)Fe^{II} \rightarrow (TPP)Fe^{III}\text{–}CH_2C_6H_4NO_2\text{-}4 \quad (3)$$

$$(TPP)Fe^{III}\text{-}CH_2C_6H_4NO_2\text{-}4 + H^+ \rightarrow (TPP)Fe^{III} + CH_3C_6H_4NO_2\text{-}4 \quad (4)$$
(**2**)

$$(TPP)Fe^{III} + e^- \text{(ascorbic acid)} \rightarrow (TPP)Fe^{II} \quad (5)$$

The involvement of reaction (2) is consistent with the propensity of (**1**) to give the 4-nitrobenzyl radical upon one-electron reduction[11] and is in agreement with the mechanism indicated by Castro *et al.* for the reduction of halogenated compounds by iron(II)-porphyrins.[1] The formation of complex (**2**) in equation (3) is in agreement with the detection of σ-alkyl complexes by combination of Fe^{II}(deuteroporphyrin) with methyl radicals using pulse radiolysis techniques.[4] The formation of 4-nitrotoluene from equation (4), and not from the possible abstraction of a solvent (toluene) hydrogen atom by the 4-nitrobenzyl radical, is supported by the following results. (i) When the reduction is performed in a $C_6D_5CD_3$–H_2O mixture, deuteriated 4-nitrotoluene is not observed, whereas $4\text{-}NO_2C_6H_4CH_2D$ is mainly formed (91% deuterium incorporation) when toluene and D_2O are used as solvents. (ii) No product deriving from the 4-nitrobenzyl radical by dimerization or reaction with the solvent could be detected in the reaction mixture. (iii) The reduction rate increases while the steady-state concentration of complex (**2**) decreases, when the pH of the aqueous phase is lowered (Table 1).

Although formation of σ-alkyl complexes by reaction of iron(II)-porphyrins with some carbon free radicals was deduced from pulse radiolysis studies,[4] no evidence has so far been presented for the involvement of such complexes as intermediates in the catalytic cycle of the iron-porphyrin-dependent reduction of halogenated compounds. The above data support such a mechanism, equations (2)—(5), for compound (**1**) reduction by a heme system exhibiting reducing properties similar to those of cytochrome P450. This

† Because of the extreme sensitivity to O_2 of complex (**2**), we were unable to get satisfactory ^1H n.m.r. and mass spectral data. However, in the case of the analogous [Fe('C_{12}-TPP-Basket Handle') ($CH_2C_6H_4NO_2$-4)] (ref. 10) complex, which is slightly more stable than complex (**2**), we were able to observe signals at −13.04 and −13.12 p.p.m. for its pyrrole protons, very similar to those described for the corresponding protons of low-spin σ-alkyl Fe^{III} ('C_{12}-TPP-Basket Handle')(R) complexes (ref. 6).

suggests that σ-alkyl-cytochrome P450 complexes could be involved in the metabolic reduction of halogenoalkanes, and that σ-alkyl iron(III) complexes could be intermediates in the formation of carbene complexes of iron-porphyrins[2] or cytochrome P450,[3] equation (6).

$$\begin{array}{ccccc} & & \overset{-X'^-}{\longrightarrow} & & \\ R_2CXX' + (P)Fe^{II} & & \longrightarrow R_2\dot{C}X + & (P)Fe^{III} & \\ & & & \downarrow +e^- & \\ & & \overset{+e^-}{\longleftarrow} & & \\ (P)Fe^{II} \leftarrow CR_2 & \longleftarrow & [(P)Fe^{III}CXR_2] & & (6) \\ & & \underset{-X^-}{} & & \end{array}$$

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