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Halomethane Adducts of Iron(II) Porphyrins

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The second step in the reductive hydrogenolysis of alkyl halides by hemes entails the one-electron reduction of a free radical.[1,2]

We have postulated a hydrolytically unstable (porphyrin)-iron-alkyl species as an intermediate in this process (1) (P = porphyrin). The reaction (1) is extremely rapid and competes

$$R\cdot + (P)Fe^{II} \rightarrow ((P)Fe\text{–}R) \xrightarrow[H(solv)]{H^+} (P)Fe^{III} + RH \quad (1)$$

efficiently with radical–radical recombination. Thus if the iron–alkyl species is an intermediate, it must rapidly hydrolyze.

Recent pulse radiolytic work[3-5] has confirmed the swiftness of the reaction of iron(II) porphyrins with radicals ($k_1 \approx 10^9$ 1/(mol s)), but the final product of the reaction was deduced to be a (porphyrin)iron–alkyl. Major confirming evidence for the methyl case was obtained by observing the same visible spectrum from the reaction of methyl iodide with sodium dithionite and iron(II) deuteroporphyrin IX. These reactions, presumably (2) or (3) followed by (4), were conducted in 1:1 isopropyl alcohol–water containing phosphate buffer at pH 7.2 or sodium hydroxide at 0.1 M.

$$CH_3I \xrightarrow[(CH_3)_2CHOH/H_2O]{Co^{60}} CH_3\cdot + I^- \quad (2)$$

$$CH_3I + SO_2^{-}\cdot \rightarrow SO_2 + CH_3I^{-}\cdot \rightarrow CH_3\cdot + I^- \quad (3)$$

$$CH_3\cdot + (P)Fe^{II} \rightarrow (P)Fe\text{–}CH_3 \quad (4)$$

We have employed the exact system described by Brault and colleagues in an attempt to generate simple (porphyrin)iron–alkyls and delineate their general chemistry. We find, however, that the product of these reactions is not an iron–alkyl but rather a methyl iodide complex of an $S = 1$ iron(II) porphyrin.

Results and Discussion

The spectrum of an argon-purged solution of chloroiron(III) deuteroporphyrin in 1:1 isopropyl alcohol–water 0.1 N in NaOH is shown in Figure 1.[6a] Treatment with a 10% molar excess of $Na_2S_2O_4$[6b] under argon results in the iron(II) porphyrin (dashed line, Figure 1). Addition of CH_3I results in the spectrum (dotted line Figure 1) ascribed to the iron–CH_3 compound. The spectrum remained unchanged for days. The rate of complex formation is first order each in heme and CH_3I ($k_2 = 0.3$ L/(mol s)).

The addition of HCl to this solution under argon demetalated the complex *without* the production of methane (eq 1). An experiment with $^{14}CH_3I$ upon reaction and demetalation afforded only deuteroporphyrin IX. No counts could be detected in the porphyrin fraction. The counts were recovered as CH_3I and CH_3OH (the solvolysis product). Moreover, these oxygen-sensitive solutions readily formed the carbonyl and bis(*N*-methylimidazole) adducts of deuteroheme upon admission of carbon monoxide or *N*-methylimidazole. All of these reactions are characteristic of an iron(II) porphyrin. Finally, NMR analysis of the reaction solution before and after the addition of methyl iodide shows that both species, corresponding to the dashed and dotted spectra in Figure 1, are iron(II) deuteroporphyrin IX of intermediate spin $S = 1$ (Figure 2).[6c]

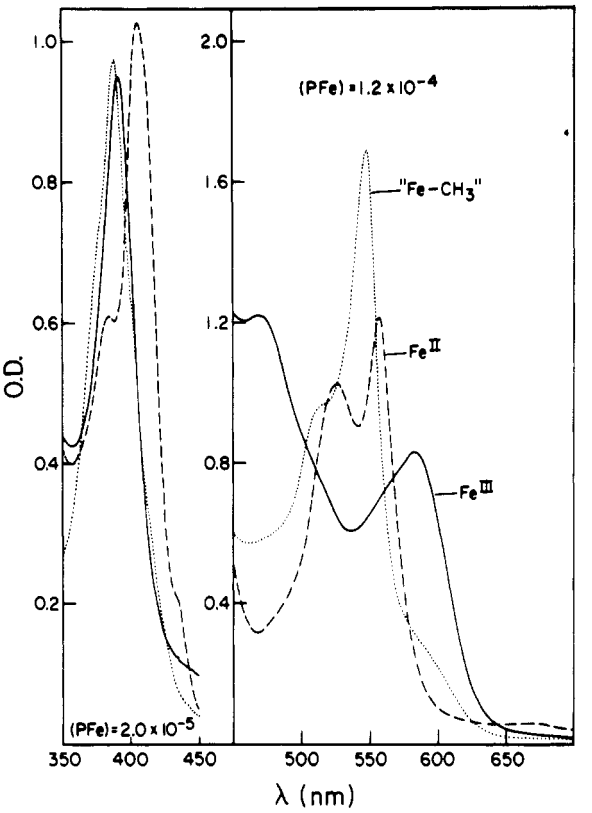

Figure 1. Visible spectrum of the reaction of iron(III) deuteroporphyrin IX with sodium dithionite and methyl iodide.

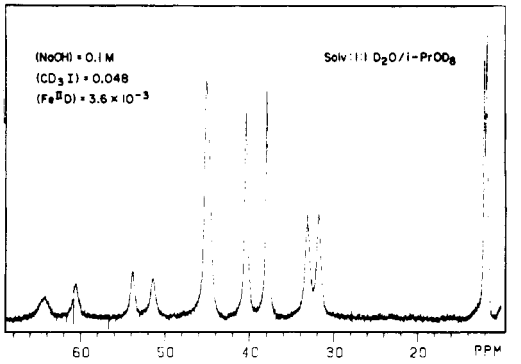

Figure 2. 300-MHz NMR spectrum of the iron(II) deuteroporphyrin IX–methyl iodide complex.

The spectrum in Figure 2 is that of the alleged iron–CH_3. It corresponds to the NMR spectrum of iron(II) deuteroporphyrin dimethyl ester in benzene,[7a] but the spectrum is somewhat compressed and broadened.[7b]

Thus, while the visible spectrum of the heme changes significantly upon addition of the halide, the NMR spectrum does not. The results suggest a simple complex formation between alkyl halide and heme (5) that does not significantly remove the iron

$$(P)Fe^{II} + RX \rightleftarrows (P)Fe^{II}(XR) \quad (5)$$

from the porphyrin plane.[8] Other halides (CH_3Cl, CH_3Br, CCl_4) previously associated with iron–alkyl generation[3-5,9] will effect the same visible spectral change elicited by CH_3I. Kinetic evidence

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(6) (a) The visible spectrum resembles a μ-oxo dimer of iron(III) porphyrin; however, magnetic measurement indicated the species is $S = {}^5/_2$. We presume it is a monohydroxy adduct. (b) A 100-fold excess of dithionite does not alter the results. (c) Visible spectra of the heme or complex were not altered at the higher NMR concentrations. The NMR spectrum of the heme was not changed by the addition of CD_3I.
(7) (7a) Goff, H.; LaMar, G. N.; Reed, C. A. *J. Am. Chem. Soc.* **1977**, *99*, 3641. (b) We presume this is due to the different solvent and the fact that in 0.1 M NaOH the disodium salt is dominant. The solution approaches the limits of solubility.
(8) For example, 2-methylimidazole adducts are pentacoordinate $S = 2$ species.[7]
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for 1:1 complex formation between alkyl halides and high-spin hemes in *N*-methylpyrrolidone–acetic acid has been obtained,[2] though no direct observation of such species has been reported. In the present system, an excess of sodium dithionite (presumably by rapidly rereducing the iron(III) porphyrin) allows observation of the halide complex formation preceding oxidation of the heme by CCl_4.

The dotted line in Figure 1 has generally been taken as characteristic of iron–alkyls in solution.[10-12] The present work suggests structures assigned on this basis may be incorrect. The exact geometry of the alkyl halide–heme binding in these complexes awaits further investigation. We tentatively formulate them as loosely affiliating with iron.[13]

Complex formation with halides appears to be a general reaction of hemes, and it is not limited to the specific system examined here. For example, iron(III) octaethylporphyrin can be reduced to the heme by group 1 and 2[17] organometals[14] in toluene. Addition of methyl iodide to these solutions produces a visible spectrum nearly identical with that of the complex shown in Figure 1. The NMR spectrum corresponds exactly to $S = 1$ octaethylheme.

Experimental Section

Materials. Chloroiron(III) deuteroporphyrin IX was obtained as previously described.[1] Methyl iodide (Aldrich, reagent grade), methyl bromide (Matheson, 99.5%), (^{14}C)methyl iodide (New England Nuclear), deuterium oxide (99.8% D), perdeuterio-iso-propanol and perdeuteriomethyl iodide, Aldrich, 99+% D, Gold Label) were used without purification. The specific activity of the (^{14}C)methyl iodide was 1.86×10^6 dpm/μL or 10 mc/millimole. Mallinckrodt AR grade isopropyl alcohol, carbon tetrachloride, and methylene chloride were freshly distilled. Sodium dithionite (Fisher Scientific) solutions were made up fresh and used within 15 min.

Solutions of deuterohemin (1.2–12.0 mg) in 1.5 mL of 0.1 M NaOH were diluted with water and phosphate buffer (10^{-2} M, pH 7.2) as described by Brault et al.[5] Forty milliliters of this solution was added to 50 mL of isopropyl alcohol and made up to 100 mL with buffer. The final concentration in these stock solutions was 2.0×10^{-5}–2.00×10^{-4} M. The visible spectrum (Figure 1) resembled that of a μ-oxo dimer.

Stock solutions of higher concentrations were also prepared in 1:1 0.1 M sodium hydroxide–isopropyl alcohol. The visible spectra were identical with those prepared in the buffer solution. Magnetic measurements by the Evans method in the manner recently described[15] indicate a μ_{eff} of 5.79 μ_B or a high-spin iron(III) complex.

NMR Analyses. Solutions of the complex for NMR analysis were prepared by adding 10 μL of 0.22 M sodium dithionite and 1 μL of perdeuteriomethyl iodide, under argon, to 550 μL of an argon-purged solution of 3.6×10^{-3} M hemin in 1:1 perdeuterioisopropyl alcohol–D_2O (0.1 M in NaOH). The solutions were prepared in a long (9-in.) NMR tube that was fitted with a 14/20 ST glass joint. To this was attached a joint that contained an in-line serum-capped stopcock and a similarly equipped splayed side arm. The argon inlet was No 22 gauge hypodermic tubing inserted through the center stopcock to the bottom of the tube. The splayed outlet stopcock was also used for reagent addition. Before it was sealed, the bottom half of the tube was cooled in an *i*-PrOH–CO_2 bath and the argon inlet tube was pulled up into the upper fitting. Properly sealed tubes exhibited the same visible spectrum (dotted line, Figure 1) for months. Visible spectra of the optically dense NMR solutions were taken of the film on the sides of the tube above the solution. An appropriately equipped Cary 118C spectrophotometer was employed for this purpose, and careful alignment was essential. NMR spectra were recorded in a 300-MHz Nicolet machine. For routine spectra of nonparamagnetic porphyrin samples a Varian EM-390 spectrometer was employed.

^{14}C Counting. A Packard Tricarb Model 3255 liquid scintillation counter was employed. The counting matrix was Packard "Instagel". Usually 0.25–100 μL of sample was counted and corrected as previously described.[16]

Reactions. In a typical reaction a four-neck flask was equipped with argon inlet and outlet stopcocks, a serum-capped stopcock, a manometer, a bottom stopcock port for a solution transfer, and a magnetic stirring bar. The flask was charged with 150 mL of 2.00×10^{-4} M hemin in buffer–*i*-PrOH. The free space was 46 mL. The solution was briefly evacuated and thoroughly purged with argon. Under slight argon pressure and purge 330 μL of 0.1 M sodium dithionite was added with stirring. The brown solution immediately became red (dashed line, Figure 1). Methyl iodide, 180 μL (3.0×10^{-3} mol), was added and the solution was stirred for 10 min. The visible spectrum corresponded to the dotted line in Figure 1. At this time the argon stopcocks were closed and 3 mL of concentrated HCl was added. The solution developed the purple color of the porphyrin dication. No pressure change was observed, and no methane could be detected in either the liquid or gas phase by gas chromatography (four-ft. Porapak Q column, detectability <0.5%). The whole was opened to air and concentrated to near-dryness on a rotary evaporator at 60 °C. The porphyrin residue was taken up entirely in methanol containing 5% HCl and allowed to stand 3 days. The solutions was stripped to dryness. The cation dimethyl ester was taken up in methylene chloride washed with sodium acetate–water, dried over sodium sulfate, filtered, and stripped to dryness. The porphyrin ester was dissolved in 0.5 mL of $CDCl_3$. The NMR spectrum of this solution was identical with that of deuteroporphyrin IX dimethyl ester.

In similar fashion 25 mL of 2.0×10^{-4} M hemin was reacted with 13 μL of 0.425 M sodium dithionite and 3 μL of $^{14}CH_3I$ (4.8×10^{-5} mol, 5.6×10^6 dpm). After 1.5 h, the red complex solution was made slightly acidic with 12 μL of concentrated HCl and opened to air. The brown hemin solution was distilled in vacuo at 25 °C and reduced to a volume of 5 mL. The distillate receiver was cooled in an *i*-PrOH–CO_2 bath. The hemin precipitated from the concentrate and was centrifuged, washed with water, and centrifuged three times. The entire hemin was dissolved in 1 mL of methanol and counted for radioactivity. No counts above background were detected (±0.5%). The combined disillate and water washes contained 99 ± 1% of the original counts. In addition to CH_3I gas chromatography of the disillate showed the presence of traces of CH_3OH.

Reactions could also be conducted in appropriately equipped spectrophotometric cells.[15] The spectra reported in Figure 1 were obtained in this way. Gassing solutions of the complex with carbon monoxide produced the spectrum of the carbonyl adduct of deuteroheme. Addition of *N*-methylimidazole produced the iron(II) bis(*N*-methylimidazole) adduct. The spectra were identical with those obtained by corresponding treatment of the iron (II) porphyrin in the absence of methyl iodide.

The rate of complex formation with methyl iodide was assessed from repeated scans of the visible spectrum over the 600–450-nm regions.

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Registry No. Chloroiron(III) deuteroporphyrin IX, 21007-21-6; iron(II) porphyrin IX, 18922-88-8.

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(16) Castro, C. E.; Wade, R. S.; Belser, N. O. *Biochemistry* **1985**, *24*, 204.
(17) In this paper the periodic group notation is in accord with recent actions by IUPAC and ACS nomenclature committees. The d-transition elements comprise groups 3 through 12, and the p-block elements comprise groups 13 through 18. (Note that the former Roman number designation is preserved in the last digit of the new numbering: e.g., III → 3 and 13.)

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A Reconsideration of the Kinetics of the Arbuzov Reaction Involving $[CpCo(dppe)X]^+$ ($X^- = Cl^-, Br^-, I^-$) and $P(OR)_3$ (R = Me, Et)

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Several conclusions about the kinetics of the Arbuzov reaction involving $[CpCo(dppe)X]^+$ ($X^- = Cl^-, Br^-, I^-$) and $P(OMe)_3$[1]

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