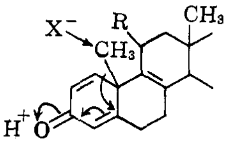
servations, in addition to others to be elaborated on in a more detailed report, suggest that the halide ion initially generated by elimination of the 9α-halogen attacks the C-19 methyl group facilitated by protonation of the C-3 oxygen. Prior to this, or perhaps concurrently, an allylic shift, elimination, and isomerization provide the double bonds required for the aromatization of ring B



$X = Cl^-$ or Br^-
R = Cl or OH

Further work is in progress on the nature of the structural features in rings B and C necessary for the aromatization reaction to take place.

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RECEIVED APRIL 11, 1964

The Rapid Oxidation of Iron(II) Porphyrins by Alkyl Halides. A Possible Mode of Intoxication of Organisms by Alkyl Halides

Sir:

Low-valent iron porphyrin complexes are manifest in all aerobic organisms and are essential to life.[1] Yet, the chemistry of these substances has remained obscure because of their difficult preparation and ready air oxidation.[2a,b] Knowledge of the kinds of molecules that are capable of undergoing oxidation–reduction reactions with iron porphyrin complexes should be helpful to an understanding of the detailed mechanism of "electron transport" in biological systems.

The author wishes to report that dilute solutions of Fe^{II} porphyrins are rapidly oxidized by alkyl halides at room temperature to the corresponding Fe^{III} halide complexes (hemins).

Thus, solutions of Fe^{II} deuterioporphyrin ($Fe^{II}D$) (λ_{max} 550, 522 mμ) in 1:1 isopropyl alcohol–acetic acid,[3] under nitrogen, saturated with KCl, are rapidly oxidized to deuteriohemin ($Fe^{III}DCl$) (λ_{max} 620, 524, 498 mμ) by the following halides: allyl chloride, phenacyl chloride, α-phenethyl chloride, 2,2-bis(*p*-chlorophenyl)-1,1,1-trichloroethane (DDT), 1,2-dibromo-3-chloropropane, hexachloroethane, and *cis*-1,3-dichloropropene. Both *n*-propyl chloride and β-phenethyl chloride were innocuous. Very dilute solutions of Fe^{II} protoporphyrin were oxidized in similar fashion.

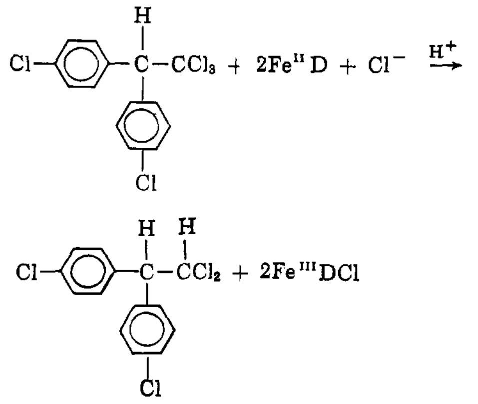
The rate of oxidation of $Fe^{II}D$ by *cis*-1,3-dichloropropene was determined spectrophotometrically by following the Fe^{III} band at 620 mμ. The third-order rate expression (1) was obtained from pseudo-second-order plots at varying high initial concentrations of halide. The rate constants[4] are presented in Table I.

$$\text{rate} = k_3[Fe^{II}D]^2[RCl] \qquad (1)$$

TABLE I

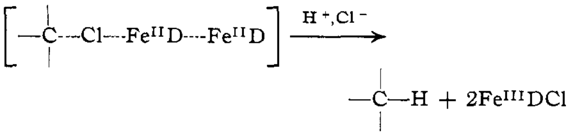
$[Fe^{II}D]_0$, *M*	$[RCl]_0$, *M*	k_3, l.²/mole²/min.
2.08×10^{-4}	0.0275	4.4×10^4
2.08×10^{-4}	0.0550	4.0×10^4
2.08×10^{-4}	0.0550	4.1×10^4
2.08×10^{-4}	0.110	4.1×10^4

Under similar conditions, allyl chloride, α-phenethyl chloride, and DDT were extremely reactive. The rate of oxidation of $Fe^{II}D$ by DDT was estimated from the slopes of concentration *vs.* time plots at various initial concentrations of reactants. The rate expression (1) was obeyed with $k_3 \sim 3 \times 10^7$ l.²/mole²/min. This reaction proceeds quantitatively to the hydrogenolysis product[5,6] (2)—a transformation of DDT recently reported to occur with yeast cells.[6a]



(2)

A plausible transition state for these oxidations might be (3) in which chlorine is transferred from carbon to iron.[7]



$$\left[-\overset{|}{\underset{|}{C}}\cdots Cl\cdots Fe^{II}D\cdots Fe^{II}D \right] \xrightarrow{H^+, Cl^-} -\overset{|}{\underset{|}{C}}-H + 2Fe^{III}DCl \qquad (3)$$

The rapidity of these reactions suggests that if a haloorganic biocide survives the nucleophilic sites[8] of a cell wall,[9] it may readily interact with an iron center in the respiratory chain.[10] This interaction should be an attractive alternate to "alkylation"[11] as a mode of intoxication.

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[1] For a recent survey, "Haematin Enzymes," J. E. Falk, R. Lemberg and R. K. Morton, Ed., Pergamon Press, London, 1961.

[2] (a) H. Fischer, A. Treibs, and K. Zeile, *Z. Physiol. Chem.*, **195**, 1 (1931); (b) D. G. Whitten, E. W. Baker, and A. H. Corwin, *J. Org. Chem.*, **28**, 2363 (1963).

[3] The preparation of these solutions by the iron powder reduction of deuteriohemin was patterned after the recent description of ferrous mesoporphyrin IX dimethyl ester; ref. 2b.

[4] Good pseudo-second-order plots were obtained in some cases through 90% completion.

[5] Gas and thin layer chromatographic properties of the product as well as a mixture melting point (111°) were identical with those of authentic material.

[6] (a) B. J. Kallman and A. K. Andrews, *Science*, **141**, 1051 (1963). A series of unusual metabolic dehalogenations have been observed; (b) T. C. Butler, *J. Pharmacol.*, **134**, 311 (1961), $CCl_4 \rightarrow CHCl_3$ (dogs); (c) R. T. Williams, "Detoxication Mechanisms," John Wiley and Sons, Inc., New York, N. Y., 1959, p. 31, $Cl_3C{-}CCl_3 \rightarrow Cl_2C{=}CCl_2 + Cl_2CHCHCl_2$ (rabbits). These conversions are not unlike those effected by low-valent metal ions [C. E. Castro and W. C. Kray, Jr., *J. Am. Chem. Soc.*, **85**, 2768 (1963)] and might be explained by a process analogous to (2).

[7] Whether or not a bridging ligand (Cl) should be present between the iron atoms remains open.

[8] S. Bartnicki-Garcia and W. J. Nickerson, *Biochem. Biophys. Acta*, **58**, 102 (1962).

[9] This is reasonable since rates of nucleophilic displacement are by comparison slow. Thus, the basic hydrolysis of *cis*-1,3-dichloropropene and related allylic chlorides proceeds with $k_2 \sim$ 0.1–0.3 l./mole/hr. at room temperature [L. J. Andrews and R. E. Kepner, *J. Am. Chem. Soc.*, **70**, 3458 (1948)].

[10] Moreover, the fact that alkyl halides can affect the respiratory system has been noted [R. L. Metcalf, Symposia Genetica et Biologica Italia Celebrazione Spallanzaniana VIII, 1961, p. 431].

[11] Reference 6b, p. 25, S. E. Lewis, *Nature*, **161**, 692 (1948); W. Moje, J. P. Martin, and R. C. Baines, *J. Agr. Food Chem.*, **5**, 32 (1957).

Acknowledgment.—This work was supported by the National Science Foundation, NSF G19145, and the National Institutes of Health, EF 00079-01, for which the author is grateful. The author wishes to thank Dr. Lyle Gaston for pure samples of DDT and DDD and for helpful analytical advice.

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RECEIVED APRIL 4, 1964

Pentacyanobenzylcobaltate(III). A New Series of Stable Organocobalt Compounds

Sir:

We wish to report the preparation and characterization of a new series of stable, water-soluble organocobalt compounds, which are formed by the reduction of organic halides with pentacyanocobaltate(II).

On addition of benzyl bromide to a water–methanol solution containing $CoCl_2$ and NaCN (which react together to form $Co(CN)_5{}^{3-}$)[1] in the absence of air, a compound which we are led to formulate as pentacyanobenzylcobaltate(III) is rapidly formed by the reaction

$$2[Co^{II}(CN)_5]^{3-} + C_6H_5CH_2Br \longrightarrow [C_6H_5CH_2Co^{III}(CN)_5]^{3-} + [Co^{III}(CN)_5Br]^{3-}$$

By fractional precipitation and recrystallization from alcohol solutions, the sodium salt of $[C_6H_5CH_2Co(CN)_5]^{3-}$ could be separated from the less soluble salts of $Co(CN)_5Br^{3-}$, $Co(CN)_6{}^{3-}$, and $Co(CN)_5OH^{3-}$, which are by-products of the reaction. *Anal.* Calcd. for $Na_3[C_6H_5CH_2Co(CN)_5]\cdot 2H_2O$: Co, 15.3; C, 37.4; H, 2.9; N, 18.2. Found: Co, 15.8; C, 37.6; H, 3.2; N, 17.6. The original yield of $C_6H_5CH_2Co(CN)_5{}^{3-}$, based on the ultraviolet spectrum of the reaction solution, is estimated to be about 70%.

$Na_3[C_6H_5CH_2Co(CN)_5]\cdot 2H_2O$ is a yellow, somewhat deliquescent, crystalline salt. It is soluble in water, methanol, and ethanol and insoluble in ether, acetone, or hydrocarbons. Thermal decomposition *in vacuo* yields dibenzyl as the organic product. Alkaline aqueous solutions of $[C_6H_5CH_2Co(CN)_5]^{3-}$ are stable in the absence of oxygen and show no immediate reaction with $NaBH_4$ or CO. The anion is decomposed slowly by oxygen and rapidly by acids, the course of the latter reaction being complex and as yet unresolved. The ultraviolet and n.m.r. spectra of $[C_6H_5CH_2Co(CN)_5]^{3-}$ are summarized in Table I. The origin of the intense band at 295.5 mμ, which is not characteristic of other pentacyanocobaltate(III) complexes, is not clear but is believed to be connected with the aromatic component of the complex, since the corresponding alkyl complexes do not exhibit this band. The chemical shifts of the benzyl protons are similar to those observed in $C_6H_5CH_2HgCl$ (CH_2, −1.85; C_6H_5, −5.86 p.p.m. from *t*-butyl alcohol, measured in $CDCl_3$).

TABLE I

Anion	C≡N stretching frequency, cm.$^{-1}$[a]	Ultraviolet absorption λ_{max} (ϵ_{max}), mμ	Proton n.m.r. spectra *in* D_2O	
			Group assignment	Chemical shift, p.p.m.[b]
$[C_6H_5CH_2Co(CN)_5]^{3-}$	2093 ± 3	295.5 (1.8×10^4)	CH_2	−1.67
			C_6H_5	−6.01
$[CH_3Co(CN)_5]^{3-}$	2094 ± 3	318 (2.9×10^2)	CH_3	+0.70
$[C_2H_5Co(CN)_5]^{3-}$[c]	2094 ± 3	. . .	CH_2	−0.35
			CH_3	+0.09

[a] Measured on the sodium salt in KBr pellet. [b] Relative to *t*-butyl alcohol. [c] Based on impure samples.

Pentacyanoalkylcobaltate(III) compounds may be similarly prepared although the study of these has not proceeded as far as that of the benzyl compound. The reaction of CH_3I with $Co(CN)_5{}^{3-}$ yields $[CH_3Co(CN)_5]^{3-}$ which has also been obtained, in nearly pure (~90%) form, as the sodium salt. The ethyl and *n*-propyl compounds can be similarly prepared in solution although these are less stable than the benzyl and methyl analogs and have not as yet been fully characterized or recovered in pure form. The ultraviolet spectrum of $[CH_3Co(CN)_5]^{3-}$ resembles that of other typical pentacyanocobaltate(III) complexes, *e.g.*, $[Co(CN)_5Cl]^{3-}$, and the band at 318 mμ (whose counterpart in the benzyl compound presumably is obscured by the tail of the much more intense 295 mμ band) may accordingly be assigned to a $(t_{2g})^5(e_g)^1 \leftarrow (t_{2g})^6$ transition. This suggests that the ligand field strength of CH_3 approaches that of CN^- (λ_{max} 311 mμ for $Co(CN)_6{}^{3-}$) and is in line with the high ligand fields exhibited by alkyl ligands in other complexes.[2] $[CH_3Co(CN)_5]^{3-}$ reacts with $HgCl_2$ to form CH_3HgCl and with I_2 to form CH_3I.

The formation of a binuclear, unsaturated organopentacyanocobalt(III) complex, $[(CN)_5Co\text{-}CH{=}CH\text{—}Co(CN)_5]^{6-}$, by a somewhat different route, namely the reduction of acetylene by $Co(CN)_5{}^{3-}$, has previously been described by Griffith and Wilkinson.[3] The $[C_6H_5CH_2Co(CN)_5]^{3-}$ anion and its alkyl analogs reported here are isoelectronic with the corresponding stable organomanganese pentacarbonyls, *e.g.*, $CH_3Mn(CO)_5$; their mode of preparation, described above, finds an analogy in the formation of another stable, water-soluble organometallic complex, $[C_6H_5CH_2Cr^{III}(H_2O)_5]^{2+}$, by the reduction of benzyl chloride with chromium(II).[4] Finally, reference should be made to some interesting points of analogy between the chemistry of $Co(CN)_5{}^{3-}$, revealed here, and that of the reduced derivatives of vitamin B_{12} (*i.e.*, vitamins B_{12r} and B_{12s}), including the reactions of the latter with alkyl halides and other alkylating agents to form stable alkyl cobalt derivatives.[5]

Further studies on the preparation and characterization of these compounds are in progress.

Acknowledgment.—Support of this work by the National Science Foundation (Grant No. GP-654) and by the National Institutes of Health of the U. S. Public Health Service (Grant No. GM-10662) is gratefully acknowledged.

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(2) J. Chatt and R. G. Hayter, *J. Chem. Soc.*, 772 (1961).

(3) W. P. Griffith and G. Wilkinson, *ibid.*, 1629 (1959).

(4) F. A. L. Anet and E. Leblanc, *J. Am. Chem. Soc.*, **79**, 2649 (1957).

(5) R. Bonnett, *Chem. Rev.*, **63**, 573 (1963).

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RECEIVED APRIL 16, 1964