Water is supporting the current study; the authors express their thanks.

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Polarography of Hemin. Evidence for a Two-Electron Transfer

Sir:

The nature of oxidation–reduction in hemoglobin-type systems has been reinvestigated by imaginative "model experiments" in recent years.[1] In this context, elucidation of the electron-transfer behavior of metalloporphyrin complexes is of considerable interest. The question whether the reduction of hemin to heme involves one or two electrons has been the subject of an important controversy. In a classical potentiometric study,[2] Conant, *et al.*, postulated that a dimeric
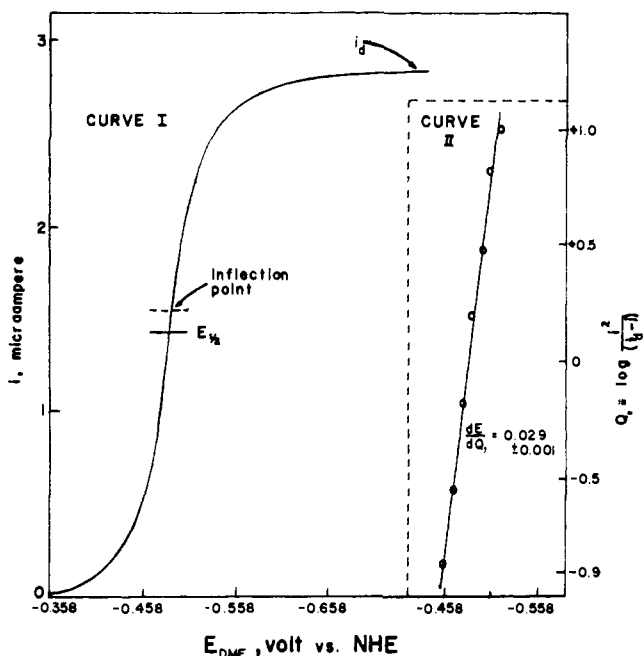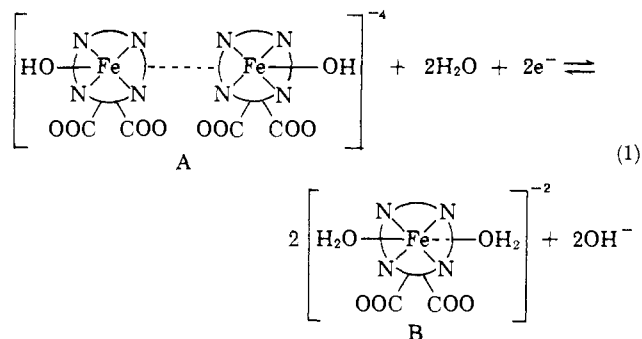
Fig. 1.—Polarography of 2.775×10^{-3} M hemin in 0.1 M aqueous KOH at 25°: curve I, current–voltage curve corrected for residual current and iR drop; curve II, wave analysis plot according to eq. 2.

hemin reactant yielded a monomeric heme product *via* a two-electron reduction. Later potentiometric investigations[3] by Barron appeared compatible with a one-electron transfer process in which the reactant as well as the product were monomeric. In contradistinction, spectrophotometric data reported by Shack and Clark[4] indicated that both were dimeric species. We have obtained conclusive evidence that the reduction of hemin chloride in 0.1 M aqueous potassium hydroxide proceeded at the dropping mercury electrode (d.m.e.) with "Nernstian reversibility" in accordance with the equation

(1) J. H. Wang, *J. Am. Chem. Soc.*, **80**, 3168 (1958).
(2) J. B. Conant, C. A. Alles, and C. O. Tongberg, *J. Biol. Chem.*, **79**, 89 (1928).
(3) E. S. Barron, *ibid.*, **121**, 285 (1937).
(4) J. Shack and W. M. Clark, *ibid.*, **171**, 143 (1947).

(1)

The electroreducible species A is a soluble ferric protoporphyrin chelate dimer. It functions as a two-electron acceptor yielding the monomeric *trans*-diaquoprotoporphyrin ferrate(II) B, which is also soluble under the prevailing experimental conditions. The formulation of A and B in eq. 1 is consistent with current knowledge of the chemistry of the prosthetic group of hemoglobin.[5]

A typical polarogram is illustrated in Fig. 1, curve I. The well-defined limiting current, i_d, varied linearly with the concentration of hemin in the bulk of the solution and was diffusion controlled (*i.e.*, proportional to the square root of the mercury pressure effective above the d.m.e.). A reversible polarogram corresponding to eq. 1, with currents controlled solely by rates of diffusion between the electrode surface and the bulk of the solution, is described by the "wave equation"[6]

$$E_{\mathrm{dme}} = E^{\circ} + \frac{\mu RT}{2\mathfrak{F}} \log \frac{f_A D_B}{f_B{}^2 D_A{}^{1/2} K_w{}^2} - \frac{\mu RT}{\mathfrak{F}} \mathrm{pH} + \frac{\mu RT}{2\mathfrak{F}} \log \frac{(i_d - i)}{i^2} \quad (2)$$

where μ ($= 2.303$) denotes the modulus which converts natural logarithms to their decadic counterparts, E° is the standard potential of the heme–hemin couple, the subscripts refer to the chemical entities identified in eq. 1, the other symbols conform to the notation used by Kolthoff and Lingane,[7] and potentials are assigned in concordance with the Stockholm IUPAC convention. The analytic geometry of a current-voltage curve governed by eq. 2 has several distinctive features. While the plot is sigmoid, it is, however, unsymmetrical about the inflection point which does not coincide with the half-wave potential. These characteristics are indeed evident in the experimental polarogram shown in Fig. 1.

The last term in eq. 2 would have the form $(\mu RT/\mathfrak{F}) \cdot \log [(i_d - i)/i]$ or $(\mu RT/2\mathfrak{F}) \cdot \log [(i_d - i)/i]$, respectively, if the hemin and heme species involved in the electrode reaction were either both monomeric or both dimeric and Nernst control prevailed. Thus the linearity and slope of plots of the quantities $Q_1 \equiv \log [(i_d - i)/i^2]$ and $Q_2 \equiv \log [(i_d - i)/i]$ *vs.* E_{dme} may provide diagnostic criteria for differentiating between the Conant, Barron, and Shack reactions. The relevant wave analysis plot of Q_1 *vs.* E_{dme} is shown in Fig. 1, curve II. This has a reciprocal slope of 0.029 $\pm$

(5) W. M. Clark, J. F. Taylor, T. H. Davies, and C. S. Vestling, *ibid.*, **135**, 543 (1940).
(6) Derived from the applicable Nernst equation; see G. Charlot, J. Badoz-Lambling, and B. Tremillon, "Electrochemical Reactions," Elsevier Publishing Co., New York, N. Y., 1962, p. 36.
(7) I. M. Kolthoff and J. J. Lingane, "Polarography," Vol. 1, Interscience Publishers, Inc., New York, N. Y., 1952, pp. 190 ff.

0.001 v., which is in excellent agreement with the theoretical slope predicted by eq. 2 for the reversible two-electron dimer–monomer reaction 1 $[(2.303)RT/2\mathfrak{F} = 0.0293$ v. at 25°]. A wave analysis plot of Q_2 *vs.* E_{dme} was rectilinear with a reciprocal slope of 0.044 v. This excludes any one-electron transfer process, whether reversible or irreversible, and is not consistent with Nernst control for a two-electron reduction. A Koutecky-type mathematical analysis[8] eliminated the possibility of a two-electron transfer "rate controlled" by slow steps other than diffusion. The remote alternative of spurious slopes,[9,10] due to extraneous effects (*e.g.*, double layer), was ruled out in our results by considerations of internal consistency.

Equation 2 predicts that the half-wave potential of hemin should shift with pH as shown in eq. 3. This

$$\frac{dE_{1/2}}{d(\mathrm{pH})} = -0.059 \tag{3}$$

dependence has been previously reported in the literature.[11] From our data and the applicable expanded form of the Ilkovic equation,[12] the diffusion coefficient of the dimeric hemin ion A was evaluated as 1.72×10^{-7} cm.^{2}/sec. at 25°. It should be noted that this assignment applies only to the species which controlled the current under the specific experimental conditions prevailing in this investigation, *i.e.*, in a dilute aqueous solution (millimolar in total hemin) containing 0.1 M potassium hydroxide as the sole supporting electrolyte in the absence of any maximum suppressor. It is well known that the degree of polymerization of hemin[4] is highly dependent on environmental conditions. Studies are in progress for elucidating the polarographic properties of iron protoporphyrin aggregates in media of biological significance.

(8) L. Meites and Y. Israel, *J. Am. Chem. Soc.*, **83**, 4903 (1961).

(9) J. Kuta and J. Koryta, Summaries of Papers, Third International Congress of Polarography, Southampton, England, 1964, p. 48.

(10) W. H. Reinmuth, L. B. Rogers, and L. E. I. Hummelstedt, *J. Am. Chem. Soc.*, **81**, 2947 (1959).

(11) R. Brdicka and K. Wiesner, *Collection Czech. Chem. Commun.*, **12**, 39 (1947).

(12) I. Kolthoff and K. Izutzu, *J. Am. Chem. Soc.*, **86**, 1275 (1964).

(13) Based on part of a doctoral thesis by T. M. B.

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The Question of Heterolytic Mechanisms for Gas-Phase Pyrolyses of Alkyl Chlorides

Sir:

At elevated temperatures in the gas phase, in reaction vessels which have been seasoned by prolonged contact with reaction products, monochlorinated hydrocarbons have usually been shown to decompose by homogeneous and unimolecular processes.[1] The prod-

(1) For reviews on pyrolytic elimination reactions see (a) A. Maccoll, "Proceedings of the Kekule Symposium on Theoretical Organic Chemistry,

ucts of such a reaction are hydrogen chloride and an olefin, and relative rates of elimination for a series of chlorides parallel the rates of solvolytic reactions for the same series.[1] Rearrangements during the thermal decomposition of neopentyl chloride[2] and bornyl chloride[3] are also observed, and all of these facts suggest "quasi-hetrolytic"[1a] mechanisms analogous to those of solvolytic eliminations. Consequently, very polar transition states[1a] or ionic pair intermediates[4] have been postulated for thermal dehydrohalogenations.

The original analogy was based upon a comparison of primary, secondary, and tertiary halides whose relative rates of elimination at 400° were in the approximate ratio 1:200:40,000, respectively.[1a,c] We choose to compare a series of secondary chlorides which differ greatly in their solvolytic reactivity. Some relative rates of dehydrochlorination in the gas phase compared with solvolytic (SN1 or E1) reactivities are presented in Table I.

TABLE I
RELATIVE RATES OF THERMAL DEHYDROCHLORINATION

Reactant	400°	500°	Solvolysis[a]
Cyclohexyl chloride	1.00	1.00	1.00
2-Butyl chloride	0.85	1.12	1.51[b]
Cyclopentyl chloride	1.20	0.93	14.1[c]
exo-Norbornyl chloride	0.67	0.77	117.[d]
α-Phenylethyl chloride	7.76	6.92	12,500[e]
t-Butyl chloride	101	71	19,100[f]

[a] Approximate values for 80% aqueous ethanol at 85°. [b] The quoted value is for isopropyl chloride: A. Streitwieser, "Solvolytic Displacement Reactions," McGraw-Hill Book Co., New York, N. Y., 1962, p. 96. [c] J. D. Roberts, L. Urbanek, and R. Armstrong, *J. Am. Chem. Soc.*, **71**, 3049 (1949). [d] J. D. Roberts, W. Bennett, and R. Armstrong, *ibid.*, **72**, 3329 (1950). [e] Extrapolated from 50°: A. M. Ward, *J. Chem. Soc.*, 445 (1927). [f] Extrapolated from 50°: E. D. Hughes, *ibid.*, 255 (1935).

Relative rates for the secondary chlorides were obtained by pyrolyzing a mixture of the required chloroalkanes in stirred flow reactor systems which have been described previously in detail.[5,6] The relative rate for *t*-butyl chloride is calculated from the Arrhenius equation since the magnitude of the rate precluded competitive experiments. Flow rates in these experiments were generally varied by a factor of ten and the usual precautions of surface inhibition were followed.[1c] Four to eight runs were made for each pair and the standard deviation of the resulting relative rate was always less than 5%. In the pyrolysis of norbornyl chloride, the corresponding olefin, bicyclo[2.2.1]heptene, was not isolated. As expected, the retro-Diels–Alder reaction of the bicyclic olefin[7] was so rapid that only cyclopentadiene and ethylene could be identified. In all of the other cases secondary processes did not occur to measurable extents.

1958," Butterworths Scientific Publications, London, 1959, p. 230; (b) C. H. DePuy and R. W. King, *Chem. Rev.*, **60**, 431 (1960); (c) A. Maccoll, "Technique of Organic Chemistry," Vol. VIII, Part I, Interscience Publishers, Inc., New York, N. Y., 1961, Chapter X; and (d) D. V. Banthorpe, "Elimination Reactions," Elsevier Publishing Co., New York, N. Y., 1963, Chapter 7.

(2) A. Maccoll and G. S. Swinbourne, *Proc. Chem. Soc.*, 409 (1960).

(3) A. Maccoll and R. Bicknell, *Chem. Ind.* (London), 1912 (1961).

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(5) W. C. Herndon, M. B. Henley, and J. M. Sullivan, *J. Phys. Chem.*, **67**, 2842 (1963).

(6) W. C. Herndon and L. L. Lowry, *J. Am. Chem. Soc.*, **86**, 1922 (1964).

(7) W. C. Herndon, W. B. Cooper, Jr., and M. J. Chambers, *J. Phys. Chem.*, **68**, 2016 (1964).