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Metalation of Etioporphyrin I with Nickel(II) 1,3-Diketonates

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The importance of metalloporphyrins in biological systems has prompted investigations concerned with the insertion of divalent metal cations into the free porphyrin base.[1-5] In these studies, porphyrins were treated with metal acetates or perchlorates. To our knowledge, no study of porphyrin metalation reactions has been reported in which the metal reactant has been systematically varied by altering the ligands associated with a given metal cation. Accordingly, we report some findings from a study in which etioporphyrin I was metalated by a series of nickel(II) 1,3-diketonates.

Experimental Section

Materials. Etioporphyrin I was synthesized by Rislove.[6] Nickel-(II) 1,3-diketonates were prepared by the general method of Charles and Pawlikowski[7] and purified by sublimation. All preparations were converted, when necessary, into anhydrous forms. Potassium 1,1,1-trifluoro-2,4-pentanedionate was prepared as described in the literature.[8] Solvents were purified by distillation and dried over alumina (Woelm).

Kinetic Techniques. Solutions of reactants were equilibrated in a thermostated bath before introduction into a triple-necked, round-bottom flask, immersed in a constant-temperature bath, and equipped with a capillary arm for sample withdrawals. Initial etioporphyrin I concentration was generally in the range, 5×10^{-5} to 1×10^{-4} M; metal chelate concentration, 1×10^{-3} to 1.5×10^{-2} M. Unless otherwise mentioned, benzonitrile was used as the solvent. Reactions were carried out under a blanket of dry nitrogen to minimize the effect of atmospheric oxygen, which provided slightly faster rates. Samples were withdrawn at time intervals into a 1-cm³ silica cell, immediately cooled to room temperature by immersion in cold water. The absorbance was measured in a Beckman DU spectrophotometer. Since the spectrum of nickel(II) etioporphyrin I varies significantly from that of etioporphyrin I, both the appearance of the metalloporphyrin (at 554 nm) and the disappearance of the porphyrin (at 496 nm) could be followed. Absorbance maxima (nm) and extinction coefficients (M^{-1} cm^{-1} $\times 10^{-4}$) for etioporphyrin I are as follows: 399, 16.7; 496, 1.48; 530, 1.06; 568, 0.675; 623, 0.603. Similarly these data for nickel(II) etioporphyrin I are as follows: 392, 19.9; 516, 1.07; 554, 3.58.

Results

The reaction studied is $H_2P + NiL_2 \rightarrow NiP + 2HL$ where H_2P is etioporphyrin I and L is the 1,3-diketonate ligand. Linear plots for log $[(A_\infty - A_t)/(A_\infty - A_0)]$ *vs.* time were obtained for the reaction of H_2P with each of the following nickel compounds: bis(2,4-pentanedionato)nickel(II), Ni(AA)$_2$; bis(2,6-dimethyl-3,5-heptanedionato)nickel(II), Ni(DIBM)$_2$; bis(1,1,1-trifluoro-2,4-pentanedionato)nickel(II),

Ni(TFA)$_2$; bis(1,1,1,5,5,5-hexafluoro-2,4-pentanedionato)-nickel(II), Ni(HFA)$_2$; bis(2,2,6,6-tetramethyl-3,5-heptane-dionato)nickel(II), Ni(DPM)$_2$; and bis(1,3-diphenyl-1,3-propanedionato)nickel(II), Ni(DBM)$_2$. The linear relationship, observed over 2-3 half-lives, established first-order dependence with respect to H_2P.

The kinetic order with respect to NiL$_2$ was obtained by varying the initial concentration of NiL$_2$ in each of several runs while maintaining initial concentration of H_2P constant. Initial concentration of NiL$_2$ was maintained at a level not less than 10 times larger than initial concentration of H_2P. The plot of the log of the slopes obtained in each of these runs *vs.* the log of the initial concentration of NiL$_2$ provided a straight line. The slope of the latter determined the kinetic order with respect to NiL$_2$. A value of essentially 1 was obtained for all reactions except when Ni(AA)$_2$ and Ni-(DIBM)$_2$ were reactants. For these latter cases, rates were found to be independent of NiL$_2$ concentrations within the range applied.

In any given run, the ratio $(A_\infty - A_t)/(A_\infty - A_0)$ is directly proportional to the amount of unreacted H_2P or of NiP formed at time t. Thus for reactions of H_2P with Ni(TFA)$_2$, Ni(HFA)$_2$, and Ni(DPM)$_2$, the slopes of the linear plots yield the second-order rate constant by the relationship

$$\text{slope} = k_2[\text{NiL}_2]/2.303$$

Presence of water, even in very small amounts, inhibited reaction. This was probably a consequence of carrying out reactions in which the initial concentration of the substrate, H_2P, was maintained at a very low level, about 10^{-5} M. Such a level was desirable since porphyrins tend to associate in more concentrated solutions.[9] Beer's law applied to H_2P and NiP over the concentration range applied; no evidence for association was detected. The degree of influence by water varied considerably with the NiL$_2$ used. In the reaction of H_2P with Ni(DPM)$_2$ at 80°, rate constants varied in the range, 5×10^{-2} to 1.3×10^{-1} M^{-1} sec^{-1}. Similarly for other NiL$_2$, ranges in rate constants (temperature, °C) were as follows: Ni(DBM)$_2$, 0.15-0.18 M^{-1} sec^{-1} (50); Ni-(HFA)$_2$, 0.3-0.4 M^{-1} sec^{-1} (48); Ni(AA)$_2$, (2-4) $\times 10^{-5}$ sec^{-1} (80); Ni(DIBM)$_2$, 0.10-0.15 sec^{-1} (80). The fastest rate was observed when the final water removal from the solvent, benzonitrile, was effected with a molecular sieve and all solution preparations were carried out in a controlled-atmosphere box. All containers used were previously scrupulously dried. The slowest rate was observed when water was azeotropically removed and normal precautions were exercised to exclude moisture including effecting reaction under a blanket of dry nitrogen. Water contained in these reaction systems would not be expected to be determinable using the Karl Fischer reagent.[10] The least sensitive system to the presence of water was the reaction of H_2P with Ni-(TFA)$_2$. Here the variation in rate at 60° was $(1.3-1.5) \times 10^{-2}$ M^{-1} sec^{-1}. Accordingly, rate data are given in Table I for this reaction at several temperatures. Activation parameters calculated from these data gave an energy of activation of 21 ± 2 kcal/mol and an entropy of activation of -5 ± 6 eu.

The rate of reaction of H_2P with Ni(TFA)$_2$ was also studied in different solvents. These data, obtained at 60°, are given in Table II.

(1) D. J. Kingham and D. A. Brisbin, *Inorg. Chem.*, **9**, 2034 (1970), and references cited therein.
(2) P. Hambright, *J. Inorg. Nucl. Chem.*, **32**, 2449 (1969), and references cited therein.
(3) D. K. Cabbiness and D. W. Margerum, *J. Amer. Chem. Soc.*, **92**, 2151 (1970).
(4) E. B. Fleischer and J. H. Wang, *J. Amer. Chem. Soc.*, **82**, 3498 (1960).
(5) B. Shah, B. Shears, and P. Hambright, *Inorg. Chem.*, **10**, 1828 (1971).
(6) D. J. Rislove, A. T. O'Brien, and J. M. Sugihara, *J. Chem. Eng. Data*, **13**, 588 (1968).
(7) R. G. Charles and M. A. Pawlikowski, *J. Phys. Chem.*, **62**, 440 (1958).
(8) R. Belcher, A. W. L. Dudeney, and W. I. Stephen, *J. Inorg. Nucl. Chem.*, **31**, 625 (1969).
(9) D. Doughty and C. W. Dwiggins, Jr., *J. Phys. Chem.*, **73**, 423 (1969).
(10) J. Mitchell, Jr., and D. M. Smith, "Aquametry," Interscience, New York, N. Y., 1948, Chapter V.

Table I. Rates of Reaction of Etioporphyrin I with Ni(TFA)$_2$ in Benzonitrile

Temp, °C	10^3 [Ni(TFA)$_2$], M	$10^2 k_2$,^{a} M^{-1} sec^{-1}
60.0 ± 0.1	15	1.37
60.0 ± 0.1	10	1.39
60.0 ± 0.1	7.5	1.38
60.0 ± 0.1	5.0	1.28
60.0 ± 0.1	3.75	1.29
64.0 ± 0.1	2.5	1.55
68.0 ± 0.1	2.5	2.18
72.0 ± 0.1	2.5	3.58
76.5 ± 0.1	2.5	5.76

^{a} Initial concentration of etioporphyrin I was 1.0×10^{-5} M.

Table II. Rates of Reaction of Etioporphyrin I with Ni(TFA)$_2$ at 60° in Various Solvents

Solvent	Dielectric constant^a (25°)	$10^2 k_2$, M^{-1} sec^{-1}
Benzene	2.27	3.02
Anisole	4.33	2.19
Chlorobenzene	5.62	6.29
o-Dichlorobenzene	9.93	3.95
Benzonitrile	25.2	1.34

^{a} A. Weissberger and E. S. Proskauer, "Technique of Organic Chemistry," Vol. VII, J. A. Riddick and E. E. Toops, Jr., Ed., 2nd ed, Interscience, New York, N. Y., 1955, pp 270-274.

The effect on the rate of reaction by addition of the ligand anion, introduced as potassium 1,1,1-trifluoro-2,4-pentanedionate, was studied. Unfortunately, its limited solubility in the reaction system allowed measurements only in the concentration range, 5×10^{-4} to 1×10^{-3} M. Inhibition was observed. Analysis of the data in the form of the plot of the log of the rate constants *vs.* the log of the concentration of added ligand anion gave a linear relationship. The slope of the plot suggested an inverse order of approximately 0.8.

Discussion

The insertion of a divalent metal ion into porphyrin rings has been interpreted[4] to involve an intermediate species. The reactions of H$_2$P with Ni(TFA)$_2$, Ni(HFA)$_2$, Ni(DPM)$_2$, and Ni(DBM)$_2$ may also be stepwise processes, *i.e.*

$$H_2P + NiL_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2PNiL^+ + L^-$$

$$H_2PNiL^+ \overset{k_2}{\rightarrow} NiP + LH + H^+$$
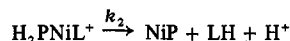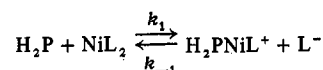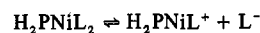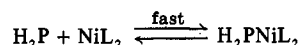
From these steps, the following rate expression derives using the steady-state approximation

$$\frac{d[NiP]}{dt} = \frac{k_2 k_1 [H_2P][NiL_2]}{k_2 + k_{-1}[L^-]}$$

The species H$_2$P NiL$^+$ may be visualized to be similar to the "sitting atop" complex, previously proposed,[4] but in our system would likely have considerable ion-pair character. The modest changes in rates observed in the reaction of H$_2$P with Ni(TFA)$_2$ in the several solvents (Table II) suggest that little change in charge separation occurs in going from the ground-state reactants to the activated complex.

The reactions of H$_2$P with Ni(AA)$_2$ and Ni(DIBM)$_2$ clearly follow a different reaction path, based on the observed first-order dependence on H$_2$P and zero-order dependence on Ni(AA)$_2$ or Ni(DIBM)$_2$. In these runs, initial concentrations of NiL$_2$ were always maintained at a level at least 10

times as large as initial concentration of H$_2$P. Accordingly, should a rapid combination of H$_2$P and NiL$_2$ occur, followed by a subsequent rate-determining step independent of NiL$_2$ concentration, the system would exhibit zero-order dependence with respect to NiL$_2$. An ionization step is

$$H_2P + NiL_2 \underset{\longleftarrow}{\overset{fast}{\longrightarrow}} H_2PNiL_2$$

$$H_2PNiL_2 \rightleftharpoons H_2PNiL^+ + L^-$$

$$H_2PNiL^+ \rightarrow NiP + LH + H^+$$

likely involved since presence of L$^-$ inhibits reaction. The mechanism is attractive since AA$^-$ and DIBM$^-$ would be expected to be poorer leaving groups than TFA$^-$, HFA$^-$, and DBM$^-$. Formation of the neutral complex likely would be precluded when the metal source is Ni(DPM)$_2$ because of the bulky *tert*-butyl groups, which could force the system to follow a displacement mechanism. An observation in support of the combination path came from studies[11] made on the competitive reaction of Ni(AA)$_2$ and Cu(AA)$_2$ with H$_2$P. In solvents of intermediate polarity, NiP was formed in spite of the much faster reaction of H$_2$P with Cu(AA)$_2$ alone. A rapid combination of H$_2$P with Ni(AA)$_2$ and not with Cu(AA)$_2$ would preclude formation of CuP. However, direct spectrophotometric evidence for rapid formation of a complex of H$_2$P and Ni(AA)$_2$ or Ni(DIBM)$_2$ was not observed.

An alternative explanation for the observed kinetic orders in the reaction of H$_2$P with Ni(AA)$_2$ and Ni(DIBM)$_2$ may be suggested. It is possible that presence of polymeric species of the metal reactants may cloud the mechanism; however, Beer's law applied to solutions of these reactants in benzonitrile over the concentration ranges used. A trimer of Ni(AA)$_2$ is well characterized.[12] Under such circumstances kinetic dependence on the metal source should not be zero but fractional orders less than 1.

In addition to the mechanistic information, these studies suggest that synthesis of nickel porphyrins may be accomplished with facility using Ni(TFA)$_2$, Ni(DIBM)$_2$, or Ni(DBM)$_2$ as metal sources. Ni(HFA)$_2$ is not a satisfactory reactant since the conjugate acid of the ligand is sufficiently acidic that protonation of H$_2$P occurs. The conventional method of refluxing the porphyrin with nickel acetate in glacial acetic acid has recently been improved by substituting Ni(AA)$_2$ in refluxing benzene.[13] Purification of product was effected with column chromatography. The conversion of H$_2$P with any of the three nickel reagents Ni(TFA)$_2$, Ni(DIBM)$_2$, and Ni(DBM)$_2$ is a faster process with quantitative conversion within several hours, as based upon spectrophotometric evidence, at temperatures of 50-60°.

(11) M. Oishi, Ph.D. Thesis, North Dakota State University, Fargo, N. D., 1968.

(12) J. P. Fackler, Jr., and F. A. Cotton, *J. Amer. Chem. Soc.*, **83**, 3775 (1961).

(13) W. P. Hambright, A. N. Thorpe, and C. C. Alexander, *J. Inorg. Nucl. Chem.*, **30**, 3139 (1968).