of initiation. We are continuing our work in this area.

Acknowledgment. This work was generously supported by National Science Foundation Grant CHE75-22453 and by Biomedical Research Support Grant RR07143 from the Department of Health, Education and Welfare, which are gratefully acknowledged.

Registry No. **3**, 70528-18-6; **4**, 72029-98-2; **6**, 78571-85-4; **7**, 78571-86-5; (teed)Cu(TCP)$_2$, 22180-39-8; (tmpd)CuCl(TCP), 78571-87-6; (teed)CuCl$_2$, 78571-93-4; TCPH, 88-06-2; (tmpdH$_2$)(CuCl$_4$), 52761-69-0.

Contribution from the Department of Chemistry,
Ithaca College, Ithaca, New York 14850

Copper(II) Incorporation into Tetraphenylporphine in Dimethyl Sulfoxide

ROBERT F. PASTERNACK,* GLENN C. VOGEL, CURTIS A. SKOWRONEK, ROGER K. HARRIS, and JAMES G. MILLER

Received February 19, 1981

A kinetic study of copper(II) ion incorporation into tetraphenylporphine (H$_2$TPP) in dimethyl sulfoxide is reported. The kinetic results suggest that the mechanism involves a rapid preequilibrium involving a copper(II) ion and H$_2$TPP prior to metal insertion and proton loss:

$$Cu^{2+} + H_2PPP \overset{K}{\rightleftharpoons} Cu^{2+};H_2TPP \qquad Cu^{2+};H_2TPP \xrightarrow{k} CuTPP + 2H^+$$

where $K = 5.5\ M^{-1}$ and $k = 1.7 \times 10^{-3}\ s^{-1}$ at 25 °C and an ionic strenth of 0.2 M (KNO$_3$ or LiNO$_3$). The thermodynamic parameters for the preequilibrium are $\Delta H^\circ = 6.5 \pm 0.1$ kcal/mol and $\Delta S^\circ = 25.2 \pm 0.5$ eu, while the activation parameters are $\Delta H^\ddagger = 11.5 \pm 0.3$ kcal/mol and $\Delta S^\ddagger = -32.6 \pm 0.1$ eu. Arguments are presented which suggest that the Cu^{2+};H$_2$TPP species is best interpreted as arising from an outer-sphere ion pair type interaction without appreciable distortion of the porphyrin ring. In the rate-determining step, the ring distorts, protons are freed, and covalent bonds are formed between the porphyrin and copper(II) ion as solvent molecules from the inner coordination sphere of the metal ion are lost.

The rates of the reactions of copper(II) ion with ligands containing four nitrogen donor groups depend markedly on whether the ligand is an open-chain polyamine or macrocyclic.[1] Thus, hematoporphyrin has been shown to be 10^9 times less reactive than the open-chain polyamine *N,N'*-bis(2-aminoethyl)-1,3-propanediamine (2,3,2-tet) under similar reaction conditions. In large part, this difference reflects the porphyrin requirement for multiple desolvation of the metal ion for complex formation while 2,3,2-tet can readily react with copper(II) by stepwise replacement of coordinated solvent.[1] Much effort has been expanded to further elucidate the detailed pathway(s) by which metal ions become incorporated into porphyrin ligands in the absence of an "insertase",[2-4] and several papers have appeared in which a general mechanism has been offered.[5-8] Although differences in detail emerge among these suggestions, several features reappear and seem to be generally accepted.

The mechanisms begin with a preequilibrium step involving the metal ion and the free-base porphyrin leading to a deformation of the porphyrin moiety. Some controversy still exists as to whether this complex is of the sitting-atop-type[3] (SAT) or if it is best represented as an outer-sphere ion pair.[8] The SAT complex involves at least partial bonding of the metal ion to two of the pyrrole nitrogens with concomitant loosening of the nitrogen to hydrogen bonds. The porphyrin deformation, while likely to be involved in metal insertion, has been shown to be rapid and would not be rate determining under ordinary conditions.[9] The rate-determining step postulated for porphyrin metalation involves either the multiple desolvation of the inserting metal ion or a dissociative loss of solvent molecule(s) from the metal and a central proton from the porphyrin prior to metal insertion. The weight of experimental evidence suggests that the free-base porphyrin (cf. Figure 1) is the reactive species in that the rate of metal incorporation into *N*-methyltetraphenylporphine (H-N-MeTPP) is more rapid than for tetraphenylporphine (H$_2$TPP) and that both reactions show little dependence on ionic strength and are unaffected by the production of protons during the reaction.[8]

Much of the experimental work upon which these suggestions are based was carried out in aqueous solution. Unfortunately, many porphyrins aggregate in water,[10] limiting the number and type of systems which can be readily investigated. Furthermore, acid/base equilibria further complicate the analysis and interpretation.[11] Studies conducted in DMF have also proven very useful[8,12] although some ambiguity exists as to the reactive form(s) of the metal ion because of the relatively low dielectric constant of the solvent. Furthermore, the rate law in DMF has the simple form:

$$\text{rate} = k[M^{II}][\text{porphyrin}]$$

which does not provide any direct evidence for a preequilibrium.

In order to avoid both the ion-pairing problem and protolytic equilibria, we have studied the incorporation of copper(II) into tetraphenylporphine in Me$_2$SO. This aprotic solvent has sufficiently high dielectric constant and good electron-donating

---

(1) D. K. Cabbiness and D. W. Margerum, *J. Am. Chem. Soc.*, **92**, 2151 (1970).
(2) P. Hambright in "Porphyrins and Metalloporphyrins", K. M. Smith, Ed., Elsevier, New York, 1975, pp 233-278.
(3) F. R. Longo, E. M. Brown, W. G. Rau, and A. D. Adler in "The Porphyrins", Vol. V, D. Dolphin, Ed., Academic Press, New York, 1979, pp 459-481.
(4) W. Schnieder, *Struct. Bonding (Berlin)*, **23**, 123 (1975).
(5) R. Khosropour and P. Hambright, *J. Chem. Soc., Chem. Commun.*, 13 (1972).
(6) P. Hambright and P. B. Chock, *J. Am. Chem. Soc.*, **96**, 3123 (1974).
(7) J. Turay and P. Hambright, *Inorg. Chem.*, **19**, 562 (1980).
(8) M. J. Bain-Ackerman and D. K. Lavallee, *Inorg. Chem.*, **18**, 3358 (1979).
(9) R. F. Pasternack, N. Sutin, and D. H. Turner, *J. Am. Chem. Soc.*, **98**, 1908 (1976).
(10) R. F. Pasternack, P. R. Huber, P. Boyd, G. Engasser, L. Francesconi, E. Gibbs, P. Fasella, G. C. Venturo, and L. de C. Hinds, *J. Am. Chem. Soc.*, **94**, 4511 (1972).
(11) H. Baker, P. Hambright, and L. Wagner, *J. Am. Chem. Soc.*, **95**, 5942 (1973).
(12) F. R. Longo, E. M. Brown, D. J. Quimby, A. D. Adler, and M. Meot-Ner, *Ann. N.Y. Acad. Sci.*, **206**, 420 (1973).

© 1981 American Chemical Society

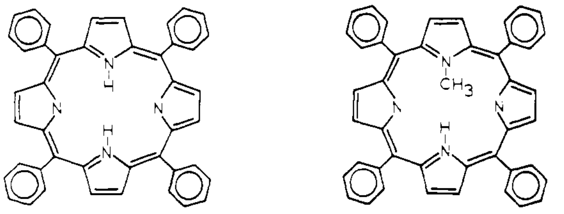

Figure 1. Structures of tetraphenylporphine and *N*-methyltetraphenylporphine.

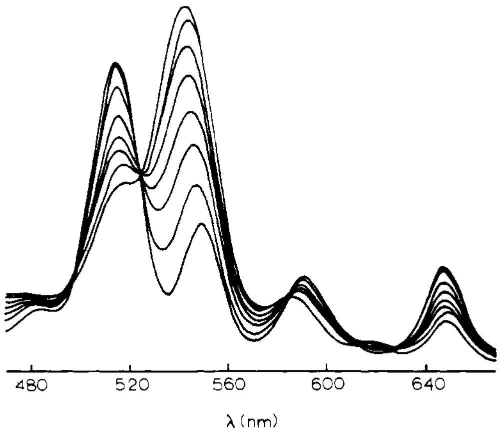

Figure 2. Absorbance changes during the reaction of Cu^{2+} with tetraphenylporphine in Me_2SO. Spectra were taken at approximately 15-min intervals ($[Cu^{2+}] = 1.72 \times 10^{-3}$ M, temp = 50 °C).

properties to prevent extensive ion pairing and to coordinate to the metal site.[13,14] Some results have been reported on the reaction of $CuCl_2$ with H_2TPP in Me_2SO, but very few details are given.[12] The authors indicate that reaction is second order and report activation parameters of $\Delta H_2^{\ddagger} = 19.4$ kcal/mol and $\Delta S_2^{\ddagger} = -2.9$ eu. However, we believe that there are other interesting features of this system which we wish to now report.

Experimental Section

Tetraphenylporphine was prepared, purified, and characterized by methods described in the literature.[15] Fisher reagent-grade anhydrous cupric chloride, potassium nitrate, and lithium nitrate were used. The salts were dried over phosphorus pentoxide in an Abderhalden apparatus (100 °C, 0.5 torr) and stored in a vacuum desiccator. Dimethyl sulfoxide from Aldrich Chemical Co. was distilled at reduced pressures (0.5 torr) from BaO. The distillate was collected in an ice bath under a nitrogen atmosphere and kept frozen until used. We preferred not using molecular sieves because we found that our solvent was modified by long standing over sieves. The stock Me_2SO was stored in a flask fitted with a septum cap, and syringe techniques were used throughout to prevent the solvent from contacting either oxygen or water. In later experiments we found that traces of oxygen and water had no significant affect on the kinetics of metal insertion, but we continued to maintain dry, anaerobic conditions.

Stock solutions were prepared within a nitrogen-filled glovebag and stored in flasks fitted with septum caps. The concentration of the cupric chloride stock solutions were determined by atomic absorption spectroscopy.

The spectra of tetraphenylporphine and (tetraphenylporphinato)copper(II) as well as the kinetic data were obtained with the use of a Cary 14 and/or a Varian 634 UV/vis spectrophotometer fitted with thermostated cell compartments. The kinetic runs were conducted under pseudo-first-order conditions with copper(II) in large excess. The ionic strength was maintained at 0.2 M with KNO_3 except in a few experiments in which $LiNO_3$ was substituted to determine if there is a specific electrolyte effect. None was found. The course of the copper ion insertion was followed at 514.5 nm which is an absorption maximum of the free-base porphyrin. Several experiments were repeated at 540 nm where CuTPP absorbs, and the observed rate constants agreed to well within experimental error to those obtained at the reactant peak.

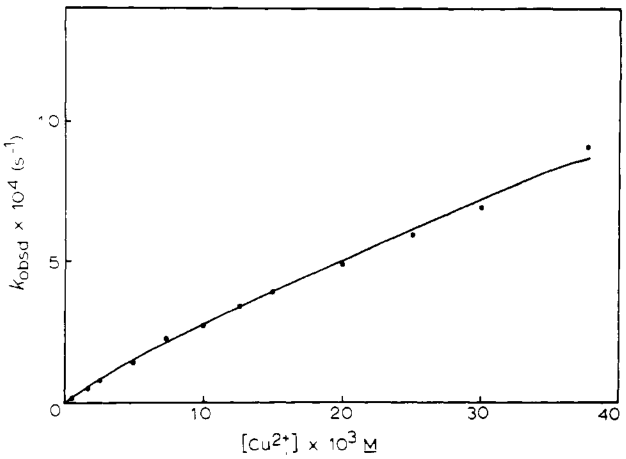

Figure 3. Plot of k_{obsd} vs. $[Cu^{2+}]$ at 35 °C. The parameters used for the theoretical curve are $k = 3.63 \times 10^{-3}$ s^{-1} and $K = 8.24$ M^{-1}.

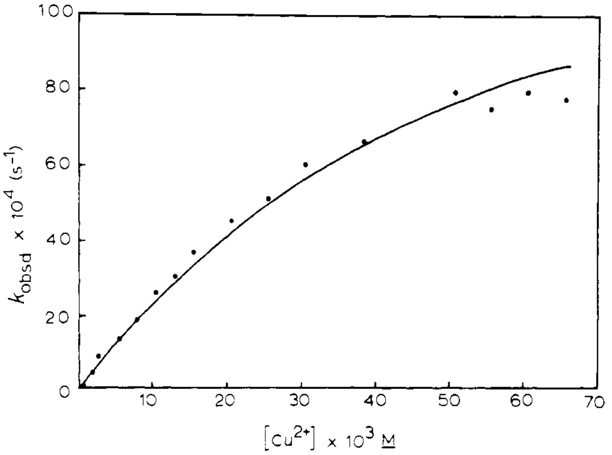

Figure 4. Plot of k_{obsd} vs. $[Cu^{2+}]$ at 50 °C. The parameters used for the theoretical curve are $k = 9.06 \times 10^{-3}$ s^{-1} and $K = 13.5$ M^{-1}.

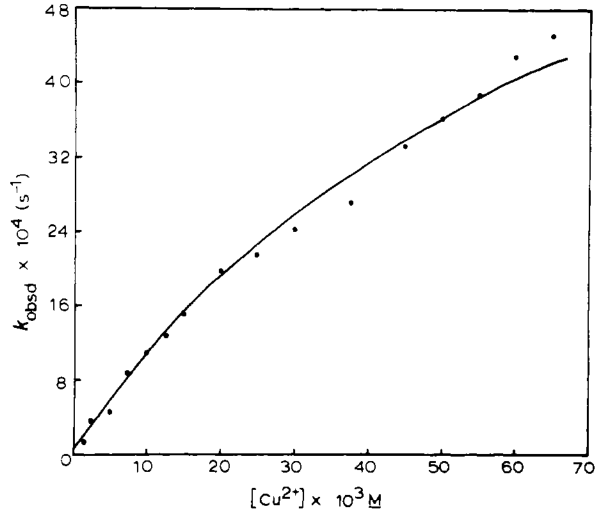

Figure 5. Plot of k_{obsd} vs. $[Cu^{2+}]$ at 60 °C. The parameters used for the theoretical curves are $k = 1.59 \times 10^{-2}$ s^{-1} and $K = 18.3$ M^{-1}.

Results

The kinetics of copper(II) insertion into tetraphenylporphine, studied at 35, 50, and 60 °C, yield good first-order data for

---

(13) U. Mayer, *Coord. Chem. Rev.*, **21**, 159 (1976).

(14) R. S. Drago, *Coord. Chem. Rev.*, **33**, 251 (1980).

(15) A. D. Adler, F. R. Longo, F. D. Finarelli, J. Goldmacher, J. Assour, and L. Korsakoff, *J. Org. Chem.*, **32**, 476 (1968).

Table I. Kinetic Results for Cu^{2+} Insertion into H_2TPP ($\mu = 0.2$ M; solvent Me_2SO)[a]

temp, °C	10^3k, s^{-1}	K, M^{-1}
35	3.63	8.24
50	9.06	13.5
60	15.9	18.3

[a] $\Delta H^{\ddagger} = 11.5 \pm 0.03$ kcal/mol; $\Delta S^{\ddagger} = -32.6 \pm 0.1$ eu. $\Delta H^\circ = 6.5 \pm 0.1$ kcal/mol; $\Delta S^\circ = 25.2 \pm 0.5$ eu.

5 half-lives or more. Experiments conducted to determine absorbance changes during the course of the reaction show isosbestic points at 490, 525, 585, 612, and 630 nm as shown in Figure 2. Although k_{obsd} does not show a linear dependence on $[Cu^{2+}]$ over the concentration range studied (cf. Figures 3–5), plots of $1/k_{obsd}$ vs. $1/[Cu^{2+}]$ are linear. These results suggest a mechanism involving a rapid preequilibrium involving copper(II) and H_2TPP prior to metal insertion and proton loss:

$$Cu^{2+} + H_2TPP \overset{K}{\rightleftharpoons} Cu^{2+};H_2TPP$$

$$Cu^{2+};H_2TPP \xrightarrow{k} CuTPP + 2H^+$$

Then

$$k_{obsd} = kK[Cu^{2+}]/(1 + K[Cu^{2+}])$$

This mechanism is consistent with the concentration dependence of k_{obsd}, the fact that the reaction is first-order over several half-lives although the solutions are unbuffered, and the presence of isosbestic points during the course of the reaction even though in some experiments *appreciable concentrations of* $Cu^{2+};H_2TPP$ *are present.*[16]

Values for k and K were obtained at each temperature with the use of a general minimization routine, SIMPLEX.[17] The results of these analyses are shown in Table I.

Discussion

When the incorporation of copper(II) into tetraphenylporphine is studied over a sufficiently wide concentration range of metal ion, significant deviations from simple second-order kinetics are observed. A comparison can be made of the present results with those obtained earlier by Longo et al. for the overall process by calculating the apparent activation parameters $\Delta H_2^{\ddagger}$ and $\Delta S_2^{\ddagger}$ by $\Delta H_2^{\ddagger} = \Delta H^\circ + \Delta H^{\ddagger}$ and $\Delta S_2^{\ddagger} = \Delta S^\circ + \Delta S^{\ddagger}$. Thus, we obtain $\Delta H_2^{\ddagger} = 18.0$ kcal/mol and $\Delta S_2^{\ddagger} = -7.4$ eu in comparison to 19.4 kcal/mol and −2.9 eu, respectively.[12] The agreement is even more dramatic for $\Delta G_2^{\ddagger}$: at 25 °C we obtain 20.2 kcal/mol while Longo et al. obtain 20.3 kcal/mol.

The preequlibrium step has been suggested as involving outer-sphere ion pair formation and porphyrin ring buckling[5,8] or alternatively the formation of a sitting-atop complex.[3,18] Estimates of the ring-buckling equlibrium constant have been provided as $K_B \approx 0.038$ in water[9] and $K_B \approx 0.025$ in DMF.[8] Therefore, if we factor a term of this magnitude out of K, we estimate $K_r \approx 175$ M^{-1} at 25 °C for the remaining part of the preequilibrium. This value of K_r is much too large to be accounted for in terms of outer-sphere ion pair formation between a 2+ ion and a neutral ligand in Me_2SO.[19,20] On this basis, it would appear that a more significant interaction between the metal ion and the porphyrin exists as, for example, the formation of a SAT. However, this interpretation leads to the following conceptual difficulties. A value for the entropy change for ring buckling is estimated as ∼−3 eu[9] and, therefore, the entropy change for the remaining portion of the preequilibrium, $\Delta S_r^\circ \approx 28$ eu. The process involves the combining of Cu^{2+} with a porphyrin ligand which in the absence of solvent effects is entropically unfavorable. Clearly, solvent structure plays a very large role in complex formation. The solvation sheaths around Cu^{2+} will be markedly affected during complex formation—solvent molecules can be expected to be released from structural constraints imposed by the free Cu^{2+} ion. However, the SAT complex involves at least partial dissociation of protons previously associated with pyrrole nitrogens. The interaction of H^+ with Me_2SO molecules is known to be very strong,[21] and solvent molecules would be ordered in this process, canceling the effect of copper ion/porphyrin interaction. Clearly, the value of ΔS_r° (or ΔS°) is not consistent with this model. Furthermore, two other factors suggest that protons do not dissociate from the porphyrin until the rate-determining step. In the present study as well as previous ones conducted in DMF,[8,12] no buffer is added to the medium. Yet the kinetics remain cleanly (pseudo) first-order for several half-lives. If a pre-rate-determining step involved protolytic equilibria, then the kinetics would not remain first order inasmuch as protons are produced during the course of the reaction. Also, the $\Delta S^{\ddagger}$ is strongly negative, and this is interpreted as due to the ordering of solvent molecules with the freeing of H^+ ions.

Therefore, we conclude that the interaction of copper(II) with H_2TPP in Me_2SO is best explained as being of the outer-sphere ion pair type without appreciable distortion of the porphyrin ring. In the rate-determining step, the ring distorts, protons are freed, and covalent bonds are formed to the metal ion as solvent molecules from the inner coordination sphere are lost; a structure similar to that proposed for the sitting-atop complex. Hence, our results suggest that in Me_2SO the SAT is probably a convenient model for the transition-state complex rather than the preequlibrium structure.[22]

Acknowledgment. We gratefully acknowledge support from the National Institutes of Health through Grant No. GM-17574.

Registry No. Cu^{2+}, 15158-11-9; H_2TPP, 917-23-7.

---

(16) R. G. Mayer and R. S. Drago, *Inorg. Chem.*, **15**, 2010 (1976).

(17) Copyrighted by J. P. Chandler, Department of Physics, University of Indiana, Bloomington, IN, 1965, and further expanded by T. Needham, Department of Chemistry, University of Illinois, Urbana, IL.

(18) P. Hambright and E. B. Fleischer, *Inorg. Chem.*, **9**, 1757 (1970).

(19) R. Fuoss, *J. Am. Chem. Soc.*, **80**, 5059 (1958).

(20) M. Eigen, *Z. Phys. Chem.* (*Wiesbaden*), **1**, 176 (1954).

(21) Y. K. Lau, P. P. S. Saluja, and P. Kebarle, *J. Am. Chem. Soc.*, **102**, 7429 (1980).

(22) A. D. Adler, W. Newman, M. Mulvaney, and J. Paone in "Porphyrin Chemistry Advanced", F. R. Longo, Ed., Ann Arbor Science, Ann Arbor, MI, 1979, pp 265–271.