Inorganica Chimica Acta, 129 (1987) L37–L39

Synthesis of Organohydroxylamine Complexes of Iron(II) Tetraphenylporphyrin

ALAN R. NEWMAN* and ANDREW N. FRENCH

Department of Chemistry, Ohio Wesleyan University,
Delaware, Ohio 43015, U.S.A.

(Received December 10, 1986)

Numerous studies have established that iron(II) and iron(III) porphyrins readily bind nitrogenous bases [1]. A category of nitrogenous bases that has not received much attention is hydroxylamine and its derivatives. Hydroxylamine is of importance as an intermediate in the interconversion of NO_2^- to NH_4^+ in the biosphere. Hydroxylamine has been identified as the first intermediate in the oxidation of NH_4^+ to NO_2^- by the nitrifying bacterium, *Nitrosomonas europaea* [2–4]. The enzyme responsible for oxidizing hydroxylamine, hydroxylamine oxidase, contains cytochrome P 460 which is believed to be involved in the oxidation [5–7]. There is also evidence of a hydroxylamine intermediate in the reduction of NO_2^- to NH_4^+ by the nitrite reductase enzyme [8] found in plants (spinach [9]), fungi (*Neurospora crassa* [10]) and bacteria (*Escherichia coli* [11] and *Achrombacter fischeri* [12]). The active site in *A. fischeri* nitrite reductase is a *c*-type cytochrome, while the active site in the other nitrite reductases is siroheme, an iron isobacteriochlorin [13]. Studies of heme-type prosthetic groups indicate that hydroxylamine is tightly bound to the iron [14].

Prior to this paper a NMR study of the reduction of ferric porphyrins with *N*-hydroxylpiperidine established that the base binds to iron(II) porphyrin [15]. In order to further study the role of hydroxylamine with iron porphyrins, we report the preparation of iron(II) porphyrin organohydroxylamine complexes of the general formula; $Fe(II)TPP(RNHOH)_2$ (TPP = dianion of *meso*-tetraphenylporphyrin; R = methyl, ethyl, propyl, and phenyl) (see Fig. 1). These complexes should be of value as models for hydroxylamine intermediates.

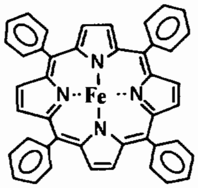

Fig. 1. Structure of FeTPP.

Experimental

Fe(III)TPP(Cl) and RNHOH were prepared following standard literature methods [16, 17]. Prior to use, toluene was refluxed in the presence of Na and dichloromethane was dried over CaH_2. Organohydroxylamines were recrystallized from methanol–ether. Under a nitrogen atmosphere, 200 mg of FeTPP(Cl) in approximately 45 ml of toluene was stirred over a zinc amalgam [18]. Following complete reduction to Fe(II)TPP, the solution was filtered and a 5–10 fold excess of RNHOH was added. After about 2 h of stirring, significant amounts of crystalline precipitate would form. Additional material could be collected by reducing the volume by about 1/3. The reddish-purple solid was collected by filtration and washed twice with deoxygenated methanol. The compound was crystallized from dichloromethane–methanol to which a small amount of the appropriate hydroxylamine derivative had been added. In the case of methyl hydroxylamine, the hydrochloride salt (MeNHOH•HCl) was used along with a slight excess of recrystallized Proton Sponge (1,8-bis(dimethylamino)naphthalene, Aldrich) to remove HCl. The reaction solution was stirred overnight. Overall yields for the complexes varied from 40 to 65% depending upon hydroxylamine derivative. Satisfactory chemical analyses were obtained for all the compounds (see Table I). Proton FT NMR spectra indicated that the complexes were diamagnetic.

When the above experimental procedure was repeated with FeTPP(Cl) and RNHOH, no evidence of complexation was observed. Besides complexing the metal, another possible reaction was the reduc-

TABLE I. C, H and N Analysis for $FeTPP(RHNOH)_2$ (%)

R	Calculated			Found		
	C	H	N	C	H	N
Me	72.43	5.03	11.03	72.45	4.85	10.34
Et	72.90	5.35	10.63	72.67	5.28	10.01
Pr	71.88	5.66	10.26	72.21	5.62	10.11
Ph	75.84	4.77	9.48	75.59	4.30	9.35

---

*Present address: Division of Environmental Chemistry, Department of Environmental Health Sciences, School of Hygiene and Public Health, Johns Hopkins University, Building 6, 3100 Wyman Park Drive, Baltimore, Md. 21211 U.S.A.

0020-1693/87/$3.50

tion of ferric porphyrin to ferrous porphyrin, typical of primary amines. However, after ~2 hours no change was observed. Eventually RNHOH decomposed and primary amines were formed.

Optical spectra were recorded on a Cary 219 spectrophotometer. Infrared spectra were obtained as Nujol mulls on a Beckman Acculab spectrometer. Satisfactory chemical analyses (Galbraith Laboratories, Inc., Knoxville, Tenn., U.S.A.) were obtained for all the compounds (see Table I). Cyclic voltammetry measurements were obtained with a PAR Model 174 Potentiostat and Model 175 Universal Programmer. Scan rates were 200 mV/s. A standard three electrode configuration was used; consisting of a glassy carbon working electrode, platinum wire counter electrode and saturated calomel reference electrode (sce). For exhaustive electrolyses, a PAR model 179 Digital Coulometer was used. A specially designed cell, generously loaned by Dr. Jack Fajer, which permits monitoring of the course of the electrolysis by optical spectra was also used [19]. Electrochemical experiments were performed under an argon atmosphere at 25 °C with tetrapropylammonium perchlorate as the electrolyte.

Results and Discussion

Solid samples of Fe(II)TPP$(RNHOH)_2$ are air stable. Nujol mull infrared spectra revealed two new weak bands at around 3200 and 3320 cm^{-1}, assigned respectively to -OH and -NH stretches of coordinated hydroxylamine [20].

A typical optical spectrum for one of the iron(II) complexes is reproduced in Fig. 2. The recorded spectrum is very similar to the spectrum of Fe(II)-TPP$(pyridine)_2$ [21]. Dichloromethane solutions of the phenylhydroxylamine complex (10^{-4} M) reacted immediately with air to form $[FeTPP]_2O$. Analogous behavior has been observed for bis pyridine complexes of iron(II) porphyrins [22]. On the other hand, solutions of the methyl-, ethyl- or propylhydroxylamine complexes, in either toluene or halogenated hydrocarbons, could be handled in air for short periods of time. However, after about 1 day the complexes reacted with air to form the μ-oxo dimer. Addition of free RNHOH to dichloromethane solutions of $FeTPP(RNHOH)_2$ did not change the optical spectrum, except in the case of the phenylhydroxylamine complex. Small amounts of phenylhydroxylamine added to the solution shifted peaks by ~5 nm, suggesting the presence in solution of five coordinate iron phenylhydroxylamine complex. These observations are consistent with the following equilibrium occurring in solution

$$FeTPP(RNHOH)_2 \rightleftharpoons FeTPP(RNHOH) + RNHOH \quad (1)$$

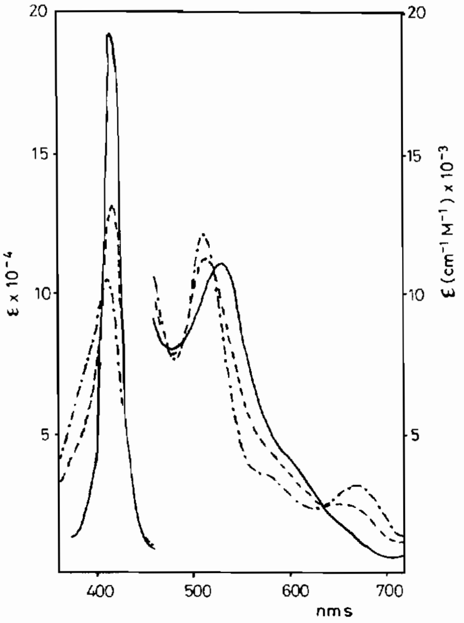

Fig. 2. Spectral changes during the exhaustive electrolysis of $FeTPP(PhNHOH)_2$ in dichloromethane. Initial spectrum (——), spectrum after 50% oxidation (— — —), spectrum after complete oxidation (— • —).

The equilibrium favors the bis organohydroxylamine complex. Loss of an axial ligand opens up a site for attack by dioxygen on the iron. The rapid oxidation of the phenylhydroxylamine complex is attributed to weaker coordination of PhNHOH due to steric hindrance of the phenyl ring.

Cyclic voltammetry studies of the iron(II) complexes in dichloromethane recorded an irreversible oxidation wave, $E_{p,anodic} = 0.6$–0.7 V *versus* sce, depending upon the complex. Exhaustive electrolysis of each complex showed that the irreversible oxidation took one electron to form an iron(III) complex. The unusually high potential for the oxidation of iron(II) is consistent with other electrochemical studies of iron porphyrins, which show an increase in Fe(III)/Fe(II) half-wave potential with axial ligands that preferentially bind Fe(II) over Fe(III) [23]. Optical changes recorded during the exhaustive electrolysis confirmed that the oxidation resulted in the loss of the organohydroxylamine. Since the oxidation took place in the presence of the electrolyte, tetrapropylammonium perchlorate, the product is Fe(III)-TPP(ClO_4) (see Fig. 2) [24]. A second oxidation was recorded, $E_{1/2} = 1.1$ V, assigned to the reversible one electron oxidation of the porphyrin [25].

We also attempted to prepare $FeTPP(NH_2OH)_2$ by the same procedure we used to prepare the organohydroxylamine complexes. When $NH_2OH \cdot HCl$ in methanol is added to FeTPP in toluene, under anaerobic conditions, the main product is FeTPP(Cl). If a base such as proton sponge or NaOMe is also added the main product is FeTPP(NO) [26]. Formation of nitrosyl from hydroxylamine in the presence of iron(III) hemes has been previously observed [27]. A similar reaction also occurs in the presence of transition metal cyanide and isocyanide complexes [28]. Based upon studies of these reactions the following reaction is proposed.

$$\begin{aligned} &\mathrm{Fe(III)TPP^+ + 2NH_2OH + B \longrightarrow} \\ &\qquad \mathrm{FeTPP(NO) + NH_3 + BH^+ + H_2O} \end{aligned} \qquad (2)$$

The above reaction begins first with the oxidation of iron(II) to iron(III). Then, in the presence of base, hydroxylamine disproportionates to give iron(II) nitrosyl, ammonia and water.

Acknowledgements

We wish to thank Dr. Keiko Koga at Ohio State University for collecting the NMR data. We also wish to thank Drs. Etsuko Fujita and Jack Fajer for communicating the results of their experiments and helpful suggestions. The Dreyfuss Fund generously provided a summer research stipend for A.N.F. Acknowledgement is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society for the support of this research.

References

1 D. Dolphin (ed.), 'The Porphyrins', Academic Press, New York, 1979.

2 D. C. Y. Tsang and I. Suzuki, *Can. J. Biochem., 60,* 1018 (1982).

3 R. D. Dua, B. Bhandari and D. J. D. Nicholas, *FEBS Letts., 106,* 401 (1979).

4 K. K. Andersson, S. B. Philson and A. B. Hooper, *Proc. Natl. Acad. Sci. U.S.A., 79,* 5871 (1982).

5 M. K. Rees, *Biochemistry, 7,* 353 (1966).

6 A. B. Hooper and K. R. Terry, *Biochemistry, 16,* 455 (1977).

7 A. B. Hooper, P. C. Maxwell and K. R. Tery, *Biochemistry, 17,* 2984 (1978).

8 E. J. Hewitt, *Annu. Rev. Plant Physiol., 26,* 73 (1975).

9 (a) P. J. Aparicio, D. B. Knaff and R. Malkin, *Arch. Biochem. Biophys., 169,* 102 (1975); (b) J. M. Vega and J. Kamin, *J. Biol. Chem., 252,* 896 (1977).

10 (a) J. M. Vega, R. H. Garret and L. M. Siegel, *J. Biol. Chem., 250,* 7980 (1975); (b) M. A. Lafferty and R. H. Garrett, *J. Biol. Chem., 249,* 7555 (1974).

11 R. H. Jackson, A. Cornish-Bowden and J. A. Cole, *Biochem. J., 193,* 861 (1981).

12 O. Prakash and J. C. Sadana, *Arch. Biochem. Biophys., 148,* 614 (1972).

13 M. G. Guerrero, J. M. Vega and M. Losada, *Annu. Rev. Plant Physiol., 107,* 4207 (1981).

14 J. C. Sadana, B. M. Khan and D. J. D. Nicholas, *FEMS Microbiol. Lett., 12,* 415 (1981).

15 J. Del Gaudio and G. N. La Mar, *J. Am. Chem. Soc., 100,* 1112 (1978).

16 A. D. Adler, R. K. Longo, F. Kampus and J. Kim, *J. Inorg. Nucl. Chem., 32,* 2443 (1970).

17 A. J. Blatt, 'Organic Synthesis', Vol. 2, Wiley, New York, 1943, p. 445.

18 J. T. Landrum, K. Hatano, W. R. Scheidt and C. A. Reed, *J. Am. Chem. Soc., 102,* 6729 (1980).

19 J. Fajer, I. Fujita, M. S. Davis, A. Forman, L. K. Hanson and K. M. Smith, in K. M. Kadish (ed.), 'Electrochemical and Spectrochemical Studies of Biological Redox Components', Adv. Chem. Ser. 201, Americal Chemical Society, Washington, D.C., 1982, p. 489.

20 K. Nakamoto, 'Infrared and Raman Spectra of Inorganic and Coordination Compounds', 3rd edn., Wiley-Interscience, New York, 1978.

21 D. Brault and M. Rougee, *Biochemistry, 22,* 4591 (1974).

22 H. Kobayashi and Y. Yanagawa, *Bull. Chem. Soc. Jpn., 45,* 450 (1972).

23 (a) K. M. Kadish and L. A. Bottomley, *Inorg. Chem., 19,* 823 (1980); (b) L. A. Bottomley and K. M. Kadish, *Inorg. Chem., 20,* 1348 (1981).

24 C. A. Reed, T. Mashiko, S. P. Bentley, M. E. Kastner, W. R. Scheidt, K. Spartalian and G. Lang, *J. Am. Chem. Soc., 101,* 2948 (1979).

25 H. M. Goff, M. A. Phillipi, A. D. Boersman and A. P. Hansen, in K. M. Kadish (ed.), 'Electrochemical and Spectrochemical Studies of Biological Redox Components', Adv. Chem. Ser. 201, American Chemical Society, Washington, D.C., 1982, p. 357.

26 B. B. Wayland and L. W. Olson, *J. Am. Chem. Soc., 96,* 6037 (1974).

27 M. F. Blokzijl-Homan and B. F. Van Gelder, *Biochim. Biophys. Acta, 234,* 493 (1971).

28 K. G. Caulton, *Coord. Chem. Rev., 14,* 317 (1975) and refs. therein.