A Bis-Pocket Porphyrin

Kenneth S. Suslick* and Mary M. Fox

Contribution from the School of Chemical Sciences, University of Illinois at Urbana—Champaign, Urbana, Illinois 61801. *Received June 4, 1982*

Abstract: The synthesis, characterization, and ligand-binding properties of a porphyrin with sterically protected pockets on both faces is described. 5,10,15,20-Tetrakis(2,4,6-triphenylphenyl)porphyrin, or the "bis-pocket" porphyrin, is synthesized by the condensation of 2,4,6-triphenylbenzaldehyde with pyrrole in refluxing propionic acid. Metalation of this porphyrin with $Fe(CO)_5/I_2$ in toluene and reduction with $(CH_3)_4NBH_4$ yields the four-coordinate Fe(II) complex. Upon addition of 1,2-dimethylimidazole, the five-coordinate adduct is produced which is capable of completely reversible oxygenation. The equilibrium constant for imidazole binding indicates that the protected pockets do not sterically interfere with axial ligation, while still providing the spacing necessary to prevent bimolecular irreversible oxidation of the Fe(II) complex. In contrast, the O_2 affinity shown by this porphyrin complex is dramatically reduced compared to other synthetic analogues or to most heme proteins. This is attributed in part to the completely nonpolar binding site present in this bis-pocket porphyrin, compared to the relatively polar and hydrogen-bonding environment of other systems. Confirmation of this interpretation comes from the effect of solvent polarity on dioxygen affinities: as the solvent is changed from mesitylene to toluene to chlorobenzene to *o*-dichlorobenzene, the $P_{1/2}$ for O_2 binding decreased from 640 torr to 508 to 299 to 227 torr, in good correlation with empirical solvolytic scales.

Heme proteins and their synthetic analogues demonstrate dramatic variation in O_2 affinities (over a range of 10^6 in equilibrium constants) due to the nature of the binding site pockets, the effects of solvation, local polarity, and hydrogen bonding, and the structural influence of the protein itself.[1] In spite of intensive study with model compounds, relative importance of these factors in regulating ligand affinities is still unclear. A number of synthetic porphyrins have been synthesized in recent years with sterically protected superstructures.[2-5] Only a few of these,[2-4] most notably the "picket-fence" and the "capped" porphyrins, bind O_2 reversibly at 300 K. Many of the others are insufficiently protected to yield stable FeO_2 complexes.[5]

We wish to report the synthesis of a completely nonpolar "bis-pocket" porphyrin, its characterization, and the reversible O_2 binding to its Fe(II) complex. The "bis-pocket" porphyrin, 5,10,15,20-tetrakis(2,4,6-triphenylphenyl)porphyrin (H_2TTPPP),[6] which has *nonpolar* pockets on *both* faces of the macrocycle, shows completely reversible oxygenation of five-coordinate Fe(II) complexes, but with dramatically reduced O_2 affinity. In contrast, the pockets do not impede the binding of axial nitrogenous ligands. We attribute the lowered O_2 affinity to the effect of local polarity. This is confirmed by the effect of solvent polarity on O_2 binding of this system, which provides a quantitative understanding of the contributions which pocket polarity and solvation make the O_2 binding.

Experimental Section

All solvents used were purchased as reagent grade or better. Each was purified[7] in the following manner and subsequently stored under N_2. Mesitylene was treated with silica gel, dried initially with $CaCl_2$, and distilled from sodium. Toluene and benzene were distilled from sodium benzophenone ketyl. Chlorobenzene was washed with concentrated H_2SO_4, aqueous Na_2CO_3, and water, dried with $CaCl_2$, and finally distilled over P_2O_5. *o*-Dichlorobenzene was washed with concentrated H_2SO_4, dried with $CaCl_2$, and distilled from CaH_2. Purity of the solvents were crucial to avoid trace concentrations of ligands which would perturb the four-coordinate Fe^{II}TTPPP optical spectrum. 1,2-Dimethylimidazole was purchased as 99% pure from Aldrich. It was vacuum distilled over Na and twice recrystallized from benzene under N_2. Prepurified O_2 and compressed air were purchased from NCG Industrial Gases and the 5.25% O_2 in N_2 mixture was purchased from Union Carbide.

The bis-pocket porphyrin (H_2TTPPP) was prepared by slow addition of a stoichiometric amount of pyrrole diluted in xylenes to a refluxing propionic acid solution of 2,4,6-triphenylbenzaldehyde (0.2 M).[8] The 2,4,6-triphenylbenzaldehyde was prepared from 2,4,6-triphenylbromobenzene[9] by treatment with 1.25 equiv of *n*-butyllithium in refluxing benzene and quenching with *N*-formylpiperidine or dimethylformamide.[10] The aldehyde was isolated by flash filtration through silica gel (yield 85%; mp 130-132 °C). The porphyrin was isolated from the crude condensation mixture by flash chromatographic separation on silica gel and further purification on C_2 reverse-phase silica gel[11] (yield 1%). The solubility of this porphyrin is surprisingly high in a wide range of solvents: >50 mM in toluene, chloroform, or dichloromethane and >10 MM even in hexane.

Metalation of the porphyrin cannot be accomplished by the usual methods[12] using Fe(II) salts but can be achieved with $Fe(CO)_5$ and I_2

(1) (a) Traylor, T. G. *Acc. Chem. Res.* **1981**, *14*, 102. (b) Collman, J. P.; Halbert, T. R.; Suslick, K. S. In "Metal Ion Activation of Dioxygen"; Spiro, T. G., Ed.; Wiley: New York, 1980; Chapter 1. (c) Perutz, M. F. *Annu. Rev. Biochem.* **1979**, *48*, 327. (d) Baldwin, J.; Chothia, C. *J. Mol. Biol.* **1979**, *129*, 175. (e) Jones, R. D.; Summerville, D. A.; Basolo, F. *Chem. Rev.* **1979**, *79*, 139.

(2) (a) Collman, J. P.; Gagne, R. R.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, W. T. *J. Am. Chem. Soc.* **1975**, *97*, 1427. (b) Jameson, G. B.; Molinaro, F. S.; Ibers, J. A.; Collman, J. P.; Brauman, J. I.; Rose, E.; Suslick, K. S. *Ibid.* **1980**, *102*, 3224. (c) Collman, J. P.; Brauman, J. I.; Collins, T. J.; Iverson, B.; Sessler, J. L. *Ibid.* **1981**, *103*, 2450.

(3) (a) Almog, J.; Baldwin, J. E.; Dyer, R. L.; Peters, M. *J. Am. Chem. Soc.* **1975**, *97*, 226. (b) Budge, J. R.; Ellis, P. E., Jr.; Jones, R. D.; Linard, J. E.; Basolo, F.; Baldwin, J. E.; Dyer, R. L. *Ibid.* **1979**, *101*, 4760. (c) Hashimoto, T.; Dyer, R. L.; Crossley, M. J.; Baldwin, J. E.; Basolo, F. *Ibid.* **1982**, *104*, 2101.

(4) Ward, B.; Wang, C. B.; Chang, C. K. *J. Am. Chem. Soc.* **1981**, *103*, 5236.

(5) (a) Diekmann, H.; Chang, C. K.; Traylor, T. G. *J. Am. Chem. Soc.* **1971**, *93*, 4068. (b) Ogoshi, H.; Sugimoto, H.; Yoshida, Z. *Tetrahedron Lett.* **1977**, *18*, 1515. (c) Battersby, A. R.; Hamilton, A. D. *J. Chem. Soc., Chem. Commun.* **1980**, 117. (d) Momenteau, M.; Loock, B. *J. Mol. Catal.* **1980**, *7*, 315. (e) Momenteau, M.; Lavalette, D. *J. Chem. Soc., Chem. Commun.* **1982**, 341. Vaska, L.; Amundsen, A. R.; Brady, R.; Flynn, B. R.; Nakai, H. *Finn. Chem. Lett.* **1974**, 66. (f) Amundsen, A. R.; Vaska, L. *Inorg. Chim. Acta* **1975**, *14*, L49. (g) Cense, J. M.; LeQuan, R. M. *Tetrahedron Lett.* **1979**, *39*, 3725.

(6) Abbreviations used in this paper include: TTPPP, 5,10,15,20-tetrakis(2,4,6-triphenylphenyl)porphyrinate(2-), the "bis-pocket" porphyrin; TPP, 5,10,15,20-tetraphenylporphyrinate(2-); C_2Cap, 5,10,15,20-[pyromellitoyltetrakis[*o*-(oxyethoxy)phenyl]]porphyrinate(2-), the "capped" porphyrin; TpivPP, 5,10,15,20-tetrakis[*o*-(pivalamido)phenyl]porphyrinate(2-), the "picket-fence" porphyrin; PocPivP, the "capped picket-fence" porphyrinate(2-) described elsewhere;[2c] $Piv_3$4ClmPP, an imidazole-tailed picket-fence porphyrinate(2-) described elsewhere;[1b] Im-chelated protoheme, protoheme-*N*-[3-(imidazolyl)propyl]amide; Mb, myoglobin; Hb, hemoglobin; Hb-T, hemoglobin the low affinity (T) state; 1,2-Me_2Im, 1,2-dimethylimidazole; 1-MeIm, 1-methylimidazole, $P_{1/2}$, partial pressure of gas at half-saturation; K_B, equilibrium constant for binding of a single axial ligand to the four-coordinate metalloporphyrin.

(7) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. "Purification of Laboratory Chemicals", 2nd ed.; Pergamon Press: Oxford, 1980.

(8) (a) Longo, F. R.; Thorne, E. J.; Adler, A. D.; Dym, S. *J. Heterocyl. Chem.* **1975**, *12*, 1305. (b) Adler, A. D.; Sklar, L.; Longo, F. R.; Finarelli, J. D.; Finarelli, M. G. *Ibid.* **1968**, *5*, 669. (c) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476.

(9) Kohler, E. P.; Blanchard, L. W. *J. Am. Chem. Soc.* **1935**, *57*, 367.

(10) Evans, E. A. *Chem. Ind. (London)* **1957**, 1596.

(11) Snyder, L. R.; Kirkland, J. J. "Introduction to Modern Liquid Chromatography", 2nd ed.; Wiley-Interscience: New York, 1979; p 276.

(12) (a) Adler, A. D.; Longo, F. R.; Kampas, F.; Kim, J. *J. Inorg. Nucl. Chem.* **1970**, *32*, 2443. (b) Fleischer, E. B.; Palmer, J. M.; Srivastava, T. S.; Chatterjee, A. *J. Am. Chem. Soc.* **1971**, *93*, 3162. (c) Chang, C. K.; DiNello, R. K.; Dolphin, D. *Inorg. Synth.* **1980**, *20*, 147.

0002-7863/83/1505-3507$01.50/0

Table I. O_2 and 1,2-Me_2Im Binding to Iron(II) Porphyrin Complexes[a]

complex	solvent	$P_{1/2}(O_2)$, torr (25 °C)	π^*	log K_B, M^{-1}	ref
Hb (T state)	water (pH 7)	9-160[b]	1.09		27
FeTPP(1,2-Me_2Im)	toluene		0.54	4.43 (5)	3c
FeTpivPP(1,2-Me_2Im)	toluene	38	0.54	4.6	14a
FePocPivP(1,2-Me_2Im)	toluene	13	0.54	4.7	2c
Fe(C_2Cap)(1,2-Me_2Im)	toluene	4000	0.54	3.06 (5)	3c
FeTTPPP(1,2-Me_2Im)	mesitylene	640	0.41		this work
	toluene	508	0.54	4.70 (5)	this work
	benzene	473	0.59		this work
	chlorobenzene	299	0.71		this work
	o-dichlorobenzene	227	0.80		this work

[a] π^* values from ref 21. [b] Depends upon phosphate and other anion concentrations.

in refluxing toluene[13] to give FeTTPPP(I) (6 h, >80% yield). All subsequent procedures were carried out under nitrogen in a Vacuum Atmospheres inert-atmosphere glovebox. Fe^{II}TTPPP was conveniently prepared by reduction of the ferric complex with $(CH_3)_4NBH_4$ in tetrahydrofuran followed by addition of toluene, vacuum evaporation of the solvent and to remove tetrahydrofuran, redissolution in toluene, and filtration to remove unreacted borohydride and byproducts.

The porphyrin has been characterized by its optical spectrum, field desorption mass spectrum, proton NMR spectrum, and elemental analysis. In all cases for which comparisons can be made, the optical spectra of TTPPP derivatives are extremely similar to but red-shifted ~30 nm from those of TPP. The optical spectrum of H_2TTPPP in benzene shows maxima (with log ϵ in parentheses) at 438 (5.33), 530 (4.11), 565 (3.83), 606 (3.61), and 655 nm (3.51) and of H_4TTPPP^{2+} in benzene shows maxima at 475 (5.22), 569 (3.37), 617 (3.82), and 675 nm (4.30). Field desorption mass spectra of H_2TTPPP showed parent ion peaks at *m/e* (relative intensity) 1527 (1.0), 1528 (1.0), 1529 (0.7), 1530 (0.3), and 1531 (0.2), corresponding to a predicted spectra of peaks due to zero, one, two, three, and four ^{13}C of *m/e* (relative intensity) 1526.6 (1.00), 1527 (1.24), 1528.6 (0.76), 1529 (0.31), and 1530.6 (0.09). Proton NMR of H_2TTPPP and FeTTPPP(I) are quite similar to those of H_2TPP and FeTPP(X), respectively; in CD_2Cl_2 referenced to tetramethylsilane, H_2TTPPP shows resonances at 8.6 ppm for the pyrrolic protons and a complex multiplet at 6–8 ppm for the phenyl protons and FeTTPPP(I) a resonance at 79 ppm for the pyrrolic protons.

Oxygenation equilibria were determined by spectrophotometric O_2 titration of the five-coordinate adduct of Fe^{II}TTPPP and 1,2-Me_2Im, a sterically hindered imidazole incapable of forming a six-coordinate complex at reasonable concentrations.[14] Base concentrations were chosen to give >99% of the five-coordinate adduct. Titrations were carried out in a 50-mL tonometer with a Hitachi 100-80A spectrophotometer equipped with thermostated cell compartment (±0.2 °C). Figure 1 shows a typical set of spectra. After equilibria measurements were made, the sample was vacuum degassed to demonstrate reversibility; in all cases >90% reversibility was achieved even after 3 h of oxygenation. Oxygen partial pressures were determined from injections of known volumes of gas into the tonometer of known volume. Corrections for variation in room temperature and solubility of O_2 in the solution were made but in all cases were <1%. Data analysis required only one limiting spectrum (i.e., the five-coordinate adduct), as described elsewhere.[14]

Results

The equilibria concerned with in this study between iron(II) porphyrins and axial bases and O_2 are

$$\text{Fe(Porph)} + \text{B} \overset{K_B}{\rightleftharpoons} \text{Fe(Porph)(B)} \quad (1)$$

$$\text{Fe(Porph)(B)} + \text{B} \overset{K_B^B}{\rightleftharpoons} \text{Fe(Porph)(B)}_2 \quad (2)$$

$$\text{Fe(Porph)(B)} + \text{O}_2 \overset{K_{O_2}}{\rightleftharpoons} \text{Fe(Porph)(B)(O}_2\text{)} \quad (3)$$

The pockets of our "bis-pocket" porphyrin do *not* impede axial ligation of imidazoles compared to either unprotected porphyrins (e.g., FeTPP) or porphyrins with one protected face (e.g., "picket-fence", FeTpivPP, or "capped-picket fence", FePocPivP, porphyrins), as seen in Table I. Not only is the binding of the first axial ligand unhindered in the bis-pocket porphyrin, but also the binding of a second imidazole is even slightly enhanced. The equilibrium constant, $K_BK_B^B$, for binding two 1-methylimidazoles is $\sim 5 \times 10^9$ M^{-2} for Fe^{II}TTPPP compared[15] to $\sim 7 \times 10^8$ M^{-2} for Fe^{II}TPP.

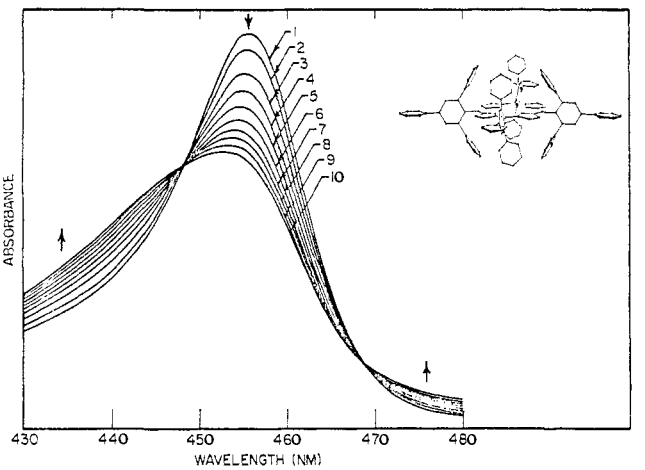

Figure 1. Spectroscopic determination of $P_{1/2}$ values for FeTTPPP(1,2-Me_2Im) in toluene at 29.8 °C. Inset is a schematic representation of the bis-pocket porphyrin ligand. O_2 partial pressures for spectra 1 through 10 are 0, 55, 143, 232, 321, 409, 498, 586, 675, and 764 torr, respectively.

In order to study the oxygenation equilibrium, eq 3, conditions must be chosen to ensure the dominant species in solution is the five-coordinate Fe(Porph)(B). Previous work has shown that Fe(II) porphyrins bind the second axial ligand more strongly than the first ($K_B^B > K_B$) for unhindered imidazoles,[15,16] but that 2-substituted imidazoles, which are sterically hindered, formed five-coordinate adducts cleanly ($K_B^B \ll K_B$).[14,15] O_2 binding to such hindered imidazole adducts has been suggested to mimic the putative restraint of T-state (deoxy, low affinity) hemoglobin.[1,14] Table I summarizes the equilibria measurements of both 1,2-Me_2Im and O_2 binding to FeTTPPP, other synthetic analogues, and heme proteins.

$P_{1/2}$ values (i.e., $K_{O_2}^{-1}$) were determined[14,17] at six wavelengths; agreement within each titration and between separate runs were better than 10%, except for the titrations in mesitylene which were within 15%. Specific values of $P_{1/2}$ used to determine the thermodynamic parameters were measured in multiple titrations at each temperature. In toluene solution, these $P_{1/2}$ values, in torr, were as follows: at −9.4 °C 20 and 21; at 0.0 °C, 52, 54, and 56; at 11.0 °C, 158, 141, and 164; at 20.4 °C, 317 and 349; at

(13) (a) Tsutsui, M.; Ichikawa, M.; Vihwinkel, F.; Suzuki, K. *J. Am. Chem. Soc.* **1966**, *88*, 854. (b) Buchler, J. W. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1975**, *30B*, 385.

(14) (a) Collman, J. P.; Brauman, J. I.; Doxsee, K. M.; Halbert, T. R.; Suslick, K. S. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 564. (b) Collman, J. P.; Brauman, J. I.; Doxsee, K. M.; Halbert, T. R.; Hayes, S. E.; Suslick, K. S. *J. Am. Chem. Soc.* **1978**, *100*, 2761.

(15) (a) Brault, D.; Rougee, M.. *Biochem. Biophys. Res. Commun.* **1974**, *57*, 654. (b) Wagner, G. C.; Kassner, R. J. *Biochem. Biophys. Acta* **1975**, *392*, 319. (c) Rougee, M.; Brault, D. *Biochemistry* **1975**, *14*, 4100. (d) Collman, J. P.; Reed, C. A. *J. Am. Chem. Soc.* **1973**, *95*, 2048.

(16) Smith, K. M. "Porphyrins and Metalloporphyrins"; Elsevier: New York, 1975.

(17) Drago, R. S. "Physical Methods in Chemistry"; W. B. Saunders: Philadelphia, PA, 1977.

Table II. Thermodynamic Data for O_2 Binding to Iron Porphyrin Complexes[a]

complex	$P_{1/2}(O_2)$, torr (25 °C)	$\Delta H°$, kcal/mol	$\Delta S°$, eu	ref
Mb, mammalian	0.5-1.3	−19 to −13.2	−50 to −38	28, 29
Fe(Im-chelated protoheme)	1.4	−14.0 ± 0.9	−35	30
Fe($Piv_3$4ClmPP)	0.60	−16.8 ± 0.8	−42 ± 3	14
Fe(C_2Cap)(1-MeIm)	23	−10.5 ± 0.3	−41 ± 1	18
Hb, mammalian[b]	~10	−10 to −15	−26 to −33	28, 31
FeTPivPP(1,2-Me_2Im), toluene	38	−14.3 ± 0.5	−42 ± 2	14
Fe(C_2Cap)(1,2-Me_2Im), toluene	4000	−9.7 ± 0.2	−49 ± 1	18
FeTTPPP(1,2-Me_2Im), toluene	508	−14.4 ± 0.2	−47.4 ± 0.7	this work

[a] Standard state 1 atm; eu = cal/(mol K). [b] Average of the four binding sites, dependent on phosphate and other ions.

25.0 °C, 506 and 510; at 29.8 °C, 753, 753, and 780; at 41.9 °C, 1649. Excellent isosbestic points were observed for oxygenation titrations for temperatures as high as 60 °C. The half-life for irreversible oxidation is >30 h at 25 °C and >2 h at 60 °C, making this iron porphyrin complex among the most stable yet reported. Thermodynamic parameters were determined by van't Hoff plots over a 50° range and are given in Table II, along with comparisons to related systems.

Discussion

Although it has been previously suggested that increased polarity should increase the observed O_2 affinities,[19] these suggestions have been based on studies of flat, unprotected porphyrins in which the specific effects of porphyrin solvation could not be evaluated. Thus it has not been previously possible to separate the effects of differential solvation of the deoxy vs. the oxy state from polarity effects.[14,20] In these present studies, however, such differential solvation has been minimized due to the nature of the steric protection afforded both axial binding sites.

The O_2 affinity of Fe^{II}TTPPP(1,2-Me_2Im) is significantly lower than those of other synthetic analogs or of T-state Hb as seen in Table I. The reduced affinity cannot be attributed to steric hindrance of the pockets or to distortion of the porphyrin, as demonstrated by base-binding equilibria.[20c] As discussed earlier, both 1,2-Me_2Im and 1-MeIm are bound even more tightly to the bis-pocket iron(II) porphyrin than to open-face iron(II) porphyrins. This is not the case in the capped porphyrins,[3] in which the distortion of the macrocycle caused by the cap affects the ability of even the four-coordinate porphyrin to bind all axial ligands and in which the steric constraints of the cap preclude formation of six-coordinate adducts except for the smallest of ligands (O_2, CO, NH_3).[25] The large difference between the dioxygen affinity of the bis-pocket porphyrin complex and those of the picket-fence[14] or pocket porphyrin[2c] must be attributed primarily to the loss of polarity in the binding pocket. Strong confirmation of this is found in the effect of changing solvent from mesitylene to toluene to benzene to chlorobenzene to *o*-dichlorobenzene (these were chosen to minimize complications due to hydrogen bonding or solvent coordination and to eliminate significant differences in solvent-solute interactions): as solvent polarity increases, O_2 affinity increases. In addition, an excellent linear correlation is found between the observed $\Delta G°$ of O_2 binding as a function of solvent with various empirical solvent polarity parameters (e.g., π^*, E_T, etc.)[21] as seen in Figure 2. These empirical solvent scales are based on solvent influence upon various spectroscopic probes ($\pi \rightarrow \pi^*$ electronic transitions, principally, but also NMR or IR) and measure the relative stability of charge separation as a function of solvent. The generally accepted presence of charge separation in end-on dioxygen complexes[22] predicts the correlation we observe in Figure 2.

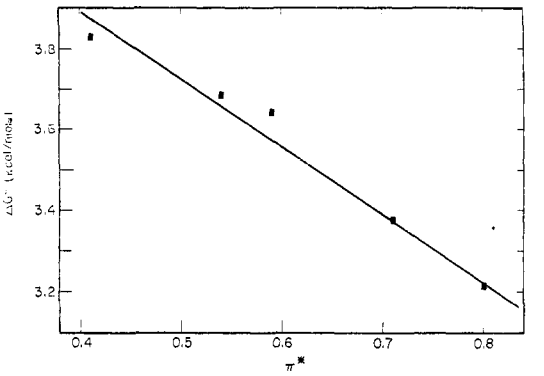

Figure 2. Correlation between π^*, an empirical solvent scale, with $\Delta G°$ of oxygenation of FeTTPPP(1,2-Me_2Im) at 25 °C in mesitylene, toluene, benzene, chlorobenzene, and *o*-dichlorobenzene (in order of increasing π^* values). The solid line represents a linear regression fit of $\Delta G° = -1.63\pi^* + 4.54$ kcal/mol for $P_{1/2}$ in torr.

In recent crystal structures of oxy-Mb and oxy-Hb, the importance of hydrogen bonding to the bound dioxygen has been demonstrated structurally.[23] EPR studies[24] have also implicated hydrogen bonding in cobalt substituted Mb. In other protected pocket porphyrins, the pocket has substantial polarity. For example, in Fe(TpivPP)(1,2-Me_2Im)(O_2), the local environment about the bound O_2 includes four amide groups, and the closest distance between the terminal oxygen atom of O_2 and an amide hydrogen is 3.1 (1) Å, as calculated from the reported data.[2b] One can now estimate that the impact which such polarity has on O_2 binding is quite significant, roughly a factor of 25 in $P_{1/2}$, compared to a completely nonpolar binding site.

One might hope to see this difference well separated in the enthalpy and entropy of the oxygenation equilibrium. The $\Delta H°$ and $\Delta S°$ (25 °C, standard state 1 atm, in toluene), shown in Table

(18) Linard, J. E.; Ellis, P. E., Jr.; Budge, J. R.; Jones, R. D.; Basolo, F. *J. Am. Chem. Soc.* **1980**, *102*, 1896.

(19) (a) Stynes, H. C.; Ibers, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 5125. (b) Carter, M. J.; Rillema, D. P.; Basolo, F. *Ibid.* **1974**, *96*, 392. (c) Weschler, C. J.; Anderson, D. L.; Basolo, F. *Ibid.* **1975**, *97*, 6707. (d) Tovrog, B. S.; Kitko, D. J.; Drago, R. S. *Ibid.* **1976**, *98*, 5144. (e) Brinigar, W. S.; Chang, C. K.; Geibel, J.; Traylor, T. G. *Ibid.* **1974**, *96*, 5597. (f) Traylor, T. G.; Berzinis, A. P. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 3171.

(20) (a) Collman, J. P.; Brauman, J. I.; Doxsee, K. M.; Halbert, T. R.; Suslick, K. S. *J. Am. Chem. Soc.* **1978**, *100*, 2761. (b) Walker, F. A.; Benson, M. *Ibid.* **1980**, *102*, 5530. (c) One could imagine that the similarity in K_B and K_B^B are due to the coincidental cancellation of destabilizing steric interactions between the pocket and the imidazole with some unspecified stabilizing interaction (e.g., π complexation). This might explain the lowered O_2 affinities observed, but would also predict lowered CO affinities as well. This is not the case, however, since the CO affinity of FeTTPPP(1,2-Me_2Im) is *very* high with $P_{1/2}(O_2)/P_{1/2}(CO) \approx 10^5$! Very recently, we have examined the solvent influence on CO binding and find that CO affinities *decrease* with increasing solvent polarity. This suggests a new mechanism by which heme proteins may discriminate[1b] against CO in favor of O_2. Suslick, K. S.; Fox, M. F., submitted for publication.

(21) Abboud, J. L. M.; Kamlet, M. J.; Taft, R. W. *Prog. Phys. Org. Chem.* **1981**, *13*, 485.

(22) (a) Vaska, L. *Acc. Chem. Res.* **1976**, *9*, 175. (b) Case, D. A.; Huynh, B. H.; Karplus, M. *J. Am. Chem. Soc.* **1979**, *101*, 4433.

(23) (a) Phillips, S. E. V.; Schoenborn, B. P. *Nature (London)* **1981**, *292*, 81. (b) Shaanan, B., *Ibid.* **1982**, *296*, 683.

(24) Ikeda-Saito, M.; Iizuka, T.; Yamamoto, H.; Kayne, F. J.; Yonetani, T. *J. Biol. Chem.* **1977**, *252*, 4882.

(25) Jameson, G. B.; Ibers, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 2823.

(26) Suslick, K. S.; Fox, M. M., unpublished work.

(27) (a) Imai, K.; Yonetani, T.; Ikeda-Saito, M. *J. Mol. Biol.* **1977**, *109*, 83. (b) MacQuarrie, R.; Gibson, G. H. *J. Biol. Chem.* **1971**, *246*, 5832. (c) Sharma, V. S.; Schmidt, M.; Ranney, H. M. *Ibid.* **1976**, *251*, 4267.

(28) Antonini, E.; Brunori, M. "Hemoglobin and Myoglobin in their Reactions with Ligands"; American Elsevier: New York, 1971.

II, are -14.4 (2) kcal/mol and -47.4 (7) cal/(mol K) for O_2 binding to FeTTPPP(1,2-Me_2Im) compared to -14.6 (5) kcal/mol and -42 (2) cal/(mol K) for FeTpivPP(1,2-Me_2Im).[14] In comparison of the picket-fence porphyrin, then, the diminished O_2 affinity of the bis-pocket porphyrin is primarily entropic. This again emphasizes the contribution which solvation of the porphyrin complexes makes to the observed equilibrium. Comparisons to the capped porphyrin[18] show the distortion induced by the cap affects the enthalpy of ligand binding primarily, as expected. Comparison to Mb shows enthalpies and entropies which are similar, but detailed comparison is difficult due to the reported variation among different species' Mb.[29] Due to the complexity of Hb's cooperative binding, meaningful comparisons to the $\Delta H°$ and $\Delta S°$ of oxygenation are difficult. The effect of steric hindrance in the axial base (i.e., 1,2-Me_2Im) within related systems is principally enthalpic for the picket-fence porphyrins but entropic for the capped porphyrin; the origin of this difference remains unknown.

Conclusion

We have described the synthesis and ligand binding of a bis-pocket iron porphyrin complex in which both faces of the macrocycle are well protected by nonpolar pockets. The steric protection provides for reversible dioxygen binding by Fe(II) complexes of the bis-pocket porphyrin with remarkable kinetic stability. The greatly diminished O_2 affinity of this system is due to the nonpolar nature of the binding site, as confirmed from the effect of polar solvents and not to conformational steric strain, as confirmed by equilibria base binding studies. Clearly, *even in protected pocket porphyrin complexes*, the local polarity and choice of solvent can have significant impact on O_2 binding. In addition to yielding stable dioxygen complexes, this bis-pocket porphyrin also allows the oxidation of its ferric complex by a wide range of oxidants, including hydroperoxides, peracids, and iodosoarenes, to produce the same intermediate stable for days at room temperature without oxidative ring cleavage of the macrocycle.[26] Further studies are presently underway to characterize this highly oxidized species.

Acknowledgment. We wish to acknowledge the assistance of J. A. Steinkamp and A. Singer in the syntheses described. This work was supported by the NIH (Grant HL 25934), the Midwest NSF Regional NMR Facility (Grant CHE 97-16100), and the UIUC Mass Spectrometry Laboratory (NIH Grant GM 27029).

Registry No. 5,10,15,20-Tetrakis(2,4,6-triphenylphenyl)porphyrin, 85390-97-2; pyrrole, 109-97-7; 2,4,6-triphenylbenzaldehyde, 85390-98-3; 2,4,6-triphenylbromobenzene, 10368-73-7; iron 5,10,15,20-tetrakis-(2,4,6-triphenylphenyl)porphyrin, 85390-99-4; 1,2-dimethylimidazole-Fe^{II}TTPPP adduct, 85391-00-0; oxygen, 7782-44-7; 1,2-dimethylimidazole, 1739-84-0.

(29) Wang, M. Y. R.; Hoffman, B. M.; Shire, S. J.; Gurd, F. R. N. *J. Am. Chem. Soc.* **1979**, *101*, 7394.
(30) Traylor, T. G.; Berzinis, A. P. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 3171.
(31) (a) Imai, K.; Yonetani, T. *J. Biol. Chem.* **1975**, *250*, 7093. (b) Imai, K.; Tyuma, I. *Biochem. Biophys. Res. Commun.* **1973**, *51*, 52.

Isolation, Purification, and Characterization of Intermediate (Iodosylbenzene)metalloporphyrin Complexes from the (Tetraphenylporphinato)manganese(III)-Iodosylbenzene Catalytic Hydrocarbon Functionalization System

John A. Smegal, Bruce C. Schardt, and Craig L. Hill*

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. *Received September 23, 1982*

Abstract: A second type of high-valent complex has been isolated from the reaction of (tetraphenylporphinato)manganese(III) derivatives, $XMn^{III}TPP$, with iodosylbenzene. This new type of complex, isolated from the $XMn^{III}TPP$-iodosylbenzene system when X = Cl^- or Br^-, is a dimeric μ-oxo manganese(IV) porphyrin complex that contains one iodosylbenzene per manganese, $[XMn^{IV}TPP(OIPh)]_2O$, **1**. These complexes are distinct from those complexes isolated from the $XMn^{III}TPP$-iodosylbenzene system when X = N_3^- or OCN^-, $[XMn^{IV}TPP]_2O$, **2**. The iodosylbenzene complexes, **1**, have been characterized by visible, infrared, and ^1H NMR spectroscopy and magnetic measurements. Absorption bands at 810 and 575 cm^{-1} have been assigned to Mn-O-Mn and Mn-O-I bands, respectively, based on ^{18}O-labeling experiments. A comparison of the NMR spectra of the complexes **1** with the well-characterized dimeric complexes **2** indicates the same dimeric structure in both types of complexes. The NMR results also indicate that the phenyl ring of the iodosyl moiety is located above the porphyrin core. The solid-state magnetic susceptibility at 28 °C gave μ_{eff} = 1.5 μ_B/atom of manganese. Oxidations of triphenylphosphine to triphenylphosphine oxide by **1** and **2** indicate that the iodosylbenzene complexes **1** contain two additional two-electron oxidizing equivalents over that of **2**. This is consistent with a formulation in which iodine is present in the 3+ oxidation state. On the basis of the low magnetic moment, the absence of an observable EPR signal, and the absence of the diagnostic π-cation radical IR absorption band, the ground electronic state of **1** is determined to be two antiferromagnetically coupled d^3 Mn(IV) atoms in neutral porphyrins.

The ability of the cytochrome P-450 enzymes to selectively oxidize alkanes through the activation of molecular oxygen has focused attention on synthetic metalloporphyrins and their potential as oxidation catalysts.[1] Synthetic metalloporphyrins have been screened for their ability to catalytically oxidize organic substrates with a variety of reduced oxygen sources.[2] Our group, as well as that of Groves, reported the use of (tetraphenyl-

* Address correspondence to Craig L. Hill, Department of Chemistry, Emory University, Atlanta, Georgia 30322.

(1) For recent reviews of cytochrome P-450 see: (a) Coon, M. J.; White, R. E. "Metal Ion Activation of Dioxygen"; Spiro, T. G., Ed.; Wiley: New York, 1980; Chapter 2. (b) Gunsalus, J. C.; Sligar, S. G. *Advan. Enzymol. Rel. Areas Mol. Biol.* **1978**, *47*, 1-44. (c) Groves, J. T. *Adv. Inorg. Biochem.* **1979**, *1*, Chapter 4. (d) Chang, C. K.; Dolphin, D. *Bioorg. Chem.* **1978**, *4*, 37.

0002-7863/83/1505-3510$01.50/0