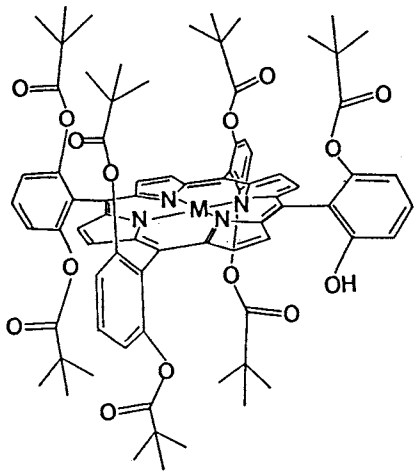
CHEMISTRY LETTERS, pp. 1071-1074, 1990.

A Bis-Fenced Porphinatoiron Having Seven Pivaloyloxy Groups on the Porphyrin Ring Plane. Synthesis and Ligand Binding

Eishun TSUCHIDA,* Etsuo HASEGAWA, Teruyuki KOMATSU,
Keisuke NAKAO, and Hiroyuki NISHIDE
Department of Polymer Chemistry, Waseda University, Tokyo 169

A new tetraphenylporphyrin derivative having two pockets on both sides of the porphyrin ring plane, 5,10,15-tri(2',6'-bis(pivaloyloxy)phenyl)-20-((2'-hydroxy-6'-pivaloyloxy)phenyl)porphine, and its iron complex were synthesized. The 1,2-dimethylimidazole binding to the iron(II) was enhanced by the presence of a steric-hindrance reduced pocket. The complex formed a stable dioxygen adduct in toluene at 25 °C.

Various porphyrins have been synthesized and studied in detail as models for natural hemoproteins.[1] Reactivity of metalloporphyrins has been controlled by preventing their dimerization process. For this purpose, both faces hindered porphyrins are considered to be more effective than single face hindered ones. For example, a both faces hindered porphinatoiron(II) gives a stable dioxygen adduct against irreversible oxidation.[2] However, the preparation is not easy and the yield was very low. The present authors have also synthesized the tetraphenylporphyrin having eight pivaloyloxy groups on both sides of a porphyrin ring plane (bis-fenced heme) and found that the iron(II) complex can form a stable dioxygen complex in toluene at 25 °C.[3] Among these both faces hindered porphyrins, one having two different pockets for ligand binding is interesting because ligands bound



1: M=-H H-, 2: M=Fe

to iron can be distinguished and controlled by their bulkiness through the steric interaction with bulky substituted groups. In this work, a both-faces hindered porphyrin (1) and its iron complex (5,10,15-tri(2',6'-bis-(pivaloyloxy)phenyl)-20-((2'-hydroxy-6'-pivaloyloxy)phenyl)porphinatoiron, 2) was designed and synthesized. 1 and 2 have two pockets with different cavity-size for axial ligand binding on the porphyrin ring plane. The binding of imidazoles to the central iron(II) was studied in toluene at ambient temperature to prove the effect of the two asymmetric pockets.

The synthetic route for the both-faces heterogeneously hindered porphyrin and its iron complex is as follows. First, 5,10,15,20-tetra-(2',6'-bis(hydroxy)phenyl)porphinatoiron(III) bromide[3] (0.36 g, 0.411 mmol) and 4-(N,N-dimethylamino)pyridine (0.30 g, 2.91 mmol) were dissolved in dry tetrahydrofuran (100 ml). To this pivaloyl chloride (0.30 ml, 2.47 mmol) was added under argon atmosphere and the reaction mixture was stirred for 1 h and then for 12 h at 60 °C. Solvents were removed by evaporation and the residue dissolved in chloroform was washed with 4% $NaHCO_3$ and then water. The organic phase dried over Na_2SO_4 was concentrated and the residue was purified by column chromatography on silica gel eluted with chloroform/methanol (100/1(v/v)) to give 2 (yield, 5.0%)).[4] To 5,10,15,-20-tetra(2',6'-di(hydroxy)phenyl)porphine[3] (0.30 g, 0.404 mmol) (3) and 4-(N,N-dimethylamino)pyridine (0.36 g, 2.91 mmol) dissolved in tetrahydrofuran was added pivaloyl chloride (0.36 ml, 2.91 mmol) under argon atmosphere and then the mixture was allowed to react at room temperature for 1 h and then at 60 °C for 12 h. After removing solvent by an aspirator, the residue was dissolved in chloroform, washed with 4% $NaHCO_3$, water and dried over Na_2SO_4. It was purified by column chromatography on silica gel eluted by chloroform/diethyl ether (10/1(v/v)) to give 1 (yield, 9.2%).[5] The structures were confirmed by FAB MS, ^1H NMR and IR spectral measurements, TLC and elemental analyses.

2 dissolved in toluene was reduced to the corresponding Fe(II) derivative by stirring with an aqueous solution containing an excess amount of sodium dithionite under argon atmosphere at room temperature. The organic phase was collected, dried over Na_2SO_4 and transferred into a UV/Vis cell. To the solution was then added a imidazole ligand (1,2-dimethylimidazole (1,2-Me_2Im) or 1-methylimidazole (1-MeIm)). The base titration curves were determined by measuring absorbance change with increasing a ligand concentration at 435 nm for 1,2-Me_2Im and 430 nm for 1-MeIm respectively and were analyzed by the Drago's method[6] and the Rougee and Brault's

$$FeP + B \rightleftharpoons FeP(B) \qquad K_B = [FeP(B)]/[FeP][B] \qquad (1)$$

$$FeP(B) + B \rightleftharpoons FeP(B)_2 \qquad K_B^B = [FeP(B)_2]/[FeP(B)][B] \qquad (2)$$

Table 1. Ligation Constants of Imidazoles to Various Porphinatoiron(II) Complexes Having Fences on a Porphyrin Ring Plane in Toluene at 25 °C

Heme	Ligand[a]	λ_{max}/nm	K_B / $dm^3 mol^{-1}$	K_B^B / $dm^3 mol^{-1}$	ΔH[d]	ΔS[e]
Bis-fenced heme	1-MeIm	561,535,429	13	50		
	1,2-Me_2Im	566,535,436	36	-	-6.8	-16
2	1-MeIm	562,535,430	21	147		
	1,2-Me_2Im	557,535,435	60	-	-10.4	-27
Picket fence heme[b]	1,2-Me_2Im	562,535,439	3.7×10^4	-		
TPP Fe(II)[c]	Imidazole	560,535	8.8×10^3	7.9×10^4		
	2-MeIm	565,537,436	2.4×10^4	-		

a)1-MeIm: 1-methylimidazole; 1,2-Me_2Im: 1,2-dimethylimidazole; 2-MeIm: 2-methylimidazole. b)From Ref. 8. c)From Ref. 7, solvent: benzene. d)In kcal mol^{-1} unit. e)In cal $mol^{-1}deg^{-1}$ unit (1 J=4.184 cal).

method.[7] It is clear from Table 1 that the ligation equilibrium constants of the both faces-hindered porphinatoiron complexes (5,10,15,20-tetra-(2',6'-bis(pivaloyloxy)phenyl)porphinatoiron(II) (bis-fenced heme[3] and 2) were much smaller than those of the single face-hindered one (picket fence heme).[8] This indicates the steric hindrance of the fence groups (pivaloyl residues) on both sides of a porphyrin ring plane. On the other hand, the ligation constants of 2 were larger than those of the bis-fenced heme by a factor of 3. This suggests that the reduction of the steric hindrance on one side of the bis-fenced porphyrin by substituting one pivaloyl group by hydrogen forms a less sterically hindered pocket enhancing imidazole ligation to iron(II). The fact that the enthalpy change for the 1,2-Me_2Im ligation is larger in the 2 complex than in the bis-fenced heme also supports this consideration. In the case of 1-MeIm ligation, the increase of K_B^B is explained by the increase of π-back donation to iron from the first imidazole ligand in the less hindered pocket.

The 2 complexes with 1-MeIm or 1,2-Me_2Im gave dioxygen adducts in toluene at 25 °C. The absorption maxima were 546 and 422 nm for 1-MeIm and 545 and 423 nm for 1,2-Me_2Im, which are similar to those of the bis-fenced heme[3] and the picket fenced heme.[8] The half-life time of the dioxygen adduct of 1-MeIm against irreversible oxidation was 25 h which is similar to that of the bis-fenced heme (26 h). The dioxygen binding affinity (the oxygen pressure at half-oxygenation of heme: P_{50}) was 503

mmHg at 25 ℃ for 1,2-Me_2Im, of which value is smaller than that of the bis-fenced heme (866 mmHg). The increase of oxygen affinity in the 2 complex could be explained by the reduction of the steric hindrance in the imidazole-binding pocket, inducing better ligation of an imidazole to the iron. The enthalpy change (ΔH: -13 kcal mol^{-1}(-53 kJ mol^{-1})), which is smaller than that of the bis-fenced heme (-9.3 kcal mol^{-1}(-38 kJ mol^{-1})), also supports the formation of a strong oxygen adduct of 2 with a sterically reduced pocket.

Thus, the introduction of heterogeneously hindered pockets on a both-faces hindered porphinatoiron resulted in the increase of affinity of imidazole and dioxygen to the central iron in comparison with the porphyrin having four pivaloyloxy groups in the both side of a porphyrin ring plane.

This work is supported by Grant-in-Aid for Scientific Research on Priority Area of "Macromolecular Complexes" from the Ministry of Education.

References

1) R. D. Jones, D. A. Summerville, and F. Basolo, Chem. Rev., 79, 139 (1979); J. E. Baldwin and A. Perlmutter, Top. Curr. Chem., 121, 181 (1984); M. Momenteau, Pure Appl. Chem., 58, 1493 (1986); E. Tsuchida and H. Nishide, Top. Curr. Chem., 132, 64 (1986); E. Hasegawa and E. Tsuchida, Kobunshi, 38, 728 (1989).

2) K S. Suslick and M. M. Fox, J. Am. Chem. Soc., 105, 3507 (1983); J. E. Baldwin, J. H. Cameron, I. J. Dagley, and T. Close, J. Chem. Soc., Dalton Trans., 1984, 1739; M. Momenteau, B. Loock, C. Tetreau, C. Huel, and J. M. Lhoste, ibid., Perkin Trans. 2, 1987, 249.

3) T. Komatsu, E. Hasegawa, H. Nishide, and E. Tsuchida, J. Chem. Soc., Chem. Commun., 1990, 66.

4) 2: IR(KBr) 3450 and 1760 cm^{-1}. λ_{max} ($CHCl_3$) 680, 649, 586, 507, 411 nm. Anal. FAB MS: 1385 $[M-Br]^+$. Found. C, 65.22; H, 6.30, N, 3.83%. Calcd for $C_{79}H_{84}N_4O_{15}FeBr$ $0.5C_6H_6$: C, 65.47; H, 5.83; N, 3.72.

5) 1: IR(KBr) 3450 and 1760 cm^{-1}. λ_{max} ($CHCl_3$) 636, 583, 538, 506, 412 nm. ^1H NMR ($CDCl_3$, TMS)δ -2.9(2H, s, NH), -0.5-1.0 (63H, m, pivaloyl), 7.2-8.0(12H, m, phenyl). FAB MS: 1331 $[M]^+$. Anal. Found. C, 71.30; H, 6.51, N, 4.15%. Calcd for $C_{79}H_{86}N_4O_{15}$: C, 70.45; H, 6.77; N, 4.03%.

6) R. S. Drago, "Physical Method in Chemistry," W. B. Saunders, Philadelphia, Pa. (1977), p.88.

7) D. Brault and M. Rougee, Biochem. Biophys. Res. Commun., 57, 654(1974).

8) J. P. Collman, J. I. Brauman, K. M. Doxsee, T. R. Halbert, S. Haynes, and K. S. Suslick, Proc. Nat. Acad. Sci., U.S.A., 75, 564 (1978).

(Received March 20, 1990)