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Steric Effects on the Rates of Dissociation of Axially Coordinated Imidazoles in Hindered Low Spin Ferric Porphyrins

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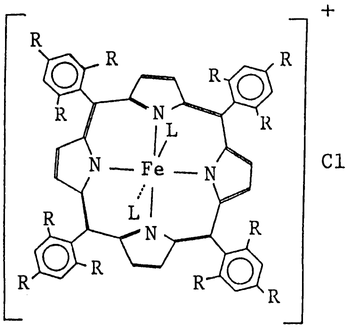
Axially coordinated imidazoles in some low spin ferric complexes derived from meso-tetraphenylporphyrin (TPP) dissociate more rapidly than those derived from meso-tetramesitylporphyrin (TMP). The results have been ascribed to the stability of bis-ligated TMP complex relative to the sterically less hindered TPP analogue.

Kinetic and thermodynamic behavior of low spin iron(III) complexes of synthetic porphyrins is of great importance to understand the physicochemical properties of naturally occurring heme proteins such as cytochrome b and c. Although such studies have been done in some complexes derived from octaethylporphyrin and meso-tetraphenylporphyrin,[1-3] little is done in sterically hindered complexes. In this paper, we would like to present the unexpected results on stability and lability of axially coordinated imidazoles in some complexes derived from sterically hindered meso-tetramesitylporphyrin.

Treatment of meso-tetraphenylporphinatoiron(III) chloride, Fe(TPP)Cl, or meso-tetramesitylporphinatoiron(III) chloride, Fe(TMP)Cl,[4] with 6.0 equiv. of 1-methylimidazole (1-MeIm), 2-methylimidazole (2-MeIm), or 1,2-dimethylimidazole (1,2-Me_2Im) in $CDCl_3$ gave low spin complexes, 1 - 6, as shown below. The ^{1}H NMR spectra of these complexes were recorded on a JEOL FX90Q spectrometer operating at 89.55 MHz. The methyl signals of the coordinated imidazoles were assigned unambiguously based on the results of saturation transfer experiments.[5] These methyl signals showed temperature dependence, indicating that the axial ligands dissociate according to (1), where P is a porphyrin, X^- is a halide ion, and L is



Complex	R	L	Abbreviation
1	H	1-MeIm	Fe(TPP)(1-MeIm)$_2$
2	H	2-MeIm	Fe(TPP)(2-MeIm)$_2$
3	H	1,2-Me_2Im	Fe(TPP)(1,2-Me_2Im)$_2$
4	CH_3	1-MeIm	Fe(TMP)(1-MeIm)$_2$
5	CH_3	2-MeIm	Fe(TMP)(2-MeIm)$_2$
6	CH_3	1,2-Me_2Im	Fe(TMP)(1,2-Me_2Im)$_2$

$$\mathrm{Fe(P)LL^{+}X^{-} + L^{*} \rightleftharpoons Fe(P)L^{+}X^{-} + L + L^{*} \rightleftharpoons Fe(P)LL^{*+}X^{-} + L} \qquad (1)$$

an axial ligand. In complexes 2, 3, and 5, the dissociation rates were determined by dynamic NMR method.[6)] The activation parameters for dissociation were listed in Table 1. The application of this method to 1, 4, and 6 was, however, impossible since they partially decomposed to the high spin complexes at the temperature where the methyl signals showed considerable broadening. Thus, the rates were measured by saturation transfer method which gives the rate constants at lower temperature.[7,8)] The kinetic data obtained by this method were also listed in Table 1. The reliability of the data was verified since the activation parameters of 5, measured by the two different methods, were quite similar. The rate constants were independent of the concentration of added imidazoles as in the case of 1.[1)] The results, together with the large positive values of activation entropies, support the dissociation mechanism (1) through five-coordinated activated complex, $\mathrm{Fe(P)L^{+}X^{-}}$.

Table 1. Activation parameters for dissociation of axial ligands at 25 °C

Complex		k / s^{-1}	$\Delta H^{\ddagger}$ / kJ mol^{-1}	$\Delta S^{\ddagger}$ / J mol^{-1} K^{-1}	$\Delta G^{\ddagger}$ / kJ mol^{-1}	Method$^{a)}$
$\mathrm{Fe(TPP)(1\text{-}MeIm)_2}$	1	120$^{b)}$	85.2± 9.6	81.1± 33.9	61.0	S
		66$^{c)}$	84.0± 8.4	72.3± 28.4	62.3	W
$\mathrm{Fe(TPP)(2\text{-}MeIm)_2}$	2	8900$^{b)}$	70.6± 2.5	67.3± 9.6	50.6	D
$\mathrm{Fe(TPP)(1,2\text{-}Me_2Im)_2}$	3	110000$^{b)}$	61.4± 2.1	58.1± 8.4	44.3	D
$\mathrm{Fe(TMP)(1\text{-}MeIm)_2}$	4	5.4	98.6±12.5	100 ± 41.0	68.5	S
$\mathrm{Fe(TMP)(2\text{-}MeIm)_2}$	5	18$^{b)}$	89.5± 2.9	79.8± 8.8	65.6	D
		17	93.2± 5.9	91.5± 18.8	66.0	S
$\mathrm{Fe(TMP)(1,2\text{-}Me_2Im)_2}$	6	100	83.2± 1.7	73.2± 5.4	61.4	S

a) S, saturation transfer; W, line width analysis; D, dynamic NMR. b) Rate constant extrapolated to 25 °C. c) Data in Ref. 1.

The data in Table 1 indicate that the dissociation rates increase in the order 1-MeIm < 2-MeIm < 1,2-$\mathrm{Me_2Im}$ in both series. Since the steric repulsion between ligand and porphyrin is expected to increase in the same order, the results suggest that the complex with sterically hindered imidazoles becomes unstable. If this is the reason for the difference in lability, it may be reflected on the formation constant, β_2, defined by (2). Thus, the relative

$$\mathrm{Fe(P)X + 2L \rightleftharpoons Fe(P)L_2{}^{+}X^{-}} \qquad (2)$$

values of formation constants were measured by the competitive ligation of mixed imidazoles. The ^{1}H NMR spectrum of a mixture of Fe(TPP)Cl (1.0 equiv.), 1-MeIm (4.0 equiv.) and 2-MeIm (4.0 equiv.) showed three peaks at -25.2, -23.1, and -21.0 ppm at -35 °C with integral intensities of 0.36 : 0.44 : 0.20. These signals were assigned to the pyrrole protons of 1, Fe(TPP)(1-MeIm)(2-MeIm), and 2, respectively. Based on these results, the ratio of formation constants of 1 and 2, $\beta_2(1)/\beta_2(2) = [1][2\text{-MeIm}]^2/[2][1\text{-MeIm}]^2$, was calculated to be 2.2. The ratio showed no appreciable dependence on temperature in the range -30 °C and

-50 °C where pyrrole protons of three species gave separate signals. The ^{1}H NMR spectrum obtained with Fe(TMP)Cl (1.0 equiv.), 1-MeIm (4.0 equiv.), and 2-MeIm (4.0 equiv.) at 16.°C also showed three signals due to the pyrrole protons of 4, Fe(TMP)(1-MeIm)(2-MeIm), and 5 at -18.1, -13.7, and -11.4 ppm, respectively, with integral intensities of 0.06 : 0.41 : 0.53. By a similar treatment, the ratio of formation constants, $\beta_2(4)/\beta_2(5)$, was determined to be 0.060. The addition of equimolar mixture of 1-MeIm and 1,2-Me$_2$Im into Fe(TPP)Cl and Fe(TMP)Cl gave $\beta_2(1)/\beta_2(3)$ and $\beta_2(4)/\beta_2(6)$. In the first column of Table 2 were listed the formation constants relative to 1 in TPP system and 4 in TMP system. In order to find the relation of the data between two systems, 2.0 equiv. of 1-MeIm was added to the CDCl$_3$ solution containing Fe(TPP)Cl (1.0 equiv.) and Fe(TMP)Cl (1.0 equiv.) at -20 °C. The ^{1}H NMR spectrum showed two broad methyl signals of the coordinated 1-MeIm of 1 and 4 at 23.2 and 20.5 ppm, respectively, with integral intensities of 1 : 4. No signals due to complexes other than two kinds of high spin species, 1, and 4 were detected in the spectrum. Further addition of the imidazole increased the signals of 1 and 4. When 4.0 equiv. of 1-MeIm was added, all the high spin complexes were converted into the low spin complexes. The results indicate that the equilibrium constant of (3), which is equal to the ratio of formation constants, $\beta_2(4)/\beta_2(1)$, is 16. Thus, the β_2 values of TMP system were multiplied by 16 for the direct comparison

$$\mathrm{Fe(TMP)Cl} + 1 \rightleftharpoons 4 + \mathrm{Fe(TPP)Cl} \tag{3}$$

with those of TPP system and they were given in the second column of Table 2.

Table 2. Relative values of formation constants

Complex	β_2 a)	β_2 b)
1	1	1
2	0.45	0.45
3	≦0.00006	≦0.00006
4	1	16
5	17	270
6	0.008	0.13

a) Formation constants relative to 1 in TPP system and 4 in TMP system.
b) Formation constants relative to 1 in both systems.

The data in Tables 1 and 2 indicate that the rates of dissociation showed little correlation with the magnitude of formation constants especially in the case of TMP complexes; while the formation constants increased by 17 times on going from 4 to 5 due to the intermolecular N-H•••Cl$^-$ hydrogen bond between coordinated 2-MeIm and chloride ion2) in 5, rate constant also increased by 3.3 times. The results suggest that the labile nature of 5 relative to 4 is ascribed to the steric acceleration; steric repulsion between the 2-methyl of imidazole and the porphyrin ring in 5 is expected to decrease at the transition state of dissociation where iron is replaced out of the porphyrin plane and the distance between two interacting groups becomes longer. The same hypothesis can be applied to explain a large increase in dissociation rate on going from 1 to 2 in TPP system. Extremely labile nature of 3 and 6 relative to 2 and 5, respectively, is thus ascribed to 1) the instability of the former complexes due to the lack of hydrogen bond, 2) the severer steric repulsion caused by the buttressing effect9) of the 1-methyl group, and 3) the stability of the five-coordinated activated complex by the release of the strain energy.

The most interesting point in the data of Table 2 is that axial imidazoles bind more strongly to Fe(TMP)Cl than to the sterically less hindered TPP analogue; the ratios of formation constants between TMP and the corresponding TPP complexes, β_2(TMP)/β_2(TPP), are calculated to be 16, 600, and ≧2000 for axial ligand = 1-MeIm, 2-MeIm, and 1,2-Me_2Im, respectively. Correspondingly, axial imidazoles dissociate more slowly from low spin TMP than from the TPP analogues; the ratios of rate constants, k(TMP)/k(TPP), are 0.045, 0.0020, and 0.00091 at 25 °C for the same change in axial ligands. Since the ratios of rate constants correlate with the corresponding ratios of formation constants, the lability of TPP complexes relative to the TMP analogues can be ascribed to the stability of the latter relative to the former complexes

The question arises as to why the formation constants of hindered complexes are larger than those of the less hindered analogues. One possible reason is the electronic effects of phenyl substituents; substituents with electron donating ability are known to increase the formation constant through resonance effect.2) This effect is, however, ruled out because of the perpendicular conformation of the mesityl groups relative to the porphyrin ring. Another possiblity is the orientation effect of coordinated imidazoles.10) Because of the bulky mesityl groups, coordinated imidazoles are supposed to lie over nitrogen-nitrogen axis of the porphyrin ring and be perpendicular each other. This orientation may be suitable for the π bond formation between metal p or d orbitals and imidazole p orbitals. As a result, TMP complexes are expected to be less labile than the corresponding TPP complexes. It is difficult, however, to explain this anomaly from the results obtained here and further study is planned in our laboratory.

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