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A New System of Autoreduction of Hemin with Isocyanide

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A new autoreduction system of hemin was established in the case of synthetic hemins with hydroquinone and isocyanide. The reduction of hemin needed both of hydroquinone and isocyanide. Kinetic studies suggested that a six-coordinated and low-spin iron porphyrin complex was an intermediate of the reduction.[1,2)]

Hemoproteins have important roles in natural systems such as oxygen carriers, oxygenation enzymes, and energy transfers and the redox reaction of heme is a common feature for these hemoproteins. It has been known that in some hemoproteins hemin is reduced spontaneously when they were kept under carbon monoxide or nitrogen monoxide to give ferrous complexes of CO or NO.[3)] On the other hand, chemical systems of hemins with cyanide,[4a)] carbon monoxide and base,[4b)] pyridine and base,[4c)] piperidine,[4d)] thiols,[4e)] and phosphines[4f)] have been reported to get autoreduced without any apparent reductants. In some cases mechanisms were proposed, most of which were electron migrations through the axial ligands involving radicals. Recently iron chlorophyll showed the similar reduction with pyridine[5)] in the conditions where hemin(FeTPPCl) did not reduce.

We now report a new autoreduction[6)] system of hemins in aprotic solvent with hydroquinone in the presence of isocyanide which was not known to be a ligand to Fe(III) porphyrins, and the situation which remained ambiguous is now clear.

Hemin needed both of hydroquinone and isocyanide in aprotic solvents to get reduced as shown in Eq. 1.

$$\mathrm{Fe(III)TPPCl} + \frac{1}{2}\ \mathrm{Hydroquinone} + 2\ \mathrm{Isocyanide} \longrightarrow \mathrm{Fe(II)TPP(isocyanide)_2} + \frac{1}{2}\ \mathrm{Quinone} + \mathrm{HCl} \qquad (1)$$

Hydroquinone is a potential reductant in the system but it does not reduce hemin chloride without isocyanide. The role of isocyanide should be similar to that of carbon monoxide: carbon monoxide and isocyanide have the same electronic structure and are known to coordinate not to Fe(III)-porphyrin but to Fe(II)-porphyrin complex. The spectral change accompanying the reduction of hemin in acetonitrile was typically shown in Fig. 1. The sharp Soret peak at 431 nm appeared after additions of H_2Q and t-BuNC indicating the formation of Fe(II)-

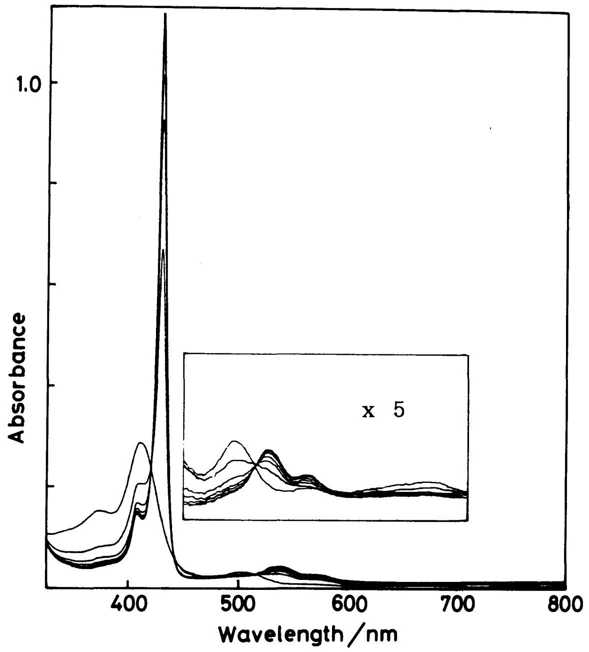


Fig.1 Spectral change of FeTPPCl in acetonitrile.

Conditions were the same as in Table 1; ambient temp., scanning speed: 60 nm/min; interval: 30 min. The inset was recorded separately.

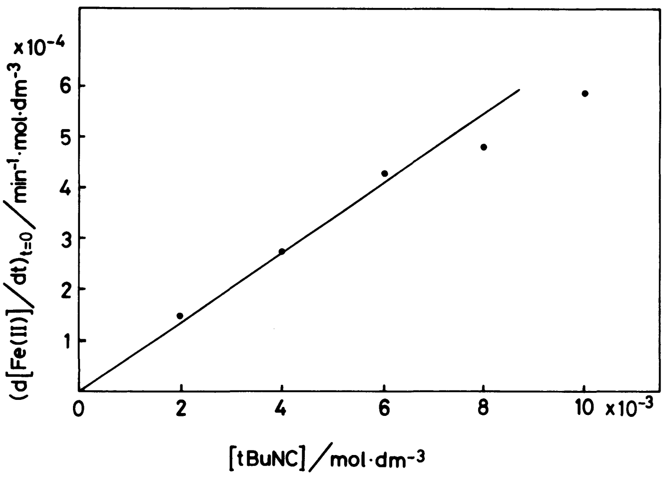


Fig.2 Plot of rate vs. [t-BuNC].

Solvent: CH_3CN. See reaction conditions in Table 1 but [t-BuNC].

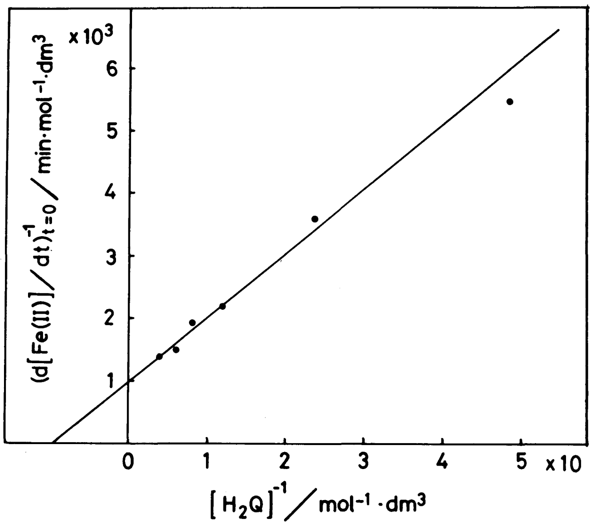


Fig.3 Plot of rate vs. $1/[H_2Q]$.

Solvent: CH_3CN. See reaction conditions in Table 1 but $[H_2Q]$.

TPP(t-BuNC)$_2$[7] with clean isosbestic points: 407, 421, 442, 478, and 516 nm.

Similar autoreductions were observed in the cases of FeOEPCl and FeTPPCl$_8$Cl with t-BuNC and H_2Q in CH_2Cl_2 and that benzyl isocyanide had the same effect on FeTPPCl.[8] The reaction was followed kinetically measuring the absorbance at the Soret peak of the formed complex in a Tonometer with a 1.0 mm cuvette under nitrogen atmosphere.

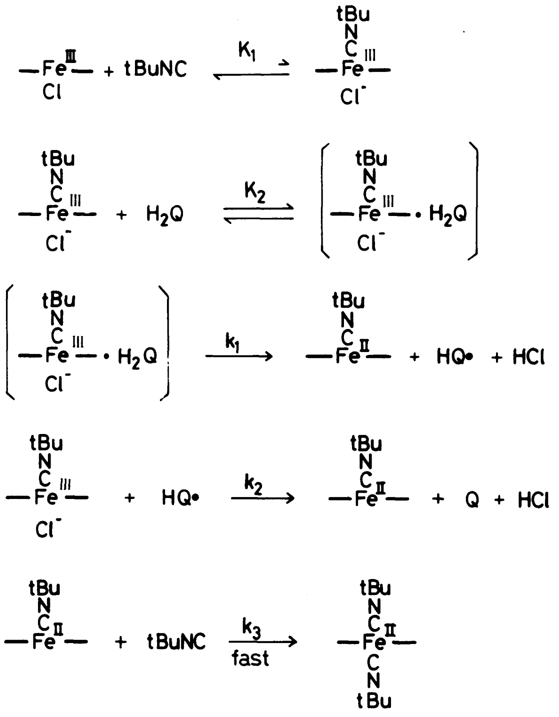
After the correction needed, suppression of absorbance of FeTPPCl, the initial rates of the increases of reduced heme were shown in Figs. 2 and 3. The rate was revealed to be dependent on the concentrations of hydroquinone and isocyanide, and the rate equation was $(d[Fe(II)TPP(t\text{-}BuNC)_2]/dt)_{t=0} = k[Fe(III)TPPCl][t\text{-}BuNC][H_2Q]/(1 + K[H_2Q])$.

Two possibilities should be taken for the reduction mechanism. The first is an initial reduction by hydroquinone followed by the formation of bisisocyanide complex. The second is an initial formation of isocyanide complex which is supposed to have a six coordinated iron complex. And the step is followed by the reduction by H_2Q. The first possibility is excluded because isocyanide binds to iron(II) at the rate of a diffusion control, $\sim 10^{10}$ s^{-1},[9)] and hence the reaction should be independent of the concentration of isocyanide. The second is reasonably elucidated by the mechanism in the scheme 1. The partial formation of a six-coordinate and low-spin iron porphyrin complex was essential, affecting the redox potential.[10)] Because the reaction was first order with respect to isocyanide, an initial formation of bisisocyanide complex is unlikely. Following the scheme the rate equation is obtained to be

$$\text{Rate} = \frac{k_1K_1K_2[\text{Fe(III)TPPCl}][H_2Q][\text{t-BuNC}]}{1 + K_2[H_2Q]} \qquad (2)$$

Here $k_1K_1 = 1.1 \times 10^3\ \text{min}\cdot\text{mol}^{-1}\cdot\text{dm}^3$ and $K_2 = 1.0 \times 10\ \text{mol}\cdot\text{dm}^{-3}$.

A possibility of π-cation radical on porphyrin ring or of electron delocalization between iron and porphyrin ring which has been the subject to be argued[11-13)] still remains. Detailed study is necessary.



Scheme 1.

Proposed Mechanism of Autoreduction.

Table 1. Solvent Effect on Autoreduction

Solvent	$(d[\text{Fe(II)}]/dt)_{t=0}/\text{min}\cdot\text{mol}\cdot\text{dm}^{-3}$
C_6H_6	$0.15 \pm 0.03 \times 10^{-4}$
$CHCl_3$	$0.75 \pm 0.05 \times 10^{-4}$
CH_2Cl_2	$0.91 \pm 0.07 \times 10^{-4}$
C_6H_5CN	$1.07 \pm 0.14 \times 10^{-4}$
CH_3CN	$2.75 \pm 0.23 \times 10^{-4}$

FeTPPCl: 2.3×10^{-5} mol/dm^3,
H_2Q: 4.1×10^{-3} mol/dm^3,
t-BuNC: 4.0×10^{-2} mol/dm^3, 25 °C.

The solvent effect on the rate in aprotic solvents was summarized in Table 1. The reduction was accelerated in polar solvents. Preliminary experiments in FeOEPCl suggested that acetonitriles affected on the pre-equilibrium in the scheme to accelerate the reaction.

Interestingly, experiments in CH_2Cl_2 showed that the reduction completed in dark and the reverse oxidation to hemin chloride occurred under the light, which means that this system would be a good model for redox reaction of enzymatic system. The detailed study is under way.

References

1) The paper was presented at XXVI International Conference on Coordination Chemistry, Porto(Portugal), Aug.-Sept., 1988.

2) Abb: FeTPPCl: 5,10,15,20-tetraphenylporphinatoiron(III) chloride, FeOEPCl: octaethylporphinatoiron(III) chloride, FeTPPCl$_8$Cl: 5,10,15,20-tetra(2,6-dichlorophenyl)porphinatoiron(III) chloride, H_2Q: 1,4-hydroquinone, Q: 1,4-benzoquinone, t-BuNC: t-butyl isocyanide.

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5) H. Inoue, Y. Matsubayashi, T. Shirai, and E. Fluck, Hyperfine Interactions, 29, 1403 (1986).

6) Though the definition of "autoreduction" is not clear so far, if molecular oxygen oxidizes substances with the aid of catalysts and the reaction is called autoxidation, the situation in this system reported here could be defined as autoreduction.

7) G. B. Jameson and J. A. Ibers, Inorg. Chem., 18, 1200 (1979).

8) In a preliminary experiment manganese complex (MnTPPCl) was not reduced under the same conditions as in FeTPPCl in CH_2Cl_2.

9) T. G. Traylor, D. Madge, D. Taube, and K. Jongeward, J. Am. Chem. Soc., 109, 5864 (1987).

10) The redox potential changed drastically when iron-porphyrin was in a six-coordinated and low-spin conformation (For example, R. C. Gurira and J. Jordan, Anal. Chem., 53,864 (1981)).

11) Recently π-cation formations were suggested in CoTPPX (M. Uchida et al., The 38th Sakuenkagaku Tohronkai Yohshishyu, 1988, 381) and Fe(III) chlorin (Morishima et al., ibid., 1988, 383, 385).

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