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ELECTRON TRANSFER REACTIONS OF AN NADH MODEL WITH IRON(III) COMPLEXES. A TWO-STEP ELECTRON TRANSFER MECHANISM

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A model of NADH, 1-benzyl-1,4-dihydronicotinamide (BzlNH), readily reduces $[Fe(N\text{-}N)_3]^{3+}$ (N-N = 2,2'-bipyridine and 1,10-phenanthroline) to $[Fe(N\text{-}N)_3]^{2+}$. The stoichiometry of the electron transfer reaction in the absence of a suitable base is such that BzlNH appears to be one-electron donor. In the presence of pyridine or *p*-cyanopyridine, however, BzlNH acts as an apparent two-electron donor, when the reduction of $[Fe(N\text{-}N)_3]^{3+}$ with BzlNH proceeds by a two-step process.

An important function of dihydropyridine coenzymes, particularly NADH, is its involvement in the electron-transport systems for biological redox reactions.1) Although there have been extensive studies on the mechanisms of hydride transfer (two-electron equivalent) in the redox reactions of NADH models,2) only a few works have been reported on the mechanisms for electron transfer reactions of NADH models with one-electron oxidants.3) We wish to report here a two-step electron transfer mechanism for reactions of an NADH model, 1-benzyl-1,4-dihydronicotinamide (BzlNH), with $[Fe(N\text{-}N)_3]^{3+}$ (N-N = 2,2'-bipyridine and 1,10-phenanthroline) in MeCN in the presence of a suitable base.

Upon mixing BzlNH with $[Fe(bpy)_3](PF_6)_3$ or $[Fe(phen)_3](ClO_4)_3$ (bpy = 2,2'-bipyridine, phen = 1,10-phenanthroline) in MeCN at 298 K, an intense absorption band due to the reduced iron(II) species was observed at 520 nm for $[Fe(bpy)_3]^{2+}$ and 507 nm for $[Fe(phen)_3]^{2+}$ without delay. The stoichiometry of the oxidation of BzlNH by $[Fe(N\text{-}N)_3]^{3+}$ was studied in a small excess of the latter. At the end of the reaction, the amount of $[Fe(N\text{-}N)_3]^{2+}$ formed was determined from the absorption spectrum4) and compared with the known amount of BzlNH initially added, as shown in Fig. 1. In the absence of a base, the result corresponds to a stoichiometry of approximately one equivalent $[Fe(N\text{-}N)_3]^{3+}$ reduced by one mole of BzlNH since the slope in Fig. 1a is 1.14 ± 0.05.5) In the presence of excess amounts of pyridine or *p*-cyanopyridine, however, the number of equivalents of $[Fe(N\text{-}N)_3]^{3+}$ reduced per one mole of BzlNH increases, reaching two, as shown in Fig. 1b (the slope is 2.03 ± 0.08). Such a change of the stoichiometry has been observed also for the electrochemical oxidation of BzlNH in the absence and the presence of pyridine.[6)] The stoichiometry in the presence of a base is thus given by Eq. 1,

$$\mathrm{BzlNH} + 2[\mathrm{Fe(N\text{-}N)_3}]^{3+} + \mathrm{B} \longrightarrow \mathrm{BzlN}^{+} + 2[\mathrm{Fe(N\text{-}N)_3}]^{2+} + \mathrm{BH}^{+} \qquad (1)$$

where B stands for a base (pyridine or *p*-cyanopyridine). A product of this reaction, BzlN^+, was identified by comparing the ^{1}H NMR spectrum of the resultant solution with that of the authentic sample.[7)]

Two opposing mechanisms (Schemes 1 and 2) are considered for the oxidation of BzlNH by $[\mathrm{Fe(N\text{-}N)_3}]^{3+}$; one is the one-electron mechanism (Scheme 1). A transfer of one-electron from BzlNH to $[\mathrm{Fe(N\text{-}N)_3}]^{3+}$ produces a protonated pyridinyl radical cation $\mathrm{BzlNH}^{+\cdot}$ which cannot be oxidized further by $[\mathrm{Fe(N\text{-}N)_3}]^{3+}$ (Eq. 2). The free radical cation $\mathrm{BzlNH}^{+\cdot}$ is known to undergo disproportionation (Eq. 3),[6)] and the resulting protonated species $\mathrm{H(BzlNH)}^+$ is deprotonated by a suitable base to regenerate BzlNH (Eq. 4).[8)] On the other hand, the two-electron mechanism (Scheme 2) involves a direct two-electron oxidation of BzlNH to give the pyridinium cation BzlN^+ (Eq. 5), and the proton formed is trapped by BzlNH in the absence of a base (Eq. 6) or by a base in its presence (Eq. 7).

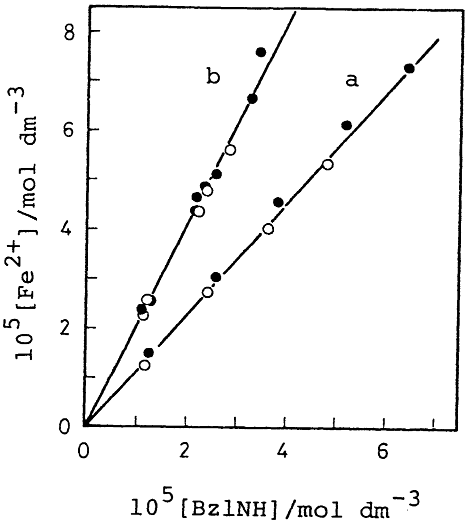

Fig. 1. Stoichiometry of the reactions of BzlNH with excess amounts of $[\mathrm{Fe(bpy)_3}]^{3+}$ (●) and $[\mathrm{Fe(phen)_3}]^{3+}$ (○) (a) in the absence of a base and (b) in the presence of pyridine (4.14×10^{-2} mol dm^{-3}) or *p*-cyanopyridine (3.3×10^{-1} mol dm^{-3}).

Scheme 1 (one-electron mechanism).

$$\mathrm{BzlNH} + [\mathrm{Fe(N\text{-}N)_3}]^{3+} \longrightarrow \mathrm{BzlNH}^{+\cdot} + [\mathrm{Fe(N\text{-}N)_3}]^{2+} \qquad (2)$$

$$2\mathrm{BzlNH}^{+\cdot} \longrightarrow \mathrm{BzlN}^{+} + \mathrm{H(BzlNH)}^{+} \qquad (3)$$

In the presence of a base

$$\mathrm{H(BzlNH)}^{+} + \mathrm{B} \longrightarrow \mathrm{BzlNH} + \mathrm{BH}^{+} \qquad (4)$$

Scheme 2 (two-electron mechanism).

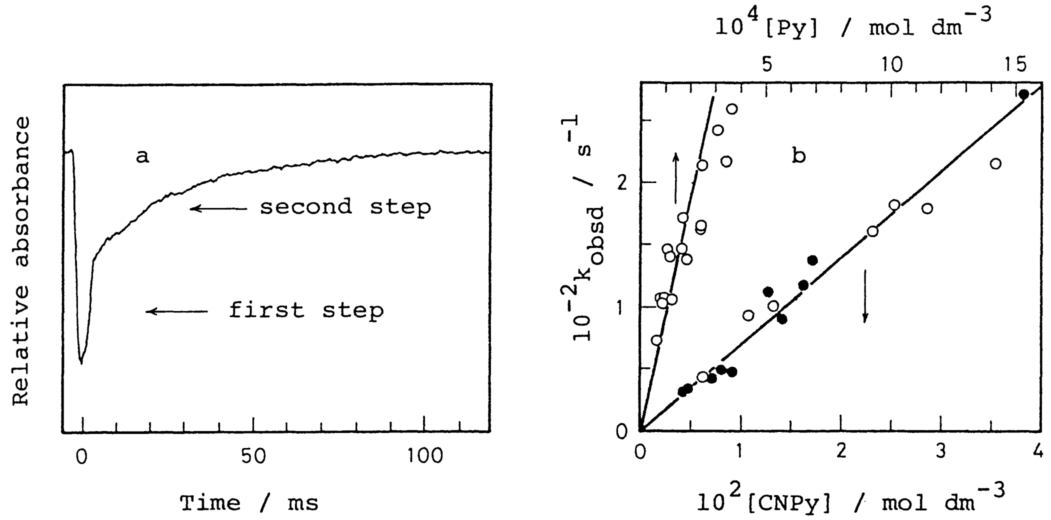

Fig. 2. (a) A kinetic curve for the two-step oxidation of BzlNH (2.00×10^{-4} mol dm^{-3}) by $[Fe(bpy)_3]^{3+}$ (7.45×10^{-4} mol dm^{-3}) in the presence of *p*-cyanopyridine (6.30×10^{-3} mol dm^{-3}), followed by the rise of absorbance at 520 nm due to $[Fe(bpy)_3]^{2+}$. (b) The pseudo-first-order rate constants for the second step (k_{obsd}) in the oxidation of BzlNH by $[Fe(bpy)_3]^{3+}$ (○) and $[Fe(phen)_3]^{3+}$ (●) plotted against the concentrations of pyridine [Py] and *p*-cyanopyridine [CNPy].

$$\mathrm{BzlNH} + 2[\mathrm{Fe(N\text{-}N)_3}]^{3+} \longrightarrow \mathrm{BzlN}^{+} + 2[\mathrm{Fe(N\text{-}N)_3}]^{2+} + \mathrm{H}^{+} \qquad (5)$$

$$\mathrm{H}^{+} + \mathrm{BzlNH} \longrightarrow \mathrm{H(BzlNH)}^{+} \qquad (6)$$

In the presence of a base

$$\mathrm{H}^{+} + \mathrm{B} \longrightarrow \mathrm{BH}^{+} \qquad (7)$$

The stoichiometry of the reaction cannot distinguish between these two mechanisms since both mechanisms give the same over-all reaction irrespective of the absence or the presence of a base. However, the kinetic curve for the formation of $[Fe(bpy)_3]^{2+}$ (Fig. 2a), measured by a Union RA-103 stopped flow spectrophotometer, clearly shows the occurrence of a two-step oxidation of BzlNH by $[Fe(bpy)_3]^{3+}$ in the presence of *p*-cyanopyridine. A similar kinetic behavior of the two-step oxidation was observed also in the presence of pyridine. Such observations of the two-step oxidation exclude the possibility of a direct two-electron oxidation (Scheme 2) and thus suggests the occurrence of two successive one-electron transfer processes (Scheme 1).

The rate constants of the first step (k_1) for the oxidation of BzlNH by both $[Fe(bpy)_3]^{3+}$ and $[Fe(phen)_3]^{3+}$ were too fast to be determined accurately with the stopped flow spectrophotometer; $k_1 > 1 \times 10^7$ mol^{-1}dm^{3}s^{-1}. Such fast one-electron transfer reactions are reconciled with negative values of the free energy change for the electron transfer reactions; ΔG^0 = -29 kJ mol^{-1} and -30 kJ mol^{-1} for $[Fe(bpy)_3]^{3+}$ and $[Fe(phen)_3]^{3+}$, respectively, obtained from the relation $\Delta G^0 = F(E^0_{ox} - E^0_{red})$ where E^0_{ox} and E^0_{red} are the oxidation potential of BzlNH (0.76 V *vs.* SCE)[9] and the reduction potentials of $[Fe(bpy)_3]^{3+}$ (1.06 V) or $[Fe(phen)_3]^{3+}$ (1.07 V).[10] The rate of the second step followed the pseudo-first-order kinetics in the presence of excess amounts of a base, and the pseudo-first-order rate constants (k_{obsd}) showed linear dependences on the concentrations of the bases as shown in Fig. 2b. Thus, the rate-limiting process of the second step is suggested to be the reaction of $H(BzlNH)^+$ with a base (Eq. 4) to regenerate BzlNH which rapidly reduces $[Fe(N\text{-}N)_3]^{3+}$ again.[11] Indeed, the weaker base *p*-cyanopyridine gave the smaller rate constant for the second step ($k_2 = (6.9 \pm 1.1) \times 10^3$ mol^{-1} dm^{3}s^{-1}) than the stronger base pyridine ($k_2 = (1.0 \pm 0.3) \times 10^6$ mol^{-1}dm^{3}s^{-1}).

References

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4) S. Fukuzumi, C. L. Wong, and J. K. Kochi, *J. Am. Chem. Soc.*, 102, 2298 (1980).

5) In the presence of a large excess of $[Fe(N\text{-}N)_3]^{3+}$ (*e.g.*, $[Fe^{3+}]/[BzlNH]$ = 13), the stoichiometry increases to 1.3 ± 0.1.

6) W. J. Blaedel and R. G. Haas, *Anal. Chem.*, 42, 918 (1970).

7) The authentic sample $BzlN^+PF_6^-$ was prepared by the addition of $NH_4^+PF_6^-$ to $BzlN^+Cl^-$ in H_2O. NMR(CD_3CN) δ(ppm) : N-CH_2, 5.77 (2H); NH_2, 6.6-7.2 (2H, broad); C_6H_5, 7.46 (5H); 5-CH, 8.10 (1H); 4-CH and 6-CH, 8.72-8.83 (2H); 2-CH, 9.15 (1H). Anal. Calcd for $C_{13}H_{13}N_2OPF_6$: C, 43.59, H, 3.66; N, 7.82. Found: C, 43.59; H, 3.80; N, 7.92.

8) In the absence of a base, the decomposition of $H(BzlNH)^+$ may occur to give several uncharacterized products.[6]

9) F. M. Martens, J. M. Verhoeven, R. A. Gase, U. K. Pandit, and T. J. D. Boer, *Tetrahedron*, 34, 443 (1978).

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11) It also is possible that the reaction of $BzlNH^{+\bullet}$ with a base ($BzlNH^{+\bullet} + B \longrightarrow BzlN\bullet + BH^+$) occurs, competing with the disproportionation reaction (Eq. 3). However, the disproportionation of $BzlNH^{+\bullet}$ may be much faster than the reaction with a base, since the free radical cation $BzlNH^{+\bullet}$ has not been detected by ESR in the course of the reaction.

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