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Na^+-Catalyzed Reduction of Semiquinone Radical Anions by NADH Analogues

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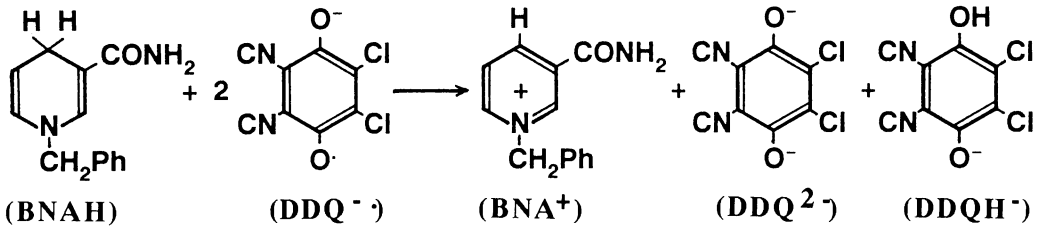
Stable radical anions such as *p*-chloranil radical anion ($Cl_4Q^{-}\cdot$) are reduced by NADH analogues, 1-benzyl-1,4-dihydronicotinamide (BNAH) and 10-methyl-9,10-dihydroacridine ($AcrH_2$), to yield the corresponding hydroquinone anions. The addition of $NaClO_4$ to the BNAH-$Cl_4Q^{-}\cdot$ system results in a significant increase in the rate of the one-electron reduction of $Cl_4Q^{-}\cdot$, while no acceleration effect has been observed by the addition of Bu_4NClO_4.

Dihydronicotinamide adenine dinucleotide (NADH) is known to act as the source of two electrons and a proton, thus formally transferring a hydride ion to a suitable substrate.[1] The nature of this oxidation as well as the catalysis, which is fundamental to the understanding of NADH-dependent enzymatic systems, has been extensively studied by using NADH analogues in the reactions with various substrates.[2-4] The substrates studied so far are mostly diamagnetic organic compounds, and thus, to our best knowledge, there has been no report on the reduction of radical anions by NADH analogues. We report herein that stable radical anions are reduced by NADH analogues and that the reduction is catalyzed effectively by Na^+ that has scarcely been regarded as a catalyst for the reduction of substrates.

2,3-Dicyano-5,6-dichloro-*p*-benzosemiquinone radical anion ($DDQ^{-}\cdot$) is stable in MeCN at 298 K. When an NADH analogue, 1-benzyl-1,4-dihydronicoinamide (BNAH) is added to an acetonitrile (MeCN) solution of $DDQ^{-}\cdot$, $DDQ^{-}\cdot$ is reduced to yield DDQ^{2-} and $DDQH_2$ (Eq. 1).[5] The monoanion $DDQH^{-}$ undergoes the



(1)

disproportionation to yield DDQ^{2-} and $DDQH_2$ (Eq. 2).[6] The BNAH also can reduce *p*-chloranil radical anion

$$2DDQH^{-} \longrightarrow DDQ^{2-} + DDQH_2 \qquad (2)$$

($Cl_4Q^{-}\cdot$) to yield Cl_4Q^{2-} and Cl_4QH_2. When BNAH is replaced by 10-methyl-9,10-dihydroacridine ($AcrH_2$), the reactivity toward radical anions is diminished significantly.

Rates of the one-electron reduction of radical anions obeyed the second-order kinetics, showing first-order dependence on each reactant concentration. The observed second-order rate constants (k_{obs}) are listed in Table 1.

Table 1. Rate Constants (k_{obs}) for the One-Electron Reduction of Radical Anions by NADH Analogues in Deaerated MeCN at 298 K

NADH analogue	k_{obs} ($DDQ^{-}\cdot$) / $dm^3\ mol^{-1}\ s^{-1}$	k_{obs} ($Cl_4Q^{-}\cdot$) / $dm^3\ mol^{-1}\ s^{-1}$
BNAH	1.1 x 10	1.1×10^{-1}
$AcrH_2$	1.7	a)
$AcrD_2$	7.6×10^{-2}	a)

a) Too slow to be determined accurately.

When $AcrH_2$ is replaced by the dideuterated compound, 10-methyl-[9,9-$^2H_2$]dihydroacridine ($AcrD_2$), the primary kinetic isotope effect is obtained as $k_H/k_D = 22$ in the reduction of $DDQ^{-}\cdot$. Such large k_H/k_D values have often been observed for other reactions involving a transfer of hydrogen nucleus (proton, hydrogen atom or hydride ion) and are generally believed to be due to quantum-mechanical tunneling.[7)]

To our surprise, the addition of $NaClO_4$ to the BNAH-$Cl_4Q^{-}\cdot$ system results in a significant increase in the rates of the one-electron reduction of $Cl_4Q^{-}\cdot$ by BNAH. The k_{obs} values increase linearly with an increase in [$NaClO_4$] as shown in Fig. 1. Similar acceleration effect on the rates is observed in the one-electron reduction of $DDQ^{-}\cdot$ by BNAH, where the k_{obs} values increase with an increase in [$NaClO_4$] to reach a constant value. In each case, no acceleration of the rates is observed in the presence of Bu_4NClO_4 (Fig. 1).

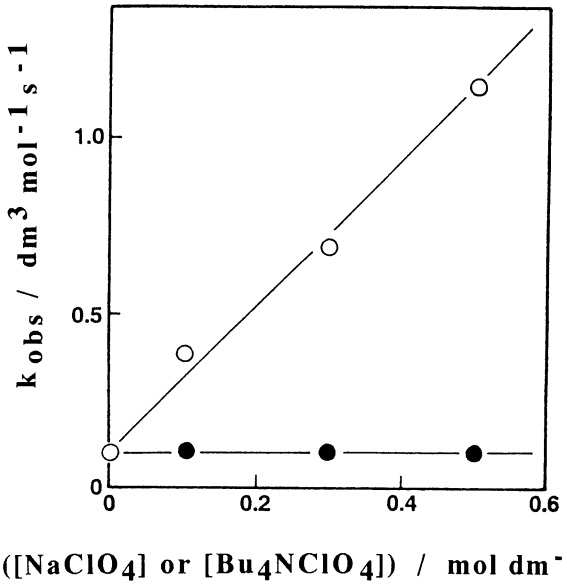


Fig. 1. Plots of k_{obs} *vs.* [$NaClO_4$] (o) or [Bu_4NClO_4] (●) for the one-electron reduction of $Cl_4Q^{-}\cdot$ (5.0×10^{-5} mol dm^{-3}) by BNAH in deaerated MeCN at 298 K.

The significant catalytic effect of $NaClO_4$ on the one-electron reduction of $Cl_4Q^{-}\cdot$ in MeCN was examined by the voltammetric study. The cyclic voltammogram (CV) of Cl_4Q in the presence of Bu_4NClO_4 (0.10 mol dm^{-3}) shows the two reversible redox couples due to $Cl_4Q/Cl_4Q^{-}\cdot$ and $Cl_4Q^{2-}/Cl_4Q^{-}\cdot$ as shown in Fig. 2a. The reduction peak potential of $Cl_4Q^{-}\cdot$ is significantly shifted to the positive direction in the presence of 0.10 mol dm^{-3} $NaClO_4$ (Fig. 2b) as compared to that in the presence of 0.10 mol dm^{-3} Bu_4NClO_4 (Fig. 2a). Such a positive shift in the presence of $NaClO_4$ indicates that the one-electron reduction of $Cl_4Q^{-}\cdot$ is accompanied by the complex formation of the one-electron reduced product (Cl_4Q^{2-}) with Na^+, since no effect of Na^+ was observed on the electronic spectrum of $Cl_4Q^{-}\cdot$. In fact, the redox couple of $Cl_4Q/Cl_4Q^{-}\cdot$ is unaffected by the presence of 0.10 mol dm^{-3} $NaClO_4$ (Fig. 2b) as compared to that in the presence of 0.10 mol dm^{-3} Bu_4NClO_4 (Fig. 2a).

Based on the catalytic effect of Na^+ on the one-electron reduction of radical anions, combined with the observation of the large primary kinetic isotope effect ($k_H/k_D = 22$ in Table 1) the reaction mechanism of the one-

electron reduction of the radical anions by NADH analogues may be given by Scheme 1 for the BNAH-$DDQ^{-}\cdot$ system as a typical case. The initial electron transfer from NADH analogues to radical anions is endergonic, judging from the one-electron oxidation potentials (E^0_{ox} *vs.* SCE) of NADH analogues (BNAH: 0.57 V, $AcrH_2$: 0.80 V)[8] and the one-electron reduction potentials (E^0_{red} *vs.* SCE) of radical anions (-0.30 and -0.70 V for $DDQ^{-}\cdot$ and $Cl_4Q^{-}\cdot$, respectively[6]). The Na^+ can form the complex with the one-electron reduced species of radical anions, *i.e.* the dianions, resulting in the positive shift of the one-electron reduction potentials of radical anions. Thus, the electron transfer becomes energetically more favorable in the presence of Na^+. This may be the reason why the rates are accelerated by the presence of Na^+ (Fig. 1). The endergonic electron transfer may be followed by proton transfer from the resulting radical cation to the dianion (Scheme 1). The large primary kinetic isotope effect (k_H/k_D = 22 in Table 1) may be ascribed to be that in the proton transfer process. The deprotonated radicals

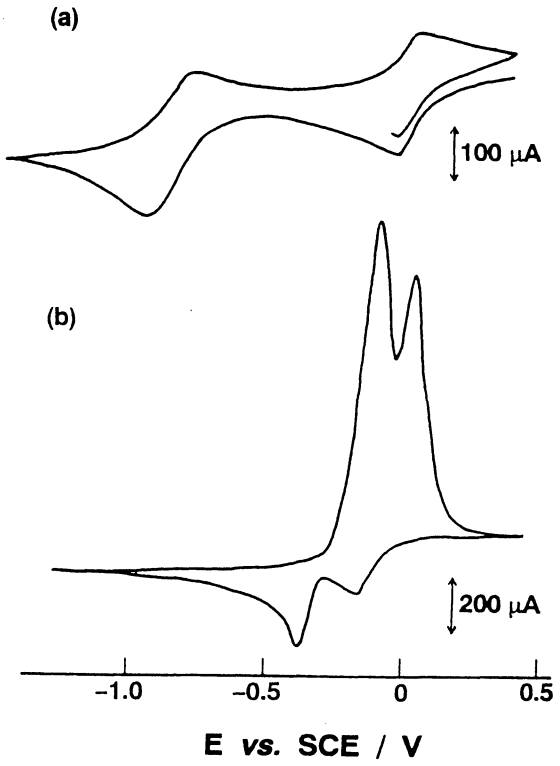
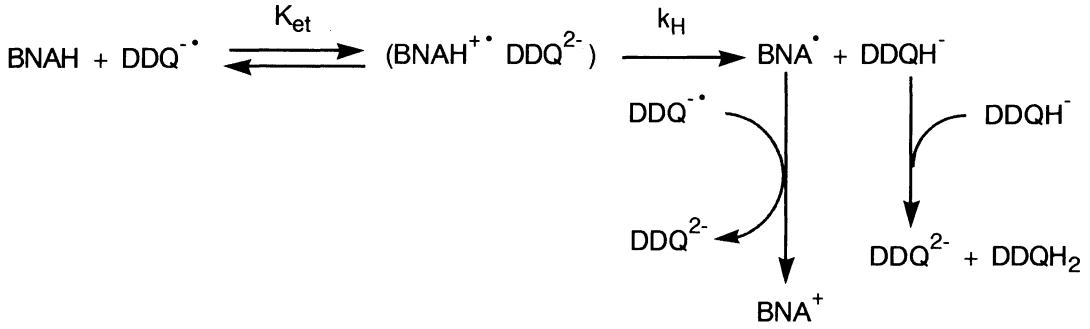


Fig. 2. Cyclic voltammograms of Cl_4Q (5.0×10^{-3} mol dm^{-3}) in the presence of (a) Bu_4NClO_4 (0.10 mol dm^{-3}) and (b) $NaClO_4$ (0.10 mol dm^{-3}) in deaerated MeCN at the sweep rate of 2 V min^{-1}.



Scheme 1.

(BNA· and AcrH·) are strong one-electron reductants judging from the negative one-electron oxidation potentials (-1.08 and -0.43 V for BNA· and AcrH·, respectively),[8] and thus, the facile electron transfer to radical anions may occur, in consistent with the stoichiometry of the reactions (Eq. 1). In the case of $AcrH_2$-$Cl_4Q^{-}\cdot$ system, the electron transfer from AcrH· to $Cl_4Q^{-}\cdot$ is highly endergonic judging from the one-electron redox potentials. This may be the reason of the diminished reactivity of $AcrH_2$ toward $Cl_4Q^{-}\cdot$.

According to Scheme 1, the observed rate constants (k_{obs}) may be given as $k_{obs} = k_H K_{et}$, where K_{et} is

the equilibrium constant for the endergonic electron transfer and k_H is the rate constant of proton transfer from the radical cation to the dianion in the solvent cage. In such a case the rate constant of overall hydrogen transfer from NADH analogues to radical anions is determined by the energetics of electron transfer and the rate constant of proton transfer. This is essentially the same as the case of hydride transfer from BNAH to *p*-benzoquinone derivatives (Q), in which the rate constant of overall hydride transfer is determined by the energetics of electron transfer from BNAH to Q and the rate constant of proton transfer from $BNAH^+ \cdot$ to $Q^- \cdot$, since the final electron transfer from BNA· to QH· is highly exergonic.[8,9] In fact, the k_{obs} value (7.6 dm^3 mol^{-1} s^{-1})[9] of hydride transfer from BNAH to chloro-*p*-benzoquinone that has a similar E^0_{red} value (-0.34 V) to the E^0_{red} value of $DDQ^- \cdot$ (-0.31 V) agrees reasonably well with the k_{obs} value (1.1 x 10 dm^3 mol^{-1} s^{-1}) of the hydrogen transfer from BNAH to $DDQ^- \cdot$.

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