Hydride transfer from NADH analogues to a nonheme manganese(IV)–oxo complex via rate-determining electron transfer†

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Hydride transfer from NADH analogues to a nonheme Mn(IV)–oxo complex, [(Bn-TPEN)MnIV(O)]2+, proceeds via a rate-determining electron transfer step with no deuterium kinetic isotope effect (KIE = 1.0 ± 0.1); a charge-transfer complex formed between the MnIV(O) complex and NADH analogues is involved in the hydride transfer reaction.

An important objective in biological oxidation reactions is to understand the nature of reactive intermediates and their reaction mechanisms occurring at the active sites of enzymes.1 High-valent metal–oxo complexes play pivotal roles as reactive intermediates in a wide range of heme2 and nonheme metalloenzymes3 as well as in their biomimetic catalysts.4 In particular, manganese–oxo complexes have attracted much attention as key intermediates in the oxygen-evolving complex (OEC) of photosystem II,5 in which four-electron oxidation of H2O to O2 is efficiently catalyzed. We have previously reported electron-transfer properties of a nonheme manganese(IV)–oxo complex, which revealed that manganese(IV)–oxo complexes are stronger one-electron oxidants than the iron(IV)–oxo analogues.6,7 Hydride transfer from dihydronicotinamide adenine dinucleotide (NADH) analogues,8 such as 10-methyl-9,10-dihydroacridine (AcrH2) and its derivatives, to nonheme iron(IV)–oxo complexes has been reported to occur via electron transfer followed by proton and electron transfer, exhibiting large deuterium kinetic effects (KIEs) to yield the corresponding NAD+ analogues and nonheme iron(n) complexes.7 In contrast to iron(IV) complexes, hydride transfer from NADH analogues to nonheme manganese(IV)–oxo complexes, which are stronger oxidants than the corresponding iron(IV)–oxo complexes may proceed via a rate-determining electron transfer step, which should exhibit no KIE. However, there has been no report on hydride-transfer reactions via a rate-determining electron-transfer step despite extensive studies on hydride-transfer reactions of NADH analogues.9–13

We report herein the first example of hydride transfer (HT) from a series of NADH analogues and their deuterated compounds to a mononuclear nonheme manganese(IV)–oxo complex, [(Bn-TPEN)MnIV(O)]2+ (1, Bn-TPEN = N-benzyl-N,N,N′,N′′-tris(2-pyridylmethyl)ethane-1,2-diamine) (Fig. 1) via a rate-determining electron-transfer step. The difference in the rate-determining steps of HT from NADH analogues to nonheme iron(IV)–oxo7b and manganese(IV)–oxo complexes is clarified by carrying out kinetic studies, including the determination of the deuterium kinetic isotope effect (KIE).

In order to compare the HT reactivities of nonheme iron(IV)–oxo and manganese(IV)–oxo complexes, we determined the rate constants of HT reactions from the same series of NADH analogues to nonheme manganese(IV)–oxo complexes, as employed in the reactions of nonheme iron(IV)–oxo complexes.22 The visible absorption changes in HT from AcrH2 to 1 in deaerated CF3CH2OH/MeCN (1:1 v/v) at 273 K are shown in Fig. 2a, where the absorption band at 358 nm due to 10-methylacridinium ion (AcrH+) increases. The rates obeyed pseudo-first-order kinetics in the presence of large excess of AcrH2, and the pseudo-first-order rate constants (kobs) increased linearly with the increase of the AcrH2 concentration (Fig. 2b). The second-order rate constant (kAcrH2) of HT from AcrH2 to 1 in deaerated CF3CH2OH/MeCN (1:1 v/v) at 273 K was determined from the slope of the linear plot in Fig. 2b (blue) to be 1.4 × 103 M−1 s−1. When AcrH2 was replaced by the deuterated

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compound (AcrD2), the same second-order rate constant was obtained as shown in Fig. 2b (red), exhibiting no deuterium kinetic isotope effect in the HT reaction (KIE = $k_{D}/k_{H} = 1.0 \pm 0.1$).

This is in sharp contrast to HT reactions by [(Bn-TPEN)FeIV(O)]$^{2+}$, in which a large KIE value of 18 was obtained.$^{27}$ In the case of 1, which has a higher one-electron reduction potential $E_{\text{red}} = 0.78$ V versus SCE$^{6}$ than [(Bn-TPEN)FeIV(O)]$^{2+}$ ($E_{\text{red}} = 0.49$ V versus SCE$^{27}$), electron transfer (ET) from AcrH2 ($E_{\text{ox}} = 0.81$ V versus SCE$^{27}$) to 1 is thermodynamically feasible, whereas ET from AcrH2 to [(Bn-TPEN)FeIV(O)]$^{2+}$ is endergonic ($\Delta G_{\text{et}} > 0$). Thus, HT from AcrH2 to 1 occurs via rate-determining ET, followed by fast proton and electron transfer to yield AcrH$^+$ and [(Bn-TPEN)MnIV(OH)]$^{2+}$ (see ESI, Fig. S1); we have shown previously that HT from AcrH2 to [(Bn-TPEN)FeIV(O)]$^{2+}$ occurs via uphill ET followed by rate-determining proton transfer (PT) in competition with the back ET, followed by fast ET to yield AcrH$^+$ and [(Bn-TPEN)FeII(OH)]$^{2+}$.$^{27}$

The $k_{A}$ values of HT from other NADH analogues (AcrHR: R = Ph, CH$_3$Ph, Et and AcrDPh) were also determined (ESI, Table S1 and Fig. S2). The substitution of one H by Ph in AcrH2 (i.e., AcrHPh) results in a higher $E_{\text{ox}}$ value (0.88 V versus SCE$^{6}$) than AcrH2 (0.81 V versus SCE$^{27}$), thus a slower deprotonation from AcrHPh$^*$ occurs compared to AcrH$^+$.$^{7h,14}$ In such a case, ET from AcrHPh to 1 becomes endergonic, followed by slower PT from AcrHPh$^*$ to [(Bn-TPEN)MnIV(O)]$^{2+}$ as compared with the case of AcrH2. Thus, the rate constant of HT from AcrHPh and AcrDPh to 1 exhibits a KIE value of $k_{D}/k_{H} = 1.9$ (see ESI, Fig. S3). In this case, PT from AcrDPh$^*$ to [(Bn-TPEN)MnIV(O)]$^{2+}$ becomes partially a rate-determining step in competition with the back ET from [(Bn-TPEN)MnIV(O)]$^{2+}$ to AcrDPh$^*$ following endergonic ET from AcrDPh to 1.

We have previously reported that the rate constant of outer sphere electron transfer from ferrocene derivatives to 1 is well fitted by the Marcus theory of outer-sphere electron transfer$^{15}$

$$k_{et} = Z \exp[-(\lambda/4)(1 + \Delta G_{et}/\lambda)]k_{b}T$$

(1)

where $Z$ is the collision efficiency taken as $1 \times 10^{11}$ M$^{-1}$ s$^{-1}$, $\lambda$ is the reorganization energy of ET, $k_{b}$ is the Boltzmann constant, and $T$ is the absolute temperature.$^{6,7,17}$ The driving force dependence of logarithm of the rate constants of outer-sphere electron transfer is shown in Fig. 3 (red circles), where the log $k_{et}$ values are plotted against the $-\Delta G_{et}$ values. The driving force dependence of $k_{et}$ is well fitted by the red line in Fig. 3 using eqn (1) with a $\lambda$ value of 2.24 eV.$^{54}$

The rate constants ($k_{A}$) of HT from AcrHR to 1 are also plotted in Fig. 3 (blue and green circles), where the $k_{A}$ values are much larger than those expected from outer-sphere electron transfer (red line). Such a difference in the $k_{A}$ and $k_{et}$ values at the same driving force results from the difference in the equilibrium constants of precursor complexes formed prior to ET (vide infra)$^{16}$.

The dependence of the pseudo-first-order rate constant ($k_{1}$) on the concentration of AcrH2 at larger concentrations is shown in the ESI, Fig. S4a, where the $k_{1}$ value increases with increasing concentrations of AcrH2 to approach the constant value. Such a saturation behaviour of $k_{1}$ on the concentration of NADH analogues is given by eqn (2), where $k_{et}$ is the rate constant in the precursor complex, $K$ is the formation constant of the precursor complex, and [S] is the concentration of a substrate.$^{15}$

$\log k_{et} = K[S]/[1 + K[S]]$ (2)

$K_{et} = (k_{et}[S])^{-1} + k_{et}^{-1}$ (3)

The $K$ value was determined from the linear plot of $k_{et}^{-1}$ versus [S]$^{-1}$ (ESI, Fig. S4b) to be $2.1 \times 10^{2}$ M$^{-1}$, which is much larger than that expected from outer-sphere electron transfer. The larger $K$ value of the precursor complex prior to ET results in the larger $k_{et}$ values than those expected from outer-sphere electron transfer, as shown in Fig. 3.

The $K$ values may be different depending on the $E_{\text{ox}}$ values of NADH analogues; therefore, the $k_{et}$ values were evaluated to be $2.0 \times 10^{2}$ M$^{-1}$ by using average $K$ values with AcrH2 (2.1 $\times$ 10$^{5}$ M$^{-1}$) and AcrHPh (1.9 $\times$ 10$^{2}$ M$^{-1}$; ESI, Fig. S4). The $K$ value of the precursor complexes of 1 with Br$_2$Fe, which is adapted as a one-electron donor, was determined to be 6.4 M$^{-1}$ (ESI, Fig. S5), indicating that the $K$ values of NADH analogues are much larger than that of a ferrocene derivative. Fig. 4 shows unified plots of log $\Delta G_{et}$ versus $k_{et}$ for AcrHR: R = Ph, CH$_3$Ph, Et and AcrDPh with AcrH2 (2.1 $\times$ 10$^{5}$ M$^{-1}$) and AcrHPh (1.9 $\times$ 10$^{2}$ M$^{-1}$; ESI, Fig. S4).
deprotonation from AcrDPh

higher one-electron oxidation potential of AcrDPh and slower

replaced by AcrDPh, which exhibits a KIE of 1.9 because of the

between AcrH2 and

PT from AcrH2 [(Bn-TPEN)Fe IV(O)]2 indentifying when AcrH2 was

gonic ET with a large KIE value of 18.7

analogues to

1 analogues to high-valent metal–oxo complexes, depending on

the one-electron redox potentials of NADH analogues and the

metal–oxo complexes.

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Notes and references


