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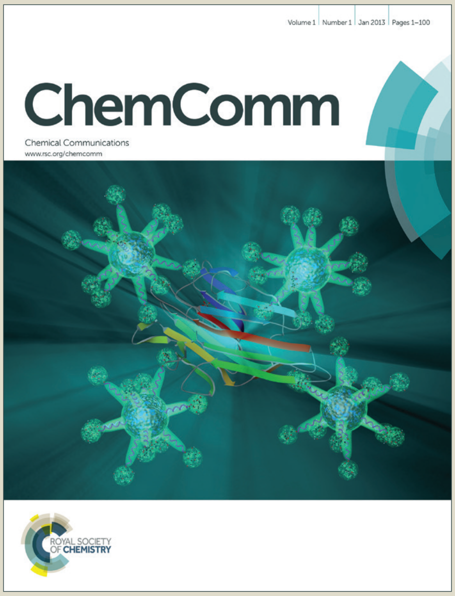

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Hydride transfer from NADH analogues to a nonheme manganese(IV)-oxo complex via rate-determining electron transfer†

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Hydride transfer from NADH analogues to a nonheme Mn(IV)-oxo complex, $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$, proceeds via a rate-determining electron transfer with no deuterium kinetic isotope effect (KIE = 1.0 ± 0.1); a charge-transfer complex formed between the $Mn^{IV}(O)$ 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 heme[2] and nonheme metalloenzymes[3] as well as in their biomimetic catalysts.[4] In particular, manganese-oxo complexes have attracted much attention as key intermediates in oxygen-evolving complex (OEC) in photosystem II,[5] in which four-electron oxidation of H_2O to O_2 is efficiently catalyzed. We have previously reported electron-transfer properties of a nonheme manganese(IV)–oxo complex, which revealed that manganese(IV)–oxo complex is a stronger one-electron oxidant than the iron(IV)–oxo analogues.[6,7] Hydride transfer from dihydronicotinamide adenine dinucleotide (NADH) analogues,[8] such as 10-methyl-9,10-dihydroacridine ($AcrH_2$) 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(II) 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]

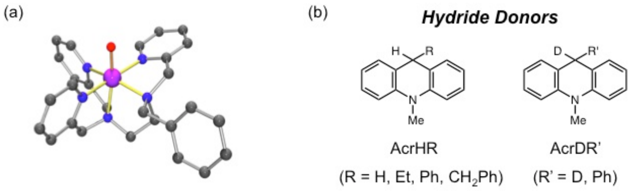


Fig. 1 (a) Chemical structures of (a) $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ and (b) NADH analogues used in HT reactions.

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, $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ (1, Bn-TPEN = *N*-benzyl-*N*,*N′*,*N′*-tris(2-pyridylmethyl)ethane-1,2-diamine) (Fig. 1)[6] via a rate-determining electron-transfer step. The difference in the rate-determining steps of HT from NADH analogues to nonheme iron(IV)-oxo[7b] and manganese(IV)-oxo complexes is clarified by carrying out kinetic studies, including the determination of 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.[7b] The visible absorption changes in HT from $AcrH_2$ to 1 in deaerated CF_3CH_2OH/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 $AcrH_2$, and the pseudo-first-order rate constants (k_{obs}) increased linearly with the increase of the $AcrH_2$ concentration (Fig. 2b). The second-order rate constant (k_H) of HT from $AcrH_2$ to 1 in deaerated CF_3CH_2OH/MeCN (1:1 v/v) at 273 K

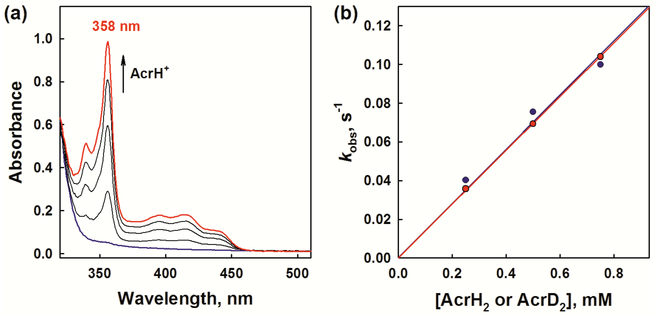


Fig. 2 (a) UV-vis spectral changes observed in HT from $AcrH_2$ (5.0×10^{-4} M) to $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ (5.0×10^{-5} M) in CF_3CH_2OH/MeCN (1:1 v/v) at 273 K. (b) Plots of the pseudo-first-order constants (k_{obs}) of $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ *versus* $AcrH_2$ (blue) or $AcrD_2$ (red).

was determined from the slope of the linear plot in Fig. 2b (blue) to be 1.4×10^2 M^{-1} s^{-1}. When $AcrH_2$ was replaced by the deuterated compound ($AcrD_2$), 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 = $k_H/k_D = 1.0 \pm 0.1$). This is in sharp contrast to HT reactions by $[(Bn\text{-}TPEN)Fe^{IV}(O)]^{2+}$, in which a large KIE value of 18 was obtained.[7b] In the case of 1, which has a higher one-electron reduction potential (E_{red} = 0.78 V *versus* SCE)[6c] than $[(Bn\text{-}TPEN)Fe^{IV}(O)]^{2+}$ (E_{red} = 0.49 V *versus* SCE),[7a] electron transfer (ET) from $AcrH_2$ (E_{ox} = 0.81 V *versus* SCE)[14] to 1 is thermodynamically feasible, whereas ET from $AcrH_2$ to $[(Bn\text{-}TPEN)Fe^{IV}(O)]^{2+}$ is endergonic ($\Delta G_{et} > 0$). Thus, HT from $AcrH_2$ to 1 occurs via rate-determining ET, followed by fast proton and electron transfer to yield $AcrH^+$ and $[(Bn\text{-}TPEN)Mn^{II}(OH)]^{2+}$ (see ESI,† Fig. S1); we have shown previously that HT from $AcrH_2$ to $[(Bn\text{-}TPEN)Fe^{IV}(O)]^{2+}$ 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 $[(Bn\text{-}TPEN)Fe^{II}(OH)]^{2+}$.[7b]

The k_H values of HT from other NADH analogues (AcrHR: R = Ph, CH_2Ph, Et and AcrDPh) were also determined (ESI,† Table S1 and Fig. S2). The substitution of one H by Ph in $AcrH_2$ (i.e., AcrHPh) results in the higher E_{ox} value (0.88 V *versus* SCE) than $AcrH_2$ (0.81 V *versus* SCE), thus a slower deprotonation from $AcrHPh^{\bullet+}$ occurs compared to $AcrH_2^{\bullet+}$.[7b,14] In such a case, ET from AcrHPh to 1 becomes endergonic, followed by slower PT from $AcrHPh^{\bullet+}$ to $[(Bn\text{-}TPEN)Mn^{III}(O)]^+$ as compared with the case of $AcrH_2$. Thus, the rate constant of HT from AcrHPh and AcrDPh to 1 exhibits a KIE value of $k_H/k_D = 1.9$ (see ESI,† Fig. S3). In this case, PT from $AcrDPh^{\bullet+}$ to $[(Bn\text{-}TPEN)Mn^{III}(O)]^+$ becomes partially a rate-determining step in competition with the back ET from $[(Bn\text{-}TPEN)Mn^{III}(O)]^+$ to $AcrDPh^{\bullet+}$ 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] [eqn (1)],

$$k_{et} = Z\exp[-(\lambda/4)(1 + \Delta G_{et}/\lambda)^2/k_BT] \qquad (1)$$

where Z is the collision frequency taken as 1×10^{11} M^{-1} s^{-1}, λ is the reorganization energy of ET, k_B is the Boltzmann constant, and T is the absolute temperature.[6,7,15] 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 the λ value of 2.24 eV.[6c]

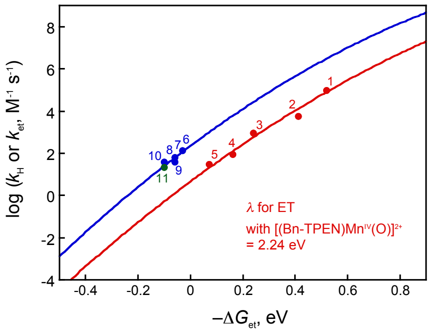


Fig. 3 Driving force of the ET ($-\Delta G_{et}$) dependence of log k_{et} of ET from one electron donors (1, dimethylferrocene; 2, ferrocene; 3, bromoferrocene; 4, acetylferrocene; 5, dibromoferrocene) to $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ (red) and the HT from NADH analogues (6, $AcrH_2$; 7, $AcrD_2$; 8, AcrHEt; 9, $AcrHCH_2Ph$; 10, AcrHPh; 11, AcrDPh) to $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ (blue) in CF_3CH_2OH/MeCN (1:1 v/v) at 273 K. The red line is drawn according to eqn (1) with the λ value of 2.24 eV.

The rate constants (k_H) of HT from AcrHR to 1 are also plotted in Fig. 3 (blue circles), where the k_H values are much larger than those expected from outer-sphere electron transfer (red line). Such difference in the k_H 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_f) on concentration of $AcrH_2$ at larger concentrations is shown in ESI,† Fig. S4a, where the k_f value increases with increasing concentration of $AcrH_2$ to approach the constant value. Such a saturation behaviour of k_f on 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.[16] Eqn (2) is rewritten by eqn (3), which predicts a linear correlation between k_f^{-1} vs $[S]^{-1}$, which was confirmed in ESI,† Fig. S4b.

$$k_f = k_{ET}K[S]/(1 + K[S]) \qquad (2)$$

$$k_f^{-1} = (k_{ET}K[S])^{-1} + k_{ET}^{-1} \qquad (3)$$

The K value was determined from linear plot of k_f^{-1} *versus* $[S]^{-1}$ (ESI,† Fig. S4b) to be 2.1×10^2 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 in Fig. 3.

The K values may be different depending on the E_{ox} values of NADH analogues; therefore, the k_{ET} values were evaluated as 2.0×10^2 M^{-1} by using average K values with $AcrH_2$ (2.1×10^2 M^{-1}) and AcrHPh (1.9×10^2 M^{-1}; ESI,† Fig. S4). The K value of the precursor complexes of $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ with Br_2Fc, which is adapted as 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 k_{ET} of ET and HT from ferrocene derivatives and NADH analogues to $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$, respectively. The driving force dependence of log k_{ET} of ET in deaerated CF_3CH_2OH/MeCN (1:1 v/v) at 273 K is unified as a single red line using the same λ value of 2.24 eV,[6c] confirming that the HT of NADH analogues by $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ proceeds via the rate-determining ET step.

In summary, HT from $AcrH_2$ to $[(Bn\text{-}TPEN)Mn^{IV}(O)]^{2+}$ occurs via rate-determining ET, followed by rapid PT and ET with no KIE. In contrast, HT from $AcrH_2$ to $[(Bn\text{-}TPEN)Fe^{IV}(O)]^{2+}$ occurs via rate-determining PT from $AcrH_2^{\bullet+}$ to $[(Bn\text{-}TPEN)Fe^{III}(O)]^+$ in

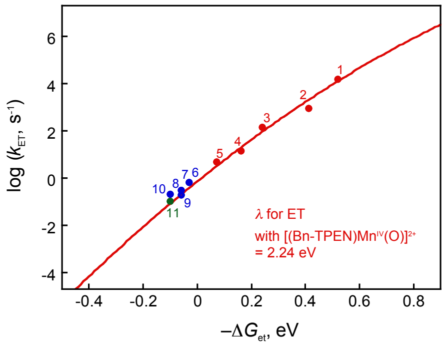
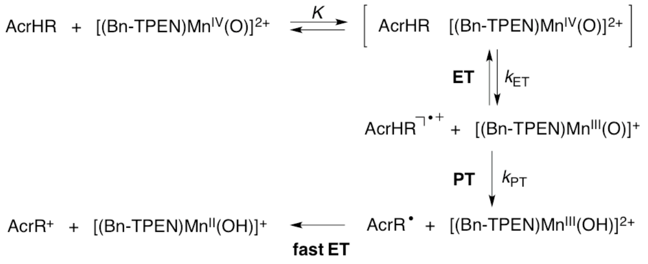


Fig. 4 Driving force of the ET ($-\Delta G_{et}$) dependence of log k_{ET} of ET from one electron donors (1, dimethylferrocene; 2, ferrocene; 3, bromoferrocene; 4, acetylferrocene; 5, dibromoferrocene) to [(Bn-TPEN)Mn^{IV}(O)]$^{2+}$ (red) and the HT from NADH analogues (6, AcrH$_2$; 7, AcrD$_2$; 8, AcrHEt; 9, AcrHCH$_2$Ph; 10, AcrHPh; 11, AcrDPh) to [(Bn-TPEN)Mn^{IV}(O)]$^{2+}$ (blue) in CF$_3$CH$_2$OH/MeCN (1:1 v/v) at 273 K. The red line is the Marcus line calculated with λ value of 2.24 eV.

competition with back ET from [(Bn-TPEN)Fe^{III}(O)]$^{+}$ to AcrH$_2^{\bullet+}$ following endergonic ET with a large KIE value of 18.[7b] Such a change in the rate-determining step was also observed when AcrH$_2$ is replaced by AcrDPh, which exhibits KIE of 1.9 because of the higher one-electron oxidation potential of AcrDPh and slower deprotonation from AcrDPh$^{\bullet+}$ as compared with AcrH$_2^{\bullet+}$.[14] ET from AcrH$_2$ to 1 occurs via formation of a precursor complex between AcrH$_2$ and 1 with a much larger formation constant (K) in Scheme 1 as compared with outer-sphere electron transfer from ferrocene derivatives to 1. This study has revealed the switch of the rate-determining step in HT from NADH analogues to high-valent metal-oxo complexes, depending on the one-electron redox potentials of NADH analogues and the metal-oxo complexes.

Scheme 1. Proposed Mechanism of HT from AcrHR to [(Bn-TPEN)Mn^{IV}(O)]$^{2+}$



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Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental and kinetic details. See DOI: 10.1039/c000000x/

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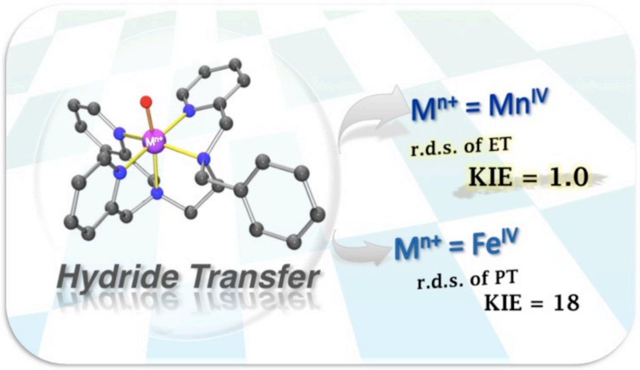
TOC Graphics



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