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Reversed effects of DNA on hydride transfer and electron transfer reactions of acridinium and quinolinium ions

Mari Nishimine, Kei Ohkubo, Takashi Komori and Shunichi Fukuzumi*

Department of Material and Life Science, Graduate School of Engineering, Osaka University, CREST, Japan Science and Technology Corporation (JST), Suita, Osaka 565-0871, Japan.
E-mail: fukuzumi@chem.eng.osaka-u.ac.jp; Fax: +81-6-6879-7370; Tel: +81-6-6879-7368

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DNA inhibits hydride transfer from 1-benzyl-1,4-dihydronicotinamide to the 10-methylacridinium ion, whereas DNA accelerates photoinduced electron transfer from the excited state of $Ru(bpy)_3^{2+}$ to the 1-methylquinolinium ion. The reason of such reversed effects of DNA on the hydride transfer and electron transfer reactions is clarified.

The rate of electron transfer is known to be controlled by the environment surrounding electron donors and acceptors. In particular, the role of the DNA double helix in mediating electron transfer has attracted much attention.[1–5] In the case of electron transfer, it is very important to know the driving force which is determined by the difference in the one-electron redox potentials of electron donors and acceptors. The driving force of electron transfer between intercalators in DNA is expected to be changed as compared with that in an aqueous solution due to the significant difference in their environment. However, significant change in the redox potentials in DNA as compared to those in an aqueous solution has yet to be reported.[6] In addition, there has been no report on the effect of DNA on reactions other than photoinduced electron transfer or energy transfer.

The present study reports that the one-electron reduction potential of the 1-methylquinolinium ion (QuH^+) is shifted significantly in a positive direction by intercalation into DNA and that electron transfer from the photoexcited state of $Ru(bpy)_3^{2+}$ (bpy = 2,2′-bipyridine) to QuH^+ is enhanced significantly in the presence of DNA. In contrast, hydride transfer from an NADH model compound to the 10-methylacridinium ion ($AcrH^+$), which can also intercalate into DNA, has been found to be retarded in the presence of DNA. Thus, DNA has reverse effects depending on the type of reaction.

Hydride transfer from an NADH model compound, 1-benzyl-1,4-dihydronicotinamide (BNAH), to $AcrH^+$ occurs in deaerated 5 mmol dm^{-3} Tris–HCl buffer (pH 7.0) at 298 K to yield the 1-benzylnicotinamidinium ion (BNA^+) and 10-methyl-9,10-dihydroacridine ($AcrH_2$).[7] When DNA is added to the BNAH–$AcrH^+$ system, the hydride transfer is retarded significantly. The second-order plots for the rate of hydride transfer from BNAH to an equivalent amount of $AcrH^+$ in the absence and presence of various concentrations of DNA gave straight lines. From the slopes of the linear plots of $1/([AcrH^+] - [AcrH^+]_\infty)$ *vs.* time the second-order rate constants (k_{obs}) of the hydride transfer reaction are obtained. The k_{obs} value decreases with an increase in the ratio of [DNA bases] : $[AcrH^+]_0$ as shown in Fig. 1a. Such a retarding effect of DNA on the hydride transfer reaction indicates that the reactivity of $AcrH^+$ toward BNAH is diminished when $AcrH^+$ is bound with DNA. If one assumes that hydride transfer from BNAH occurs only to unbound $AcrH^+$ as shown in Scheme 1, k_{obs} can be expressed as a function of [DNA bases] by eqn. (1), where k_{obs}^0 is the rate constant in the absence of DNA and K is the binding constant of $AcrH^+$ with DNA. From eqn. (1) is derived the ratio of the intercalated $AcrH^+$ molecules as shown in eqn. (2).

$$k_{obs} = k_{obs}^0/(1 + K[\text{DNA bases}]) \quad (1)$$

$$[\text{DNA bases–AcrH}^+]/[AcrH^+]_0 = (k_{obs}^0 - k_{obs})/k_{obs}^0 \quad (2)$$

Plots of $[\text{DNA bases–AcrH}^+]/[AcrH^+]_0$ *vs* [DNA bases]/$[AcrH^+]_0$ are shown in (Fig. 1b), where the data obtained from the rate constants of hydride transfer (○) agree well with those obtained from the change in absorbance due to $AcrH^+$ in the presence of DNA (●).[8] Such agreement indicates strongly that $AcrH^+$ is intercalated between the nucleic acid base pair to show no reactivity toward BNAH in solution.

Effects of DNA on photoinduced electron transfer of 1-methylquinolinium ion (QuH^+), which can also be intercalated into DNA, were examined by the emission lifetime measurements of the excited state of $Ru(bpy)_3^{2+}$ used as an electron donor that is known to be groove binding with DNA.[1,2] In the absence of DNA, the emission of $Ru(bpy)_3^{2+}$ is little quenched as indicated by an increase in the decay rate constant (k_d) with increasing QuH^+ concentration (○ in Fig. 2a). This is consistent with a slightly positive free energy change of electron transfer from $Ru(bpy)_3^{2+}$* (* denotes the excited state) to QuH^+ (ΔG^0_{et} = +0.13 eV), obtained from the one-electron reduction potential of QuH^+ in the absence of DNA (*vide infra*) and the one-electron oxidation potential of the excited state of $Ru(bpy)_3^{2+}$ (E^0_{ox} = −0.81 V *vs.* SCE).[9] The rate constant of photoinduced electron transfer (k_{et}) from $Ru(bpy)_3^{2+}$* to QuH^+ is determined as 3.1×10^7 mol^{-1} dm^3 s^{-1} in 5 mmol dm^{-3} Tris–HCl buffer (pH 7.0) at 298 K from the slope of the linear plot in Fig. 2a (□).

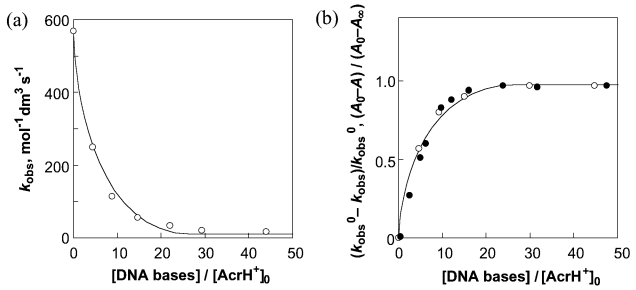
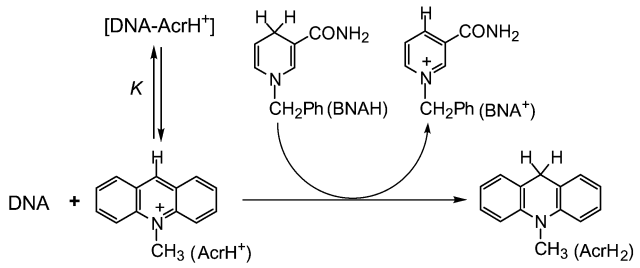


Fig. 1 (a) Plot of rate constants (k_{obs}) *vs.* [DNA bases]/$[AcrH^+]_0$ for hydride transfer from BNAH (3.2×10^{-5} mol dm^{-3}) to $AcrH^+$ (3.2×10^{-5} mol dm^{-3}) in the absence and presence of DNA in deaerated 5 mmol dm^{-3} Tris–HCl buffer (pH 7.0) at 298 K; [DNA bases] = 0, 1.4×10^{-4}, 2.8×10^{-4}, 4.7×10^{-4}, 7.1×10^{-4}, 9.4×10^{-4}, 1.4×10^{-3} mol dm^{-3}. (b) Ratio of intercalated $AcrH^+$ (3.1×10^{-5} mol dm^{-3}) to DNA (0–1.4×10^{-3} mol dm^{-3}) *vs* [DNA bases]/$[AcrH^+]_0$ in 5 mmol dm^{-3} Tris–HCl buffer (pH = 7.0) at 298 K, obtained from the second-order rate constants of hydride transfer, $(k_{obs}^0 - k_{obs})/k_{obs}^0$ (○) and from the UV-vis spectral change of $AcrH^+$ in the presence of DNA, $(A_0 - A)/(A_0 - A_\infty)$ (●).



Scheme 1

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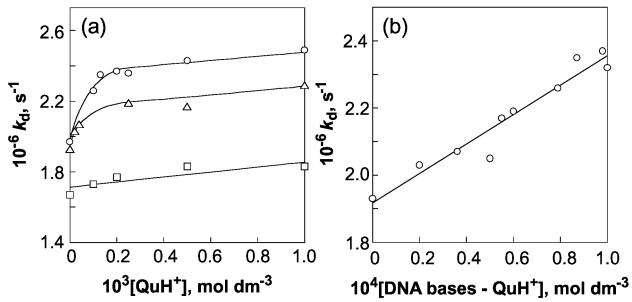

Fig. 2 (a) Plots of the decay rate constants (k_d) of Ru(bpy)$_3^{2+}$* *vs.* concentration of QuH$^+$ in 5 mmol dm^{-3} Tris–HCl buffer (pH 7.0) in the absence of DNA (□) and presence of DNA [1.0 × 10^{-3} mol dm^{-3} (△), 2.0 × 10^{-3} mol dm^{-3} (○)]; (b) Plot of k_d *vs* concentration of DNA bases–QuH$^+$.

In the presence of DNA, however, the k_d value increases significantly with increasing QuH$^+$ concentration to reach a nearly constant value which increases slightly with a further increase in QuH$^+$ concentration as shown in open circles in (Fig. 2a), where the magnitude of the initial increase in the k_d value increases with increasing DNA concentration.[10,11] Such an accelerating effect on photoinduced electron transfer from Ru(bpy)$_3^{2+}$* to QuH$^+$ may be ascribed to the intercalation of QuH$^+$ into DNA (*vide infra*).

The one-electron reduction potential (E^0_{red}) of QuH$^+$ in a 5 mmol dm^{-3} Tris–HCl buffer (pH 7.0) is determined as −0.94 V (*vs.* SCE) by second harmonic AC voltammetry (SHACV).[12] The E^0_{red} value is shifted to a positive direction in the presence of DNA, increasing with an increase in DNA concentration to reach a constant value (−0.81 V). The change in the E^0_{red} value with [DNA bases]/[QuH$^+$] is in parallel with the amount of intercalated molecule relative to the initial amount of QuH$^+$ which is determined from a bathochromic shift in the absorption band due to QuH$^+$ as well as the fluorescence quenching of QuH$^+$ by intercalation into DNA.[13] This indicates that the positive shift in E^0_{red} results from intercalation of QuH$^+$ into DNA. The QuH$^\cdot$ radical produced by the one-electron reduction of QuH$^+$ may be more stabilized by the π–π interaction with base pairs of DNA as compared to that in an aqueous solution. Thus, the free energy change of electron transfer from Ru(bpy)$_3^{2+}$* to QuH$^+$ in the presence of DNA becomes zero (ΔG^0_{et} = 0.00 eV) in contrast with the case in the absence of DNA (ΔG^0_{et} = +0.13 eV). No transient absorption spectrum due to QuH$^\cdot$ was observed in the laser flash photolysis experiments of the QuH$^+$–Ru(bpy)$_3^{2+}$ system in the absence of DNA as shown in Fig. 3 (○). In contrast, the addition of DNA to the QuH$^+$–Ru(bpy)$_3^{2+}$ system results in the observation of the transient absorption band at 520 nm due to QuH$^\cdot$ (● in Fig. 3).[14]

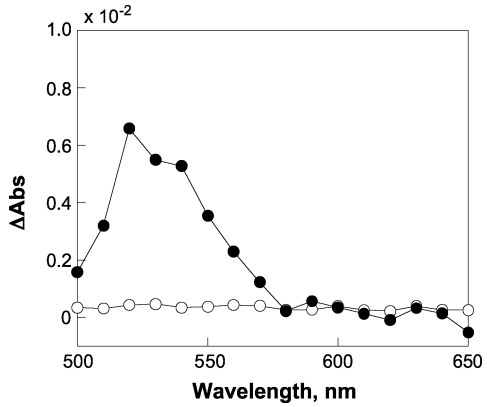

Fig. 3 Transient absorption spectra of an aqueous solution of QuH$^+$ (1.0 × 10^{-3} mol dm^{-3}) with Ru(bpy)$_3^{2+}$ (1.0 × 10^{-4} mol dm^{-3}) in the absence of DNA (○) and in the presence of DNA [2.0 × 10^{-3} mol dm^{-3}, (●)] at 298 K taken at 50 μs after laser excitation at 355 nm.

Thus, DNA makes the electron transfer from Ru(bpy)$_3^{2+}$* to QuH$^+$ thermodynamically much more favorable.

The rate constant of electron transfer (k_{et}) from Ru(bpy)$_3^{2+}$* to QuH$^+$ which is intercalated into DNA is determined as 4.4 × 10^9 mol^{-1} dm^3 s^{-1} from the linear Stern–Volmer plot of k_d *vs.* concentration of intercalated QuH$^+$, [DNA bases–QuH$^+$] which is determined from the absorption change by the intercalation (Fig. 2b). The k_{et} value is 140 times larger than the value in the absence of DNA (3.1 × 10^7 mol^{-1} dm^3 s^{-1}). Such large acceleration of electron transfer by DNA is ascribed to an increase in the driving force of electron transfer by the intercalation of QuH$^+$ into DNA. This shows sharp contrast with the case of hydride transfer from BNAH to AcrH$^+$ in which the intercalation of AcrH$^+$ into DNA prohibits the reaction due to the steric hindrance of the base pairs toward BNAH (Scheme 1).

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11 In the case of photoinduced electron transfer from Ru(bpy)$_3^{2+}$* to AcrH$^+$ which is a much stronger oxidant than QuH$^+$, the emission decay exhibits two-exponential decay which consists of both intermolecular electron transfer from Ru(bpy)$_3^{2+}$* to AcrH$^+$ which is intercalated into DNA and unimolecular electron transfer from Ru(bpy)$_3^{2+}$ which is groove binding with DNA to AcrH$^+$ intercalated into the same DNA molecule. The faster component corresponds to the quenching of glove binding Ru(bpy)$_3^{2+}$* by nearest-neighbor AcrH$^+$ intercalated into the DNA molecule, since this component increased with increasing DNA concentration.

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