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Hole transfer in DNA: DNA as a scaffold for hole transfer between two organic molecules

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Abstract—Hole transfer process in ODNs conjugated with two organic molecules, pyrene (Py) and phenothiazine (Ptz) was investigated with the pulse radiolysis measurements. Monitoring the transient absorption of Py$^{\bullet+}$ and Ptz$^{\bullet+}$, it was shown that the hole transfer rate was dependent on the distance and sequence between Py and Ptz. © 2003 Elsevier Science Ltd. All rights reserved.

Duplex DNA forming one-dimensional π-stacked array can be utilized to construct high-ordered structures in nanoscale devices.[1] A hole generated by one-electron oxidation of DNA has been demonstrated to migrate over a distance of 100 Å on the basis of strand cleavage experiments using polyacrylamide gel electrophoresis,[2] suggesting that DNA may be applied as nanowires for long range charge transportation.[3] However, DNA is inherently unstable upon oxidation.[4] Thus, DNA itself cannot be a good conductive material. In contrast, there are such organic molecules whose radical cations are stable in water. Therefore, for the construction of DNA wires, it may be better to use DNA as a scaffold for arranging such organic molecules. In order to explore such possibility of DNA wires, it is necessary to investigate the mechanism of the hole transfer between organic molecules conjugated to DNA.

Table 1. Sequences of ODN conjugated with Ptz and Py (PtzPy-**n**), and the rate constant of the hole transfer from Py to Ptz for PtzPy-**n**

ODN	Sequence	k_{ht}[a] / 10^{4} s^{-1}
PtzPy-**1**	$^{5'}$**Ptz**-AAA- A-CGCGATA TTT-**PyU**-GCGCTAT$^{5'}$	> 10
PtzPy-**2**	$^{5'}$**Ptz**-ACA- A-CGCGATA TGT-**PyU**-GCGCTAT$^{5'}$	> 10
PtzPy-**3**	$^{5'}$**Ptz**-AAAAA- A-CGCGA TTTTT-**PyU**-GCGCT$^{5'}$	2.0
PtzPy-**4**	$^{5'}$**Ptz**-AACAA- A-CGCGA TTGTT-**PyU**-GCGCT$^{5'}$	2.6
PtzPy-**5**	$^{5'}$**Ptz**-ACACA- A-CGCGA TGTGT-**PyU**-GCGCT$^{5'}$	3.3

[a] Obtained from the decay of the transient absorption of Py$^{\bullet+}$ at 470 nm.

Time-resolved absorption measurements are desired to clarify the kinetics of the hole transfer in DNA. There are several reports on the transient behavior of hole generated in DNA.[5] We have previously studied the multi-step and single-step hole transfer processes during pulse radiolysis of pyrene-conjugated ODN, and elucidated the rate and distance dependence of the hole transfer from monitoring the transient absorption of pyrene radical cation.[6] Since the hole is irreversibly generated in DNA during pulse radiolysis of ODN conjugated with probe molecule, this is a good method to investigate the hole transfer process occurring in the μs time scale.

There are only a few reports in which photoinduced electron transfer process between two organic molecules was examined by monitoring respective transient absorption spectra.[5f–h] It is expected that the observation of the hole transfer process gives us a valuable information of the mechanism. In the present study, we have carried out pulse radiolysis of ODN conjugated with pyrene (Py) and phenothiazine (Ptz) to investigate the possibility of modulation of the hole transfer rate and direction by means of introducing several organic molecules into DNA. Monitoring the transient absorption of radical cations of Py and Ptz (Py$^{\bullet+}$ and Ptz$^{\bullet+}$),

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we have measured the hole transfer rate depending on the distance and sequence.

Planar Py and Ptz are expected to stack well among nucleobases, and were used as the probe molecule to measure the hole transfer rate. The oxidation potentials of Py ($E_{ox} = 1.40$ V versus NHE in CH_3CN)[6] and Ptz ($E_{ox} = 0.76$ V versus NHE in CH_3CN)[7] were lower than those of four nucleobases, in particular G ($E_{ox} = 1.47$ V versus NHE in CH_3CN).[6] We examined the distance and sequence dependences of the hole transfer rate with monitoring the decay and formation of the transient absorption of $Py^{\bullet+}$ and $Ptz^{\bullet+}$ during pulse radiolysis of ODN conjugated with Py and Ptz (PtzPy-**n** (**n**=**1**–**5**)) (Table 1).

Synthesis of ODN conjugated with Py and Ptz followed the procedure reported previously.[7,8] Ptz was covalently bonded at 5′-end, while Py was linked to the ribose 2′-site by amide bond. The chemical structures of ODN conjugated with Py and Ptz and sequence of ODN used in this study were shown in Figure 1 and Table 1. Introduction of Py and Ptz into ODN caused an increase in T_m for PtzPy-**1** compared to unmodified ODN-**1**,[9] suggesting that Py intercalated into ODN duplex at the 3′-side and the 5′-linked-Ptz associated with the 5′-terminus by end-capping.[10]

Oxidizing reagent $TlOH^+$ was generated by pulse radiolysis (28 MeV, 8 ns) of N_2O-saturated (22 mM) aqueous solution containing 2 mM Tl_2SO_4, 20 mM Na phosphate buffer and 0.2 mM (strand conc.) ODN.[11] The hydrated electrons react with N_2O to give $^{\bullet}OH$, and $TlOH^+$ is produced within 20 ns by the reaction of Tl^+ with $^{\bullet}OH$ (Scheme 1). It is expected that random oxidation of ODN occurs because $TlOH^+$ has high oxidation potential enough to oxidize all four nucleobases, and direct oxidation of ODN by $TlOH^+$ is completed within 20 μs (Scheme 1, path a).[12]

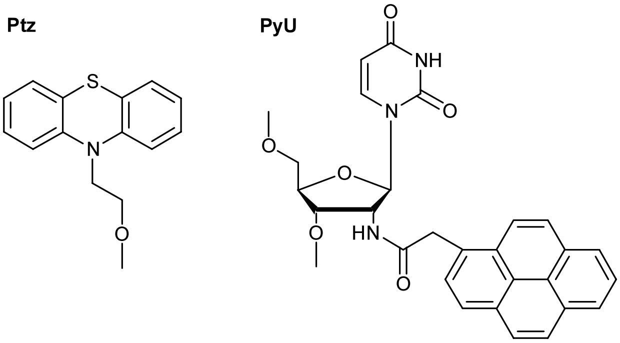
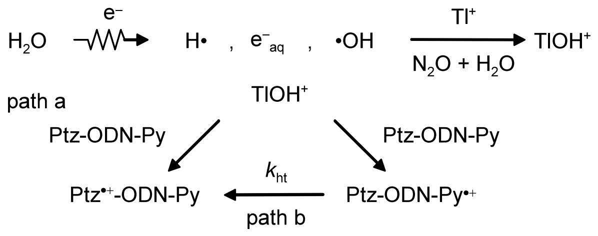


Figure 1. Chemical structures of phenothiazine attached at 5′-end (Ptz) and pyrene linked to the ribose 2′-site (PyU).



Scheme 1.

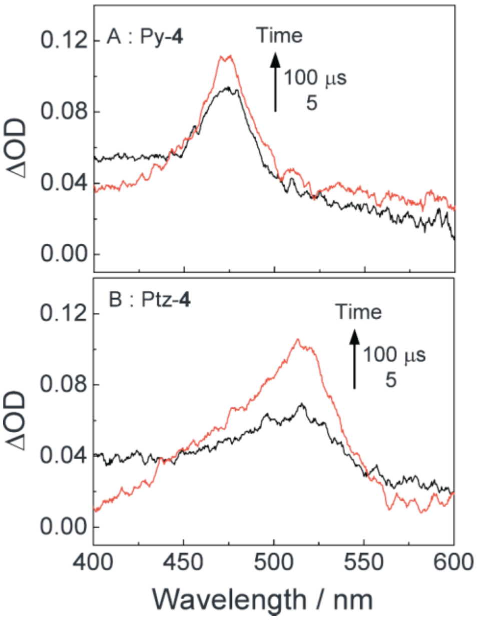


Figure 2. Transient absorption spectra of (A) Ptz-**4** and (B) Py-**4** obtained 5 and 100 μs in N_2O-saturated aqueous solution containing 0.2 mM ODN(strand conc.), 20 mM Na phosphate buffer (pH 7.0) and 2 mM Tl_2SO_4.

The pulse radiolysis of ODN conjugated with Py and Ptz (Ptz-**4** and Py-**4**) showed a transient absorption spectrum with a peak at 470 or 520 nm assigned to $Py^{\bullet+}$ or $Ptz^{\bullet+}$, respectively (Fig. 2). The formation rates of $Py^{\bullet+}$ and $Ptz^{\bullet+}$ obtained for Py-**1** and Ptz-**1** were almost identical to that of decay of $TlOH^+$ and no secondary formation was observed. These results indicate that hole migrates from G-region to Py or Ptz within the diffusional process.[13]

Transient absorption spectral changes and time profiles observed during pulse radiolysis of PtzPy-**n** are shown in Figure 3. When Ptz was separated from Py by three A-T base pairs (PtzPy-**1**), no formation of $Py^{\bullet+}$ was observed (Fig. 3A). Since oxidation of Ptz and Py by $TlOH^+$ occurs competitively,[14] the hole transfer from $Py^{\bullet+}$ to Ptz occurs faster than the diffusional oxidation of ODN by $TlOH^+$ at the rate constant of $k_{obs} = 10^5$ s^{-1} for PtzPy-**1**. On the other hand, when the distance between Py and Ptz was longer (PtzPy-**3**) with five A-T base pairs, formation and decay of $Py^{\bullet+}$ were observed in the time range of 0–100 μs after an electron pulse. At 100 μs only $Ptz^{\bullet+}$ was observed (Fig. 3B). This result indicates that hole migrates from $Py^{\bullet+}$ to Ptz within 100 μs. From the time profiles of absorption peaks at 470 nm for $Py^{\bullet+}$ and 520 nm for $Ptz^{\bullet+}$, secondary formation of $Ptz^{\bullet+}$ was also observed concomitant with the decay of $Py^{\bullet+}$ for PtzPy-**3**,[15] while no secondary formation of $Ptz^{\bullet+}$ was observed for PtzPy-**1** due to the rapid hole transfer (Fig. 3C, D). The rate constant of the hole

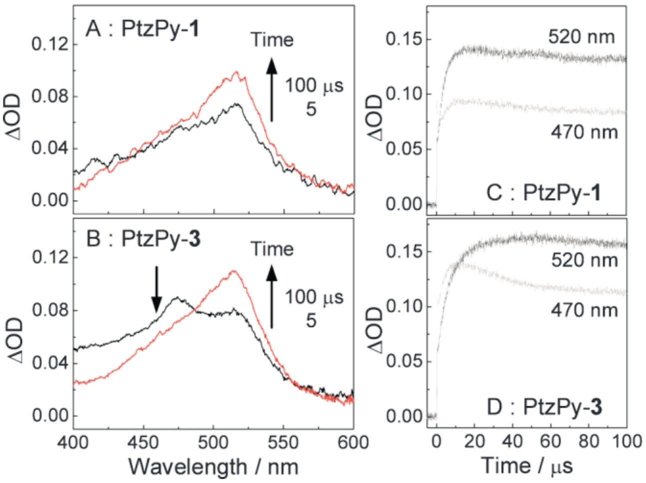


Figure 3. Transient absorption spectra observed at 5 and 100 μs after the electron pulse during pulse radiolyses of (A) PtzPy-**1** and (B) PtzPy-**3**. Time profiles of the transient absorption of Py$^{\bullet+}$ and Ptz$^{\bullet+}$ observed at 470 and 520 nm for (C) PtzPy-**1** and (D) PtzPy-**3**, respectively.

transfer from Py$^{\bullet+}$ to Ptz was determined to be 2.0×10^4 s^{-1} for PtzPy-**3** from the decay of Py$^{\bullet+}$. These results demonstrate that the hole transfer rate decreases with the increase of the distance between Py and Ptz (Scheme 1, path b).

Previously, we reported that the rate constants of the hole transfer from Py$^{\bullet+}$ to 8-oxo-7,8-dihydroguanine (oxG) ($E_{ox}=1.09$ V versus NHE in CH_3CN) were 3×10^4 s^{-1} for Py-TTT-oxG and smaller than 1×10^3 s^{-1} for Py-TTTTT-oxG.[6] Compared with the rate constant for Py-oxG-ODN, the hole transfer rates for PtzPy-**1** and PtzPy-**3** were much faster. This result is probably explained by difference of thermodynamic driving force (ΔG). The energy gap (ΔE) between Py and oxG is 0.31 eV, whereas ΔE between Py and Ptz is 0.64 eV. Namely, the lower oxidation potential of Ptz is considered to be responsible for the increase in the hole transfer rate.

Next, in order to elucidate effect of the sequence on the hole transfer rate, ODN containing G in the bridged base pairs between Py and Ptz was examined. Monitoring the decay of the transient absorption of Py$^{\bullet+}$ for PtzPy-**n** (**n**=**3**–**5**) in which Ptz and Py are separated by five base pairs, the hole transfer was accelerated slightly with increasing the number of G (Table 1). This result indicates that the hole transfer process from Py$^{\bullet+}$ to Ptz is mediated by G between Py and Ptz, indicating increases of the electronic coupling for the superexchange interaction. Similar results have been reported by Saito et al.[16] However, it may be possible to consider the contribution of G as a stepping stone for the hole transfer.[2c–e,5c]

In conclusion, the hole transfer rate between Py and Ptz was determined with the transient absorption measurements of Py$^{\bullet+}$ and Ptz$^{\bullet+}$, and it is shown that the hole transfer rate from Py$^{\bullet+}$ to Ptz depends on the distance and sequence between Ptz and Py. In other words, the hole transfer rate in DNA is modulated by designing the sequence of DNA and conjugated molecules. It is suggested that DNA may be utilized as a molecular wire by introducing several organic molecules at the appropriate positions in DNA.

Acknowledgements

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9. We examined the melting behavior of ODN conjugated with Ptz and Py. The T_m for PtzPy-**1** was 39.4°C, which was 6.9°C higher than that of unmodified ODN (32.5°C). Similarly, introduction of Ptz or Py into ODN showed increase (1.2°C) for Ptz-**1** and (6.6°C) for Py-**1** in T_m

compared with unmodified ODN. The structure of ODN conjugated with Py and Ptz was examined by circular dichroism (CD) spectrum in 20 mM phosphate buffer, which indicated the characteristic B-form.

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13. Considering lower oxidation potential of Py and Ptz compared to G, a hole generated in ODN migrates from G to Py or Ptz, and it is expected that this process occurred within several μs according to our previous reports (Ref. 6). Therefore, contribution of the hole transfer from G-region was almost ignored in the examined time region (>10 μs). As a result, a hole is trapped on Py and Ptz-site after completion of oxidant $TlOH^+$.
14. From the time profile of $Ptz^{\bullet+}$ for Ptz-**1** and $Py^{\bullet+}$ for Py-**1**, the rate constants of oxidation reaction with $TlOH^+$ were determined to be about 10^5 s^{-1}, indicating that competitive oxidation of Ptz and Py-moiety occurred.
15. When Ptz and Py were separately conjugated to different ODNs, both $Py^{\bullet+}$ and $Ptz^{\bullet+}$ were observed at 100 μs after the electron pulse during pulse radiolysis of the mixture of 0.2 mM each of Py and Ptz conjugated ODNs.
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