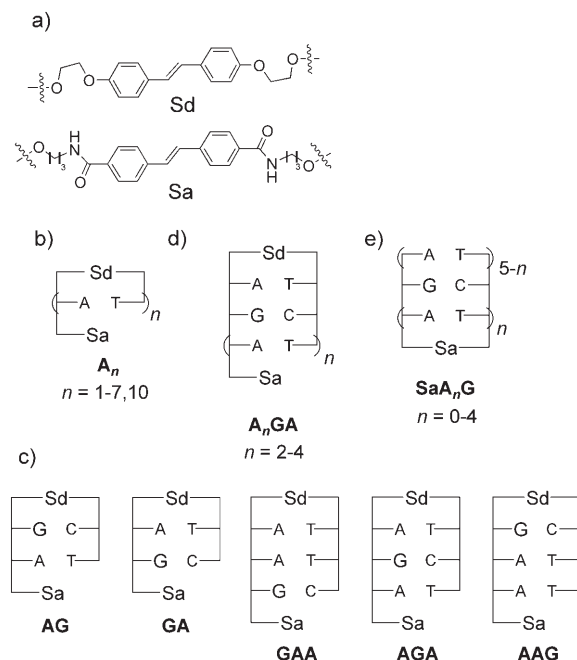


The Influence of Guanine on DNA Hole Transport Efficiency**

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Guanine plays a central role in studies of charge transfer and oxidative strand cleavage in duplex DNA.^[1,2] It is the most readily oxidized of the nucleobases and thus positive charges (holes) reside preferentially on guanine. The initial studies of DNA charge transfer dynamics by ourselves and others employed guanine or its analog deazaguanine as the hole acceptor.^[3–7] The dynamics of forward and return hole transport in these systems were inferred from the kinetic behavior of the excited state hole donor. Studies based on oxidative strand cleavage at G, GG, and GGG sites provided the initial evidence for long-range charge transport in DNA.^[8–13] Unfortunately, the efficiency of hole transport was not readily determined in these systems because the guanine cation radical is difficult to detect spectroscopically and oxidative strand cleavage is inherently slow and inefficient.

We recently described procedures for determining both the efficiency and dynamics of charge separation between a stilbenedicarboxamide electron acceptor (Sa) and a stilbene-diether electron donor (Sd) separated by a variable number of A–T base pairs in capped hairpins (Scheme 1a,b).^[14–17] Charge separation in these hairpins occurs via a multistep hole hopping mechanism when Sa and Sd are separated by two or more base pairs. The mechanism consists of hole injection from ¹Sa* to the adjacent A followed by hole migration and hole trapping by Sd. Replacement of poly(A) sequences with alternating AT base sequences results in a marked decrease in both the rate constant and efficiency of hole transport for short Sa–Sd distances.^[17] We report here the effect of a single G–C base pair on the efficiency and dynamics of photoinduced charge separation in synthetic DNA capped hairpins in which a poly(A)–poly(T) base pair domain separates the electron acceptor Sa and electron donor Sd (Scheme 1c,d). Charge separation in G-containing hair-



Scheme 1. Structures of a) stilbenes Sa and Sd, b) Sa/Sd hairpins with A-tract base sequences, c) Sa/Sd hairpins with polypurine sequences, d) Sa/Sd hairpins with A_nGA sequences, and e) Sa hairpins with A_nGA_{n-5} sequences.

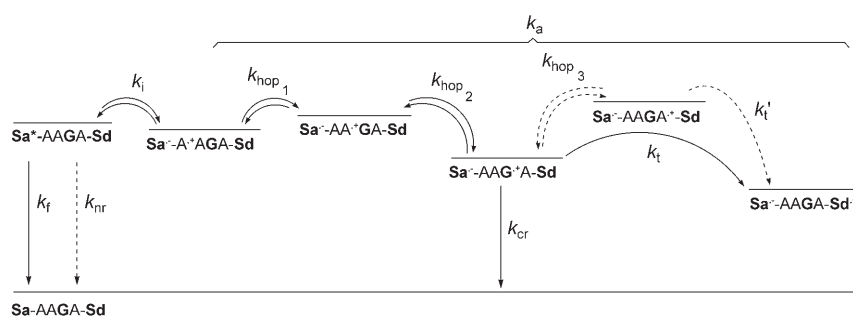
pins occurs via a hole hopping mechanism in which G serves as the primary hole acceptor and Sd as the hole trap, as shown in Scheme 2 for the sequence A_2GA (Scheme 1d). We find that the efficiency of hole arrival and trapping at Sd is dependent upon both the total length of the base pair domain and the base pair sequence. Location of G near Sa results in inefficient charge separation, whereas location three or four base pairs away from Sa can result in enhanced charge separation efficiency when compared to poly(A) analogs of the same length. These results establish that efficient photoinduced charge separation can be achieved over six or more base pairs by means of base sequence design.

The G-containing hairpins (Scheme 1c,d) were synthesized and characterized by the procedures used for the synthesis of the A_n hairpins (Scheme 1b).^[14–17] Femtosecond (fs) time resolved transient absorption spectra in aqueous solution were obtained using 350 nm excitation (providing selective excitation of Sa) from a Ti-sapphire based system having a time resolution of ca. 180 fs, a spectral range of 425–850 nm, and a time window of 0–6 ns.^[16] Typical transient spectra are shown in Figure 1 for hairpin **AGA**. Laser excitation initially yields a single band with a maximum at 575 nm attributed to the locally excited ¹Sa* singlet state. For

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Scheme 2. Kinetic scheme for charge separation in hairpin **A₂GA**.

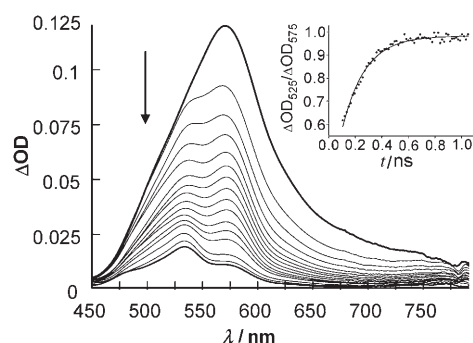


Figure 1. Pump-probe transient absorption spectra of **AGA** in the time range of 4.0 ps to 1.0 ns after excitation at 350 nm. The arrow indicates time-dependent decrease in intensity. Inset shows rise in the 525/575 nm band intensity ratio.

sequences containing three or more base pairs, the initial growth of a 525 nm shoulder over 50–100 ps results from the formation of Sa^- (Scheme 2), which has a 525/575 nm band intensity ratio of ca. 0.4 (neither A^{++} nor G^{++} has appreciable absorption in this wavelength region).^[15] Continued growth of the 525/575 nm band intensity ratio (inset in Figure 1) is attributed to formation of Sd^{++} which has an absorption maximum at 535 nm.

Plots of the time dependence of the 525/575 nm band intensity ratio have fast and slow components attributed to hole injection (τ_i) and hole arrival at Sd (τ_a), respectively (Scheme 2).^[15] In the case of hairpins having only one or two base pairs separating Sa and Sd, only one rising component of the 525/575 nm ratio is observed and is attributed to charge separation which may occur via either a single step superexchange or a multistep hole hopping mechanism. For hairpins possessing five or more base pairs the exponential growth in the band ratio resulting from hole arrival at Sd is too slow to be fully observed within the 0–6 ns time window of our fs experiments. The hole arrival times for these hairpins were thus determined using an initial slope method.^[16] Quantum yields for charge separation were estimated by comparing the integrated band intensities of the transient absorption spectra with those for **A₁** ($\Phi_{\text{cs}} = 1$). Values of τ_a and Φ_{cs} for the G-containing hairpins are reported in Table 1 along with previously reported values for the **A_n** hairpins.^[16]

The quantum yields for charge separation and the hole arrival times at Sd have been determined for all possible di- and trinucleotide sequences containing a single G (Table 1).

Location of G adjacent to Sd results in little or no change in Φ_{cs} and in a decrease in τ_a for sequences **AG** vs. **AA** and **AAG** vs. **AAA**. However, there is a marked decrease in Φ_{cs} when G is adjacent to Sa in sequences **GA** and **GAA** and a smaller decrease when G is located in the middle of the **AGA** sequence. The effect of a G:C base pair on the behavior of longer base pair sequences has been investigated for the **A_nGA** sequences ($n = 0$ to 4). Rate constants for hole arrival ($k_a = \tau_a^{-1}$) and values of Φ_{cs} for this series are shown in Figure 2 along with our data for the **A_n**

Table 1: Quantum yields for charge separation and hole arrival times for Sa-Sd hairpins.^[a]

base sequence	$\Phi_{\text{cs}}^{[b]}$	τ_a [ps] ^[c]	base sequence	$\Phi_{\text{cs}}^{[b]}$	τ_a [ns] ^[c]
A₁	1.0	5 ± 1	A₄	0.23 ± 0.01	1.3 ± 0.3
A₂	0.8 ± 0.2	39 ± 3	A₂GA	0.29 ± 0.9	0.45 ± 0.04
AG	0.7 ± 0.1	32 ± 6	A₅	0.10 ± 0.05	4.5 ± 1.5
GA	0.2 ± 0.1	80 ± 20	A₃GA	0.3 ± 0.1	1.0 ± 0.1
A₃	0.52 ± 0.08	250 ± 30	A₆	0.09 ± 0.03	9.0 ± 4
AAG	0.52 ± 0.02	120 ± 10	A₄GA	0.12	5.9 ± 0.1
AGA	0.16 ± 0.05	190 ± 20	A₇	0.06 ± 0.03	12 ± 4
GAA	0.07 ± 0.03	210 ± 70			

[a] Data in aqueous solution (standard buffer). [b] Estimated quantum yields and errors for hole trapping obtained from multiple measurements. [c] Hole arrival time ($\tau_a = k_a^{-1}$) and errors obtained from single exponential fits to the main rise of the 525/575 nm ratio curve for multiple measurements.

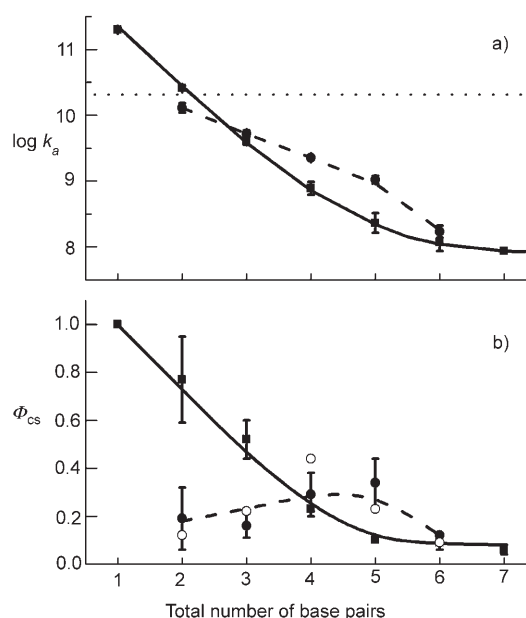


Figure 2. Rate constants for hole arrival (a), and charge separation quantum yields (b) for **A_n** ($n = 1-7$, ■) and **A_nGA** ($n = 0-4$, ●). In (a), the rate constant for hole injection into the A-trait is displayed with a horizontal dashed line. In (b), the calculated values for Φ_{cs} in **A_nGA** hairpins (see text) are displayed with open symbols.

series. For some donor–acceptor distances, the k_a values are actually larger for the A_nGA series than for the A_n series, the largest advantage being observed for the pentanucleotide A_3GA vs. A_5 (Figure 2a).

Values of Φ_{cs} increase with n for the A_nGA sequences for $n=0$ to $n=3$, reaching a maximum value of ca. 0.3 for the tetra- and pentanucleotides and then decrease for the longer polypurine sequences (Figure 2b). To our knowledge the values of $\Phi_{cs}=0.3\pm0.1$ for A_2GA and A_3GA are the largest reported to date for photoinduced charge separation over four or more base pairs, regardless of the acceptor and base sequence.^[18] We also investigated hairpins having the base sequence $AAA(GA)_n$ ($n=2$ and 3) but were unable to detect the occurrence of charge separation ($\Phi_{cs}<0.05$) on the 6 ns time scale or our measurements, presumably because of the lower overall efficiency for multiple hops. Schuster and co-workers have reported that oxidative strand cleavage efficiency in $(A_nGG)_n$ poly(purine) sequences is weakly distance-dependent and that charge migration is therefore rapid on the time scale of the chemical processes leading to strand cleavage,^[10] which is much slower than the time scale of our measurements.

The base sequence dependence of Φ_{cs} for the A_nGA hairpins can be understood in terms of the mechanism shown in Scheme 2. Assuming that hole trapping by Sd is permanent on the ns time scale of our measurements, the quantum yield of hole transport in the A_nGA hairpins can be described by Equation (1), where Φ_G and Φ_t are the efficiencies of hole arrival at G and hole transport from G to Sd, respectively.

$$\Phi_{cs} = \Phi_G \Phi_t = \Phi_G [k_t / (k_t + k_{cr})] \quad (1)$$

Calculated values of Φ_{cs} for A_nGA obtained using our values for Φ_{cs} for $Sa-A_n-Sd$ systems, $k_t = 5 \times 10^9 \text{ s}^{-1}$ for AGA , and published values for k_{cr} in SaA_nG systems (Scheme 1e are included in Figure 2b and are in reasonable agreement with the experimental values.^[19] Values of Φ_{cs} for the A_nGA hairpins initially increase with increasing n because of the decrease in k_{cr} , but ultimately decrease because of decreasing Φ_G .

In summary, the efficiency of photoinduced charge separation between donor and acceptor chromophores separated by a poly(A) sequence containing a single G is sensitive to the location of G as well as the total length of the polypurine sequence. Location of G near the point of hole injection results in low Φ_{cs} values as a consequence of rapid charge recombination of the $Sa^+A_nG^+$ radical ion pair, a process that is strongly distance-dependent.^[20] The highest Φ_{cs} values are observed when G is located near or adjacent to the secondary hole acceptor Sd. The agreement between calculated and experimental values of Φ_{cs} [Eq. (1)] provides support for the stepwise mechanism shown in Scheme 2, in

which G serves as a temporary resting place or stopover in the overall charge separation process. It should be noted that hole migration processes which are slow and inefficient on the 0–6 ns time scale of our experiments may appear to be rapid on the much slower time scale of DNA strand cleavage.^[11,21]

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