Electron Transfer

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Hole Mobility in DNA A Tracts**

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A unique feature of electron transfer in duplex DNA is the ability of positive charge (holes) to migrate over long distances in poly(dA)–poly(dT) base pair domains,[1,2] known as A tracts.[3] "A hopping" has been observed in numerous studies of oxidative strand cleavage at GG and GGG sites.[4–6] Giese et al. reported that the relative efficiency of hole transport from an isolated oxidized G to a GGG hole trap separated by a variable number of A–T base pairs (bp) displayed a highly distinctive distance dependence.[7] The relative efficiency of hole transport was observed to be highly distance dependent at short distances (1–3 bp) but weakly distance dependent at longer distances (4–16 bp). This change was attributed to a change in mechanism from tunneling at short distances to multistep hole hopping at longer distances. Giese's report prompted numerous theoretical analyses[8–12] as well as experimental efforts to determine the rate constants for hole transport through A hopping.[13–15]

We report herein the kinetics and efficiency of photoinduced hole transport across A tracts consisting of 1–7 bp in DNA hairpin conjugates, as determined by femtosecond transient absorption spectroscopy measurements. The values for these parameters are strongly distance dependent over the first 4 bp, but are relatively insensitive to distance from 5–7 bp. Hole arrival times roughly parallel the relative strand-cleavage efficiencies reported by Giese et al.[7] Competition of hole trapping with charge return of the hole while in the A tract results in low quantum yields for hole trapping in the longer base-pair domains.

We have previously investigated the dynamics of charge separation in DNA-hairpin conjugates with a stilbenedicarboxamide (**Sa**) capping group and a stilbenediether (**Sd**) hairpin linker separated by 1–4 A–T base pairs (Scheme 1).[16,17] Selective excitation of the **Sa** capping group at 350–355 nm permits observation of the decay of

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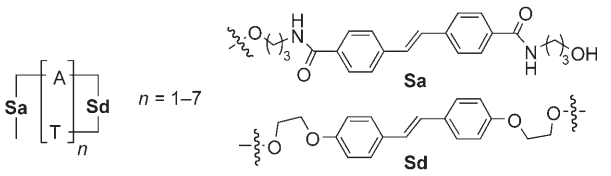
Supporting information for this article including transient absorption spectra for conjugates **3**, **4**, **6**, and **7** is available on the WWW under http://www.angewandte.org or from the author.



Scheme 1. Condensed structures for the hairpins **1**–**7**, **Sa**, and **Sd**.

^{1}**Sa*** (both fluorescence and stimulated emission with a 385-nm band maximum), and the formation of **Sa**$^{-\bullet}$ (575-nm band maximum) and **Sd**$^{+\bullet}$ (525-nm band maximum). Hole arrival times for **1**–**4** were estimated from the rise in the band ratio at 525/575 nm.[17] In the cases of **1** and **2**, decay of **Sa*** and formation of **Sd**$^{+\bullet}$ occur simultaneously, leading to the conclusion that charge separation occurs through a single-step tunneling process. In the cases of **3** and **4**, the hole arrival times are slower than the fast component of **Sa*** decay (≈40 ps) attributed to hole injection, in accord with a hole-hopping mechanism for charge separation. Hole arrival times for **5**–**7** were too long for measurement by femtosecond transient spectroscopy (2-ns time window) and too short for measurement by nanosecond transient spectroscopy (≈20-ns time resolution).[17]

We have now determined the hole arrival times for conjugates **3**–**7** from the rise of the 525/575-nm band ratio obtained from transient absorption spectra recorded with a time window of 0–6 ns. Transient spectra obtained at several delay times are shown in Figure 1 for **5** and in the Supporting Information for the other hairpins. Plots of the time-dependent 525/575-nm single wavelength intensity ratios for **1**–**7** are shown in Figure 2. The curved lines for **3**–**5** are fit to first-order kinetics by using data obtained following the initial rise in the 525/575-nm intensity ratio (≈100 ps), which occurs upon hole injection.[17] The rate constants for hole arrival (k_a) and hole arrival times ($\tau_a = k_a^{-1}$) obtained from these fits are reported in Table 1. The straight lines for **6** and **7** are the initial slopes for the rise in the 525/575-nm ratio (0.2–2.0 ns).[18] Comparison of these slopes with that for **5** provides values of k_a and τ_a for **6** and **7**. The values of τ_a = 7–12 ns for **5**–**7** are consistent with earlier estimates, which were based on the failure to observe hole arrival on longer time scales.[13–15,17]

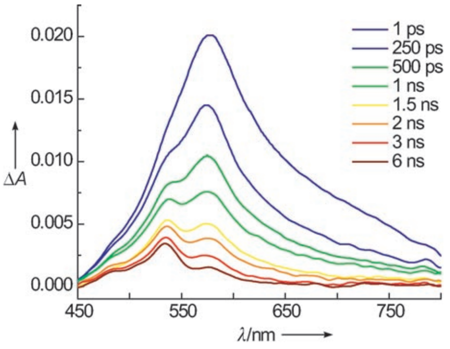


Figure 1. Transient absorption spectra of **5** at delay times of 1 ps (Δ*A*/2.5) to 6.0 ns following fs laser excitation at 350 nm.

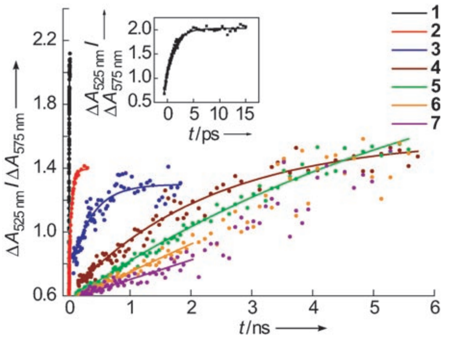


Figure 2. Time-dependent 525/575-nm band intensity ratios for **1**–**7** (data for **1** and **2** from reference [17]). The curved lines for **3**–**5** are single exponential fits to the data obtained following the initial fast rise attributed to hole injection (≈100 ps). The straight lines for **6** and **7** are linear fits to the 0.2–2.0-ns data.

Table 1: Quantum yields of hole trapping, hole arrival rate constants, and hole arrival times for charge transfer in **Sa/Sd** hairpins.

hairpin	Φ_t[a]	$k_a \times 10^{-9}$ [s^{-1}][b]	τ_a [ns][c]
1	1.0 ± 0.1	580[d]	0.0017[d]
2	1.0 ± 0.1	27[d]	0.036[d]
3	0.6 ± 0.1	2.9 ± 0.3 (3.4[d])	0.34
4	0.3 ± 0.1	0.43 ± 0.03	2.3
5	0.3 ± 0.1	0.15 ± 0.02	6.7
6	0.2 ± 0.1	0.12 ± 0.03	8.3
7	0.2 ± 0.1	0.08 ± 0.03	12

[a] Estimated quantum yields and errors for hole trapping (see text). [b] Rate constants for hole arrival and errors obtained from single exponential fits to the data for **1**–**5** and initial rates for **6** and **7** in Figure 2. [c] Hole arrival time $\tau_a = k_a^{-1}$. [d] Data from reference [17].

A plot of the distance dependence of the hole arrival rate constants for **1**–**7** is shown in Figure 3 along with Giese's plot for relative hole-transport efficiencies from G to GGG.[7] The parallel between our kinetic data and Giese's data for strand cleavage data may be fortuitous as hole injection is most likely to be the rate-determining step in Giese's study,[7] whereas hole transport is the rate-determining step for conjugates **3**–**7**.

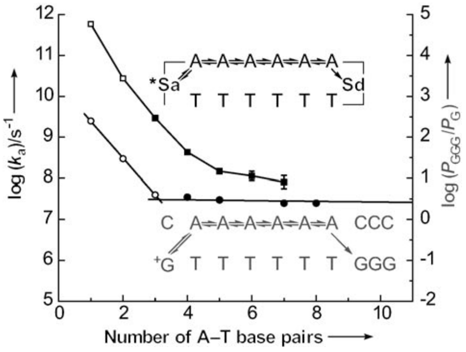
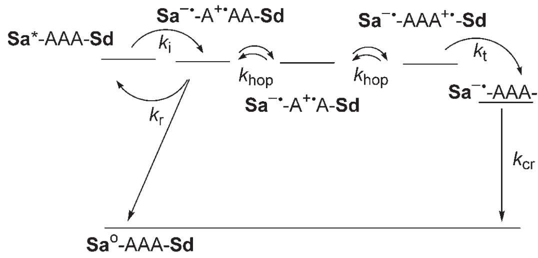


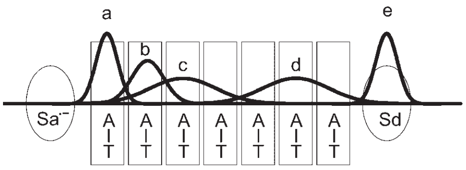
Figure 3. Rate constants for hole arrival in hairpins **1**–**7** (data from Table 1) and relative efficiencies of strand cleavage at G versus GGG (data from reference [7]). Open symbols for tunneling and filled symbols for hopping mechanisms. Our kinetic results (□, ■) parallel the DNA-strand-cleavage results of Giese et al. (○, ●).Error bars for **3**–**5** are smaller than the symbols.

Quantum yields (Φ_t) for hole trapping by **Sd** can be estimated from a comparison of the integrated area of the transient spectra at approximately 1.0 ps and after the 525/575-nm band ratio approaches its maximum value. A value of $\Phi_t \approx 1.0$ for **1** and **2** is assumed on the basis of their fast hole arrival times and absence of significant **Sa** fluorescence.[17] The values of Φ_t reported in Table 1 decrease rapidly for 2–4 bp and more gradually for 5–7 bp. The values of Φ_t for **4**–**7** are larger than those reported by Takada et al. for A-tract hole transport between a different donor–acceptor pair.[14,15]

The photoinduced charge-separation process for **3**–**7** can be described in terms of hole transport through either a localized hole-hopping model,[8] as shown in Scheme 2 for **3**, or through a delocalized hole model, as shown in Scheme 3 for **7**. In both models, hole injection (k_i) and hole trapping (k_t) are assumed to be faster than hole transport,[17] and hole transport is the rate-determining step for the hole arrival process. Hole trapping results in the formation of relatively long-lived **Sa**$^{-\bullet}$/**Sd**$^{+\bullet}$ charge-separated states, which decay through charge recombination (k_{cr}). Charge recombination of **Sa**$^{-\bullet}$/**Sd**$^{+\bullet}$ is slower than hole arrival for **3**–**7**[17] and thus does not significantly affect the efficiency of hole trapping (Φ_t). Recombination of the hole in the A tract with **Sa**$^{-\bullet}$ (k_r) does compete with hole trapping and results in formation of both the ground and excited states of **Sa**.[17] The low values of Φ_t for **4**–**7** are attributed to the competition of hole arrival with **Sa**$^{-\bullet}$/**A**$^{+\bullet}$ charge recombination (Scheme 2). In the case of **6** and **7**, the value of $\Phi_t = 0.2$ indicates that $k_r \approx 4 k_a$. As the length of the A tract increases, hole arrival times at **Sd** become slower and less efficient. Beyond 3 bp, values of Φ_t become essentially constant. Some charge return may still occur at these distances, however, the change in the value of Φ_t would be too small to measure.



Scheme 2. Simplified kinetic scheme for hole injection (k_i), hole hopping (k_{hop}), hole trapping (k_t), **Sa**$^{-\bullet}$/**A**$^{+\bullet}$ charge recombination (k_r), and **Sa**$^{-\bullet}$/**Sd**$^{+\bullet}$ charge recombination (k_{cr}) in hairpin **3**.



Scheme 3. Conceptualized hole transport in hairpin **7**: a) the **Sa**$^{-\bullet}$/**A**$^{+\bullet}$ contact radical ion pair, b) and c) hole delocalization, d) hole migration, and e) hole trapping on **Sd**.

The similar values of τ_a for **5**–**7** suggests that hole transport becomes weakly distance dependent at long distances. The differences in τ_a values for **5**–**7** provide an incremental value of approximately 2 ns per bp for a hole-hopping mechanism (Scheme 2), which may become shorter at even longer distances as the hole moves further away from **Sa**$^{-\bullet}$. This value is slower than the value of 50 ps per bp, which was estimated by Takada et al.[14] An estimated hopping rate of approximately $10^9\,s^{-1}$ can be used to calculate a value of $4 \times 10^{-5}\,cm^2\,V^{-1}\,s^{-1}$ for A-tract hole mobility, μ, from the relation $\mu = (e/kT)w\delta^2$, where e is the charge, w the hopping rate, and δ the distance between base pairs (3.4 Å).[19] This value is distinctly smaller than values of μ for discotic liquid crystals of planar aromatics such as triphenylene, which has a value of $\mu \approx 0.1\,cm^2\,V^{-1}\,s^{-1}$.[20,21] This value is also smaller than the values calculated for hypothetical poly(dG)–poly(dC) oligomers, even when corrected for static disorder.[22]

The hole-transport model shown in Scheme 3 is based upon several theoretical models that have been developed to explain Giese's results.[7] Berlin et al. have described A-tract hole migration as a motion in the tight-binding band.[9] Conwell has advanced a polaron model in which the hole is delocalized over 3–5 adenine molecules,[12,23] and an ion-gated polaron-like hole-transport model has been proposed by Schuster, Landman, and co-workers.[24] Renger and Marcus proposed a delocalized state model in which the splitting between bridge states increases as the bridge becomes longer.[11] The Conwell and Renger–Marcus models are consistent with our observation of a more-pronounced decrease in the hole-transport rate for **3**–**5** than is present at longer distances, at which point transport of the delocalized hole becomes necessary. Both static and dynamic disorders are expected to reduce A-tract hole mobility.[11,22] Basko and Conwell have considered the effects of solvent and counterions on hole mobility in DNA.[25] Their value of $\tau = 0.65$ ns calculated through Debye–Hückel screening by counterions is consistent with our estimate of the effective hole-transport rate per base pair.

In summary, we have determined the hole arrival times and efficiencies for a family of DNA conjugates with donor and acceptor stilbenes at the ends of A tracts consisting of 1–7 base pairs. The hole arrival times provide an estimated value for the A-tract hole mobility that is significantly lower than the values for columnar π-stacked discotic materials.[21] The low hole mobilities plausibly result from a combination of weak coupling, static and dynamic disorder, and solvent and ion gating. Although our estimated value for the hole mobility is lower than previous estimates, it is still significantly faster than strand cleavage at G-containing sites.[4] The relatively low hole mobility and rapid charge return in our system result in low hole-trapping efficiencies in longer A tracts.

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