J|A|C|S
COMMUNICATIONS

Dynamics of Inter- and Intrastrand Hole Transport in DNA Hairpins

Frederick D. Lewis,* Xiaobing Zuo, Jianqin Liu, Ryan T. Hayes, and Michael R. Wasielewski*

Department of Chemistry, Northwestern University, Evanston, Illinois 60208-3113

Received December 17, 2001

The migration of positive charge (holes) can occur over long distances in DNA.[1−4] Hole migration is of current interest both as it relates to oxidative strand cleavage in DNA[5] and in the development of molecular electronic devices.[6] Experimental evidence for long-distance hole migration is based on strand cleavage studies in duplexes that possess multiple guanine-containing sites. Strand cleavage occurs selectively at guanine, particularly at sites containing GG or GGG sequences. Preferential cleavage at GG or GGG has been attributed to hole trapping at these sites.[7] Several theoretical models have been proposed to account for these experimental observations.[8,9] The most widely employed is a hole-hopping model in which holes migrate between G (or GG, GGG) sites more rapidly than they react with water, which ultimately leads to strand cleavage. The dynamics of hole transport between G-containing sites in DNA are expected to be dependent upon the number of base pairs separating the hole donor and acceptor, the identity of the intervening bases (A vs T), and the location of the sites in either the same strand or complementary strands. Previous reports indicate that rate constants for hole transport from $G^{+\bullet}$ to hole donors across short (T:A) bridges decrease ca. 10-fold for each additional T:A base pair[2,10] and that transport is more rapid via polyA versus polyT sequences.[11] We report here the kinetic penalties for reversible hole transport from $G^{+\bullet}$ to GG across AA versus A, across T versus A, and for inter- versus intrastrand transport.

We have employed transient absorption spectroscopy with kinetic modeling to obtain rate constants for reversible intrastrand hole transport between a G primary donor and GG (or GGG) secondary donor (Figure 1) in synthetic DNA hairpins possessing a stilbenedicarboxamide (Sa) acceptor (Figure 2).[12] Data for the hairpins **1a** and **1b** are summarized in Table 1. Decay of ^{1}Sa* is attributed to charge separation ($\tau_s{}^{-1} = k_{cs}$), which occurs with similar rates for **1a** and **1b**. The single-exponential decay of $Sa^{-\cdot}$ for **1a** is attributed to charge recombination ($\tau_a{}^{-1} = k_{cr}$). The decay of $Sa^{-\bullet}$ for **1b** is dual exponential, the fast component being attributed to the occurrence of both charge recombination with the primary G donor and charge transport to the secondary donor and the slow component to recombination with the secondary donor. The rate constants k_{cr}, k_t, and k_{-t} are obtained from nonlinear fitting of the experimental data to the kinetic model in Figure 1 (see Supporting Information). Charge recombination of the primary ion pair formed from **1b** (k_{cs}) is more rapid than hole transport from $G^{+\bullet}$ to GG (k_t), thus accounting for the low amplitude of the longer-lived ns decay component. Attempts to observe hole transport between $G^{+\bullet}$ and GG in **1c** were unsuccessful. Presumably, charge recombination is more rapid than hole transport in this hairpin. This led us to investigate the dynamics of hole transport in hairpins in which charge recombination is slower than that for **1a,b** by virtue of a longer distance between the Sa acceptor and the primary G hole donor.[13]

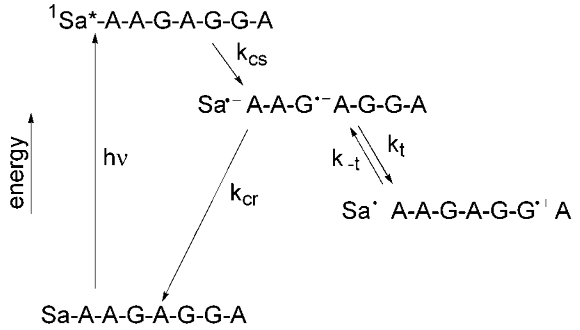

Figure 1. Kinetic scheme for charge separation (k_{cs}) and charge recombination (k_{cr}) in hairpin **1b** which can also undergo reversible hole transport from $G^{+\bullet}$ to GG (k_t and k_{-t}). Only the G-containing arm of the hairpin is shown.

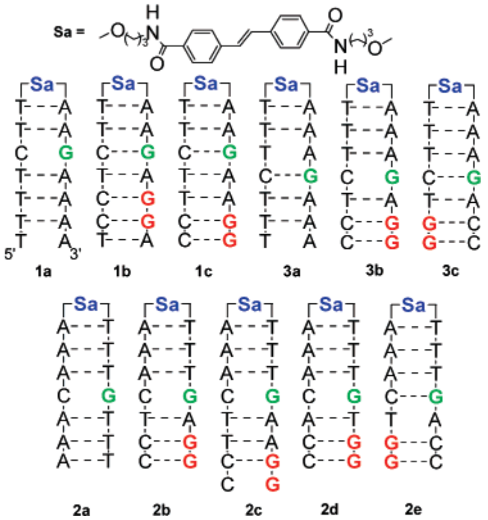

Figure 2. Structures of synthetic DNA hairpins.

The hairpins **2a** and **3a** possess a single 3′-G separated from Sa by a TTT or AAA sequence, respectively. Both have significantly longer ^{1}Sa* decay times (τ_s) and $Sa^{-\bullet}$ anion radical decay times (τ_a) than does **1a**, indicative of slower charge separation and charge recombination (Table 1). Both charge separation and charge recombination are slower for **2a** than for **3a**, in accord with our previous studies of superexchange electron transfer via polyT versus polyA sequences in Sa-linked DNA hairpins.[13] The hairpins **2b−d** and **3b** were designed to probe the dynamics of intrastrand hole transport between $G^{+\bullet}$ and GG sites, whereas hairpins **2e** and **3c** were designed to probe interstrand hole transport. The ^{1}Sa* decay times (Table 1) of **2b−e** and **3b,c** are similar to those of **2a** and **3a**, respectively, as expected for superexchange charge separation

---

* To whom correspondence should be addressed. E-mail: lewis@chem.northwestern.edu.

10.1021/ja0177859 CCC: $22.00 © 2002 American Chemical Society

Table 1. Transient Decay Times and Rate Constants for Hole Transport

hairpin[a]	τ_s,ns[b]	$\tau_{a,}$ ns[c]	$10^{-7}k_{cr}$, s^{-1} [d]	$10^{-7}k_t$, s^{-1} [d]	$10^{-7}k_{-t}$, s^{-1} [d]
1a[e]	0.031	1.9	53		
1b[e]	0.039	1.5 (77), 170 (23)	60	5.6	0.75
2a	(0.93)	250	0.40		
2b	(1.1)	60 (9), 790 (91)	0.40	0.84	0.54
2c	(1.0)	220 (88), 3600 (12)	0.38	0.04	<0.08
2d	(1.1)	240 (88), 1200 (12)	0.41	0.02	<0.04
2e	(1.1)	223 (82), 4800 (18)	0.29	0.10	<0.03
3a	0.46 (0.60)	57	1.8		
3b	0.61 (0.61)	29 (34), 233 (66)	1.5	1.3	0.90
3c	(0.67)	53 (84), 3200 (16)	1.6	0.21	<0.04

[a] See Figure 2 for hairpin structures. [b] Stilbene singlet decay time as determined by transient absorption or fluorescence decay (values in parentheses). [c] Stilbene anion radical decay time(s) determined by transient absorption (relative amplitude of kinetic components, %). [d] Rate constants for charge recombination (k_{cr}), hole transport (k_t), and return transport (k_{-t}) obtained from kinetic modeling. [e] Data from ref 12.

involving the same donor−bridge−acceptor sequence. The $Sa^{-\bullet}$ decay times (Table 1) for **2b**−**e** and **3b,c** are biexponential. Their fast components decay more rapidly and their slow components more slowly than those of **2a** or **3a**, respectively, in accord with the occurrence of reversible hole transport between $G^{+\bullet}$ and GG sites (Figure 1).[12] The amplitudes of the slow components of **2b** and **3b** are larger than those for **1b**, indicative of more efficient hole transport for the former hairpins. The amplitudes of the slow components of **2c**−**2e** and **3c** are smaller than those for **2b** and **3b**, respectively. This is indicative of slower hole transport via AA or T versus a single A and slower inter- versus intrastrand hole transport.

Nonlinear fitting of the $Sa^{-\bullet}$ decay data for **2b**−**e** and **3b,c** using the analytical solution for the kinetic model in Figure 1[12] provides the rate constants reported in Table 1. The values of k_{cr} for **2b**−**e** and **3b,c** are similar to those for **2a** and **3a**, respectively, as expected for charge recombination involving the same base sequence. The values of k_t are smaller for **2b** and **3b** than for **1b**, as are the values of k_t/k_{-t} which provide the equilibrium constants for hole transport from G to GG ($K = 7.5$ for **1b** vs 1.5 for **2b** and **3b**). We attribute these differences to the diminished stability of a terminal versus internal GG. In the case of **2c**−**e** and **3c** the slow $Sa^{-\bullet}$ decay component is sufficiently long that alternate decay pathways (e.g., reduction of $Sa^{-\bullet}$ by residual oxygen or by neighboring T or C bases) may compete with k_{-t}. Since the values of k_{-t} in Table 1 provide upper bounds for these hairpins, our analysis will rely on values of k_t rather than k_{-t}.

Comparison of the values of k_t for **2b** versus **2c** indicates that hole transport from $G^{+\bullet}$ to GG via an AA sequence is ca. 20 ± 7 times slower than that via a single A base. This kinetic penalty is similar to the values observed in several previous studies using diverse hole donors and acceptors.[2,10,11] In view of the errors inherent in these measurements, which employ highly different methodology (laser photolysis−transient absorption, strand cleavage, and pulse radiolysis−transient absorption), their agreement is satisfying.

Comparison of the values of k_t for **2b** versus **2d** indicates that hole transport from $G^{+\bullet}$ to GG via a single T is ca. 40 ± 15 times slower than via an A base. A large kinetic penalty has also been reported by Shafirovich et al.[11] for hole transport via a T_4 versus A_4 sequence. We previously observed more similar rate constants for charge separation reactions of singlet Sa with G when located in a polyT versus polyA strand (e.g., **2a** vs **3a**).[13] However, the charge-separation process (Figure 1a) is more exergonic than hole transport (Figure 1b) and involves neutral reactants. Thus, the injection energy and solvent reorganization energy for a superexchange electron-transfer reaction may be considerably smaller for the former process. The charge-separation process in **2a** may also follow an interstrand pathway which has a much smaller kinetic penalty (vide infra).

Comparison of the values of k_t for either **2b** versus **2e** or **3b** versus **3c** indicates that interstrand hole transport from $G^{+\bullet}$ to GG via a single T:A base pair is ca. 7 ± 3 times slower than the intrastrand process. This value is considerably smaller than the kinetic penalty of 10^3 estimated by Barton[4] on the basis of strand cleavage data. However, analysis of these data by Bixon and Jortner[9] provides a penalty of ca. 30 for interstrand hole transport from $G^{+\bullet}$ to G across a single A:T base pair. A somewhat smaller value might be expected for our system, in which the hole transport is more exergonic. A relatively small penalty is consistent with the observation in strand cleavage studies of efficient long-range hole migration via a zigzag pathway involving multiple interstrand hops.[2]

In summary, kinetic modeling of the transient absorption data for the hairpin families **2a**−**e** and **3a**−**c** has provided estimates of the kinetic penalties for hole transport from $G^{+\bullet}$ to GG in several different duplex structures. It should be emphasized that our kinetic data applies to short hopping steps which are presumed to occur via a superexchange mechanism and cannot be extrapolated to longer hopping steps for which alternative mechanisms may be operative.[3,9] Moreover, in the absence of hole trapping or fast chemical reactions leading to strand cleavage, kinetic penalties of the magnitude reported herein should not diminish the efficiency of long-distance multistep hole-transport process in DNA.

Acknowledgment. This research is supported by grants from the Division of Chemical Sciences, Office of Basic Energy Sciences, U.S. Department of Energy under Contracts DE-FG02-96ER14604 (F.D.L.) and by DE-FG02-99ER14999 (M.R.W.).

Supporting Information Available: Representative transient decay data, kinetic analysis, and error analysis (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Schuster, G. B. *Acc. Chem. Res.* **2000**, *33*, 253−260. (b) Núñez, M. E.; Hall, D. B.; Barton, J. K. *Chem. Biol.* **1999**, *6*, 85−97. (c) Nakatani, K.; Dohno, C.; Saito, I. *J. Am. Chem. Soc.* **2000**, *122*, 5893−5894.
(2) Giese, B. *Acc. Chem. Res.* **2000**, *33*, 631−636.
(3) Giese, B.; Amaudrut, J.; Köhler, A.-K.; Spormann, M.; Wessely, S. *Nature* **2001**, *412*, 318−320.
(4) Wagenknecht, H.-A.; Rajski, S. R.; Pasculay, M.; Stemp, E. D. A.; Barton, J. K. *J. Am. Chem. Soc.* **2001**, *123*, 4400−4407.
(5) Armitage, B. *Chem. Rev.* **1998**, *98*, 1171−1200.
(6) Porath, D.; Bezryadin, A.; de Vries, S.; Dekker: C. *Nature* **2000**, *403*, 635−638.
(7) Yoshioka, Y.; Kitagawa, Y.; Y., T.; Yamaguchi, K.; Nakamura, T.; Saito, I. *J. Am. Chem. Soc.* **1999**, *121*, 8712−8719.
(8) (a) Jortner, J.; Bixon, M.; Langenbacher, T.; Michel-Beyerle, M. E. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 12759−12765. (b) Bixon, M.; Giese, B.; Wessely, S.; Langenbacher, T.; Michel-Beyerle, M. E.; Jortner, J. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 11713−11716. (c) Voityuk, A. A.; Jortner, J.; Bixon, M.; Rösch, N. *J. Chem. Phys.* **2001**, *114*, 5614−5620. (d) Berlin, Y. A.; Burin, A. L.; Ratner, M. A. *J. Am. Chem. Soc.* **2001**, *123*, 260−268. (e) Grozema, F. C.; Berlin, Y. A.; Siebbeles, L. D. A. *J. Am. Chem. Soc.* **2000**, *122*, 10903−10909. (f) Conwell, E. M.; Basko, D. M. *J. Am. Chem. Soc.* **2001**, *123*, 11441−11445.
(9) Bixon, M.; Jortner, J. *J. Am. Chem. Soc.* **2001**, *123*, 12556−12567.
(10) (a) Kawai, K.; Takada, T.; Tojo, S.; Ichinose, N.; Majima, T. *J. Am. Chem. Soc.* **2001**, *123*, 12688−12689. (b) Lewis, F. D.; Liu, J.; Liu, X.; Zuo, X.; Hayes, R. T.; Wasielewski, M. R. *Angew. Chem., Int. Ed.* **2002**, *41*, 1026−1028.
(11) Shafirovich, V. Y.; Dourandin, A.; Huang, W.; Luneva, N. P.; Geacintov, N. E. *Phys. Chem. Chem. Phys.* **2000**, *2*, 4399−4408.
(12) (a) Lewis, F. D.; Liu, X.; Liu, J.; Miller, S. E.; Hayes, R. T.; Wasielewski, M. R. *Nature* **2000**, *406*, 51−53. (b) Lewis, F. D.; Liu, X.; Liu, J.; Hayes, R. T.; Wasielewski, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 12037−12038.
(13) Lewis, F. D.; Wu, T.; Liu, X.; Letsinger, R. L.; Greenfield, S. R.; Miller, S. E.; Wasielewski, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 2889−2902.

JA0177859