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Electron Mobility in a Mercury-mediated Duplex of Triazole-linked DNA (^{TL}DNA)

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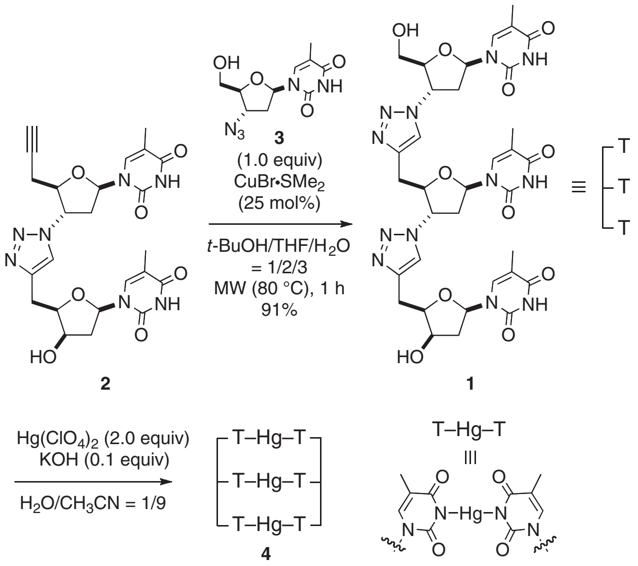
A metal-ion-mediated duplex of triazole-linked DNA (^{TL}DNA) was synthesized via thymine–mercury(II)–thymine (T–Hg–T) base pairing. The electron-transport properties of the mercury-mediated duplex deposited on a solid substrate were determined by time-resolved microwave conductivity (TRMC) measurements.

The DNA duplex, a helical combination of two strands with interior π stacks, has emerged as a unique molecular building block for nanoscale electronic devices since the discovery of charge migration through the π stacks.[1] The rich synthetic chemistry of DNA molecules also furnishes various tools to implement additional functions and properties in the duplex. Among the variants of DNA duplexes for electronic applications, a metal-ion-mediated duplex is especially attractive due to the presence of a one-dimensional metal array within the helical π stack.[2] One of the obstacles to its implementation, however, is the low thermal stability of the duplex, which may hamper deposition on a solid surface of a device. The instability mainly originates from the electrostatic repulsions between the negative charges on the phosphodiester linkage of each strand and, even in the solution phase, the duplex often requires a lengthy strand with additional natural nucleobase sequences attached to the metal-embedding core sequence to stabilize it.[2] We recently developed a new artificial DNA, ^{TL}DNA,[3] and envision that the neutral congener may provide an ideal platform for a stable metal array in the duplex. We herein report the synthesis of a mercury-mediated duplex of a short triazole-linked oligonucleotide and its electron-transport properties on a solid substrate.

We first synthesized the trimer oligothymine **1** using a copper-catalyzed Huisgen reaction.[3] An equimolar mixture of dimer **2** and azidothymidine **3** was irradiated with microwaves for 1 h to afford the desired trimer **1** in 91% yield (Scheme 1).

We then synthesized duplex **4**, utilizing the mercury-mediated pairing of thymines.[4] After screening several conditions, we found that the addition of a Brønsted base facilitated the duplex formation. The mercury-mediated duplex **4** was thus obtained by the reaction of the trimer **1** and $Hg(ClO_4)_2$ in the presence of KOH (Scheme 1), and the spectral analysis confirmed the formation of the duplex. Circular dichroism (CD) spectra showed a drastic change in the ellipticity around 240–300 nm upon the addition of mercury, indicating the formation of a helical complex (Figure 1). A titration experiment with CD measurements showed that the optimum ratio between mercury and thymine is 1:2, which confirms the mercury-mediated pairing of thymine nucleobases (T–Hg–T) (See also Figure S1[14]). The mass spectrum of **4** indicated the selective formation of the duplex, showing the duplex as the sole species (Figure 2).[5] Supporting the duplex structure, analysis



Scheme 1.

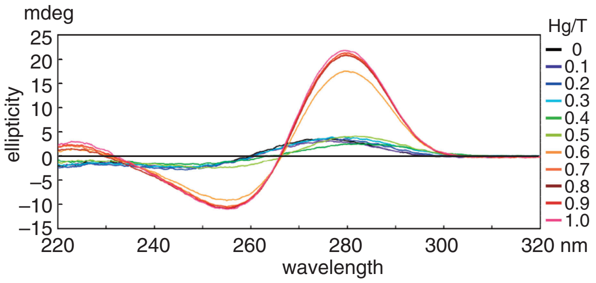


Figure 1. CD spectra of duplex **4** upon addition of mercury in 10% H_2O/CH_3CN at 20 °C. The ratio of Hg:T was varied from 0:1 to 1:1. See Figure S1[14] for the titration curve.

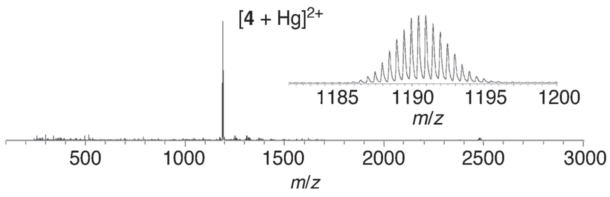


Figure 2. Mass spectrum of duplex **4** obtained by ESI-MS measurement of a solution in 10% H_2O/CH_3CN, showing the absence of other species. Upon ionization, the duplex **4** was detected as a divalent cation with an additional mercury(II) ion. Inset shows the expanded spectrum which confirms the structural identity as **4** + Hg(II).

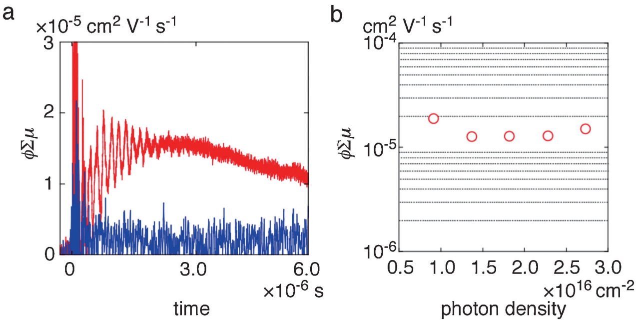


Figure 3. Conductivity transients of duplexes. (a) Transient conductivity ($\phi\Sigma\mu$) of the duplex **4** on a quartz substrate was observed under laser pulse excitation of 2.7×10^{16} photons/cm^2 at 355 nm (red). The conductivity of a mercury-mediated duplex of trimer natural oligothymines was negligible under the same conditions (blue). (b) The transient conductivity of duplex **4** at various excitation photon densities.

by NMR spectroscopy showed the symmetric environment of corresponding nucleosides in different strands (Figure S3[14]).[6]

Finally, we measured the mobility of charge carrier in the mercury-mediated duplex **4** on a solid surface using TRMC[7] and found that the duplex can function as an electron-transport material. Note that, despite the potential application as conducting materials,[2,8] the carrier transport in metal-ion-mediated duplexes has scarcely been investigated.[9] We thus deposited the mercury-mediated duplex **4** on a quartz substrate as a thin film by drop casting and measured the transient conductivity by laser pulse excitation at 355 nm. Figure 3 shows the time-dependent curves of transient conductivity $\phi\Sigma\mu$ where ϕ and $\Sigma\mu$ denote the quantum yield of photoinduced carrier generation and the sum of carrier mobilities, respectively. The maximum transient conductivity ($\phi\Sigma\mu$) measured 1.5×10^{-5} cm^2 V^{-1} s^{-1}, and the quantum yield ϕ was separately determined to be 1.1×10^{-3} by conventional direct-current integration on interdigitated electrodes under the same excitation conditions (Figure S5[14]). Under these conditions, the mobility of the carrier in the duplex **4** ($\Sigma\mu$) was determined to be 1.3×10^{-2} cm^2 V^{-1} s^{-1}, which is three times faster than that of natural base stacks.[7,10] Note that the negative charges on the natural duplex might also have affected the mobility.

Although we did not observe any change in the transient conductivity by exposing the film to air, the addition of SF_6 to the deposited duplex **4** completely quenched the transient conductivity (data not shown). The observation shows that, instead of holes that are characteristic for natural π stacks, electrons function as the predominant carrier in the mercury-mediated duplex. In addition, we did not observe any appreciable changes in $\phi\Sigma\mu$ upon varying the excitation photon density (Figure 3b) and confirmed that the effect of second-order bulk recombination processes is negligible. Considering the small absorbance of the film (ca. 0.04) and the quantum yield (1.1×10^{-3}), we can roughly estimate the charge-carrier (electron) density as ca. 10^{15} cm^{-3}. In the time region of the experiments, the carrier is free from the second-order bulk recombination and can be effectively scavenged by highly dielectric media such as SF_6. In contrast to the mercury-mediated duplex of the triazole-linked oligonucleotide, the mercury-mediated duplex of a natural trimer oligothymine[4] under the same conditions did not show the transient conductivity probably due to the disassembly of the duplex on the quartz substrate (Figure 3a).

In summary, we have synthesized a mercury-mediated duplex of triazole-linked oligothymines with a neutral backbone. The conductivity analysis of a thin film of the complex by TRMC revealed electron transport in the deposited duplex with a mobility of 1.3×10^{-2} cm^2 V^{-1} s^{-1}, which rivals that of solution-processed n-type organic semiconductors (0.001–0.2 cm^2 V^{-1} s^{-1}).[11] Note that the mobility data presented here are the first values ever reported for a metal-ion-mediated oligonucleotide duplex and may thus serve as a reference standard for their future development. Mixing the embedded metal arrays and natural base stacks bearing hole-transport ability[1,7] in a programmed sequence may allow the design of bipolar transistors or complementary circuits in a duplex. The present study also confirmed the theoretical prediction of the electron-transport properties of the T–Hg–T stacks through the effective LUMO overlaps in the mercury array[8] and further demonstrated the effective use of the artificial backbone for an air-stable electron-transporting duplex on a substrate. The combination of neutral backbones with interior modulation[2,12] and terminus click chemistry[3,13] may facilitate the fabrication of DNA devices in the future.

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References and Notes

1 J. C. Genereux, J. K. Barton, *Chem. Rev.* **2010**, *110*, 1642.
2 G. H. Clever, C. Kaul, T. Carell, *Angew. Chem., Int. Ed.* **2007**, *46*, 6226; J. Müller, *Eur. J. Inorg. Chem.* **2008**, 3749; G. H. Clever, M. Shionoya, *Coord. Chem. Rev.* **2010**, *254*, 2391.
3 H. Isobe, T. Fujino, N. Yamazaki, M. Guillot-Nieckowski, E. Nakamura, *Org. Lett.* **2008**, *10*, 3729; T. Fujino, N. Yamazaki, H. Isobe, *Tetrahedron Lett.* **2009**, *50*, 4101; T. Fujino, N. Tsunaka, M. Guillot-Nieckowski, W. Nakanishi, T. Iwamoto, E. Nakamura, H. Isobe, *Tetrahedron Lett.* **2010**, *51*, 2036.
4 Y. Miyake, H. Togashi, M. Tashiro, H. Yamaguchi, S. Oda, M. Kudo, Y. Tanaka, Y. Kondo, R. Sawa, T. Fujimoto, T. Machinami, A. Ono, *J. Am. Chem. Soc.* **2006**, *128*, 2172; Y. Tanaka, S. Oda, H. Yamaguchi, Y. Kondo, C. Kojima, A. Ono, *J. Am. Chem. Soc.* **2007**, *129*, 244.
5 A shorter triazole-linked oligothymine did not selectively give the duplex upon addition of mercury (Figure S2[14]), which shows that the trimer oligothymine has the minimal length for the mercury-mediated duplex.
6 Although the analysis confirmed the selective formation of mercury-mediated duplex, it could not give a conclusive identification to the relative orientation of the two strands (antiparallel vs. parallel).
7 R. Yamagami, K. Kobayashi, A. Saeki, S. Seki, S. Tagawa, *J. Am. Chem. Soc.* **2006**, *128*, 2212.
8 A. A. Voityuk, *J. Phys. Chem. B* **2006**, *110*, 21010.
9 As the theoretical study predicted (ref. 8), an experimental investigation on one T–Hg–T pair embedded in natural strands showed that the base pair does not accelerate the hole transport. See: J. Joseph, G. B. Schuster, *Org. Lett.* **2007**, *9*, 1843.
10 K. Kawai, T. Kimura, K. Kawabata, S. Tojo, T. Majima, *J. Phys. Chem. B* **2003**, *107*, 12838.
11 A. R. Murphy, J. M. J. Fréchet, *Chem. Rev.* **2007**, *107*, 1066.
12 E. T. Kool, *Acc. Chem. Res.* **2002**, *35*, 936; K. Kawai, H. Kodera, Y. Osakada, T. Majima, *Nat. Chem.* **2009**, *1*, 156.
13 L. Luo, C. D. Frisbie, *J. Am. Chem. Soc.* **2010**, *132*, 8854.
14 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.