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[12] Crystallographic data for **Vb**: $C_{24}F_{18}B_2 \cdot 2\,C_7H_8$; monoclinic, space group $P2_1/c$; $a = 22.855(2)$, $b = 10.865(1)$, $c = 13.750(1)$ Å, $\beta = 99.689(1)^\circ$, $V = 3366(1)$ Å^3, $Z = 4$; $\rho_{calcd} = 1.650\ \mathrm{g\,cm^{-3}}$; $\mu = 1.65\ \mathrm{cm^{-1}}$; $T = -120\,^\circ\mathrm{C}$. The structure was solved by direct methods. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in idealized positions and not refined. The final cycle of full-matrix least-squares refinement was based on 8069 observed reflections ($I > 2.00\sigma(I)$) and 523 variable parameters and converged (largest parameter shift was 0.087 times its esd) with unweighted and weighted agreement factors of $R = 0.042$ and $Rw = 0.118$. For clarity of the crystallographic discussion, note that there are two half molecules in the asymmetric unit, and consequently there are two independent bond lengths and angles for each bond length/angle of **Vb**. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-135514. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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Photocontrol of Triple-Helix Formation by Using Azobenzene-Bearing Oligo(thymidine)**

Hiroyuki Asanuma, Xingguo Liang, Takayuki Yoshida, Akira Yamazawa, and Makoto Komiyama*

Triple-helix formation by oligonucleotides is one of the most promising methods for sequence-specific recognition of DNA double helices.[1] Various applications (for example, regulation of gene expression and cell growth) have already been demonstrated.[2] However, little is known on the regulation of triple-helix formation by external signals. If triple helixes can be formed at will (as triggered by a signal), the scope of their applications would be extended.

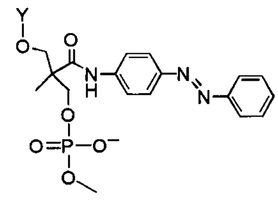
Previously, it was shown that intercalating agents stabilize triple helixes when tethered to oligonucleotides.[1b, d, h, 2a] Furthermore, formation of DNA double helices was regulated by photoisomerization of the azobenzene-tethered oligonucleotides.[3, 4] These findings have prompted us to study on photoregulation of triple-helix formation. Here, we show modified oligo(thymidine) (oligo(T)) species, which carry an azobenzene at the appropriate position, form stable triple helices with oligo(T)/oligo(dA) double helices (oligo(dA) = oligo(deoxyadenosine)). More importantly, these triple helices can be formed and dissociated repeatedly by photoinduced *cis-trans* isomerization of the azobenzene.

The double helix [**t/a**] is formed from two complementary 32-mer oligonucleotides, and involves a T_{14} and dA_{14} block (from the **t** and **a**, respectively) (Scheme 1).[5] Its melting temperature (T_m) is 73.0 °C at pH 7.0 ([$MgCl_2$] = 0.1 M; other conditions are presented in the Experimental Section). With addition of oligonucleotide $\mathbf{T_{13}}$ to the [**t/a**] double helix, the melting curve for the system is double-sigmoidal, corresponding to the formation of the [$\mathbf{T_{13}}$/**t/a**] triple helix ($T_m = 18.0\,^\circ$C). When the modified oligonucleotide $\mathbf{XT_{13}}$ is used in place of $\mathbf{T_{13}}$, a double-sigmoidal curve is also obtained (Figure 1). Here, the azobenzene mostly (90 %) takes its *trans*-form with respect to the stereochemistry of the N=N bond, as indicated by the reversed-phase HPLC analysis. The T_m for the [*trans*-$\mathbf{XT_{13}}$/**t/a**] triple helix is 26.0 °C. This T_m value is higher than that of either [$\mathbf{T_{13}}$/**t/a**] or [$\mathbf{T_{14}}$/**t/a**] triple helices (Table 1). The *trans*-azobenzene moiety stabilizes the triple helix, at least in this case, to a greater extent than thymine.

t: 5'-GCCACGAAATTTTTTTTTTTTTTAAACCGACG-3'
a: 3'-CGGTGCTTTAAAAAAAAAAAAAATTTGGCTGC-5'

$\mathbf{T_{11}}$: 5'-TTTTTTTTTTT-3'
$\mathbf{T_{12}}$: 5'-TTTTTTTTTTTT-3'
$\mathbf{XT_{11}}$: 5'-XTTTTTTTTTTT-3'
$\mathbf{TXT_{10}}$: 5'-TXTTTTTTTTTT-3'
$\mathbf{T_{13}}$: 5'-TTTTTTTTTTTTT-3'
$\mathbf{T_{14}}$: 5'-TTTTTTTTTTTTTT-3'
$\mathbf{XT_{13}}$: 5'-XTTTTTTTTTTTTT-3'

X =



(Y = H or phosphodiester linkage)

Scheme 1. The oligonucleotides used in this study; **X** denotes the residue carrying an azobenzene moiety in the side chain. The configuration of the N=N bond in **X** is noted.

Upon irradiating the [*trans*-$\mathbf{XT_{13}}$/**t/a**] solution with light ($300 < \lambda < 400$ nm), the azobenzene in $\mathbf{XT_{13}}$ isomerized to the *cis*-form. Concurrently, the melting curve for the [*cis*-$\mathbf{XT_{13}}$/**t/a**] triple helix (see Figure 1) notably shifts towards lower temperatures with respect to the [*trans*-$\mathbf{XT_{13}}$/**t/a**]

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Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

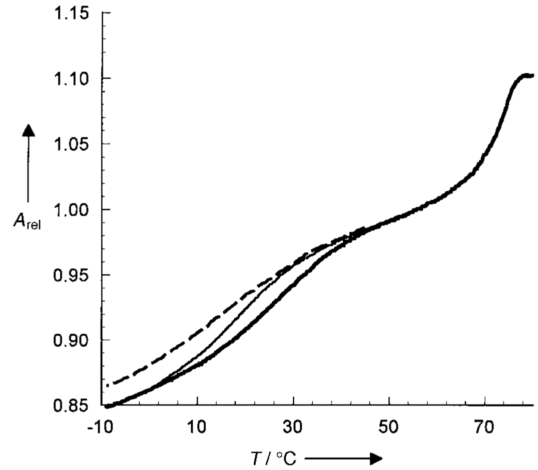

Figure 1. Melting curves (cooling profiles) for the triple-helix formation between the [**t**/**a**] double helix and *trans*-$\mathbf{XT}_{13}$ (——), *cis*-$\mathbf{XT}_{13}$ (- - - -), or $\mathbf{T}_{13}$ (——). The T_m values obtained from these curves are listed in Table 1. The heating profiles superimpose almost perfectly on the cooling ones. The conditions are described in the Experimental Section.

Table 1. The melting temperatures (T_m) of triple helixes between the [**t**/**a**] duplex and the modified oligonucleotides. Where the azobenzene moiety **X** is present, its configuration is noted.

Oligonucleotide	T_m [°C] *trans*-**X**	 *cis*-**X**	Change in T_m [°C] on *trans* → *cis* isomerization
$\mathbf{XT}_{13}$[a]	26.0	12.7	– 13.3
$\mathbf{T}_{14}$	22.5		
$\mathbf{T}_{13}$	18.0		
$\mathbf{XT}_{11}$[b]	29.1	14.3	– 14.8
$\mathbf{TXT}_{10}$	15.8	6.6	– 9.2
$\mathbf{T}_{12}$	26.8		
$\mathbf{T}_{11}$	20.6		

[a] [$MgCl_2$] = 0.1 M. [b] [$MgCl_2$] = 0.4 M.

curve. The T_m value is 12.7 °C, which is by 13.3 °C lower than that of [*trans*-$\mathbf{XT}_{13}$/**t**/**a**] (Table 1). The stability, as measured by T_m values, of the triple helix formed with the [**t**/**a**] double helix is as follows: *trans*-$\mathbf{XT}_{13}$ > $\mathbf{T}_{14}$ > $\mathbf{T}_{13}$ > *cis*-$\mathbf{XT}_{13}$. When the *cis*-azobenzene moiety is isomerized to the *trans*-form by irradiating with visible light ($\lambda > 400$ nm), the melting curve is almost superimposed with that before the UV irradiation. Thus the triple-helix formation is reversibly modulated by the photoirradiation. Similar results were obtained for the triple-helix formation with $\mathbf{XT}_{11}$. The T_m decreases in the following order: *trans*-$\mathbf{XT}_{11}$ > $\mathbf{T}_{12}$ > $\mathbf{T}_{11}$ > *cis*-$\mathbf{XT}_{11}$ (Table 1). The difference in T_m between [*trans*-$\mathbf{XT}_{11}$/**t**/**a**] and [*cis*-$\mathbf{XT}_{11}$/**t**/**a**] is 14.8 °C.

When *trans*-$\mathbf{XT}_{13}$ forms a triple helix with [**t**/**a**], circular dichroism (CD) is explicitly induced (the solid line in Figure 2 A). The azobenzene is incorporated in the chiral environment of the double helix. As expected, no CD is induced at temperatures higher than the T_m (the dotted line). The induced CD around 360 nm (the π-π* transition of azobenzene) is negative and rather weak, showing that the long axis of the azobenzene

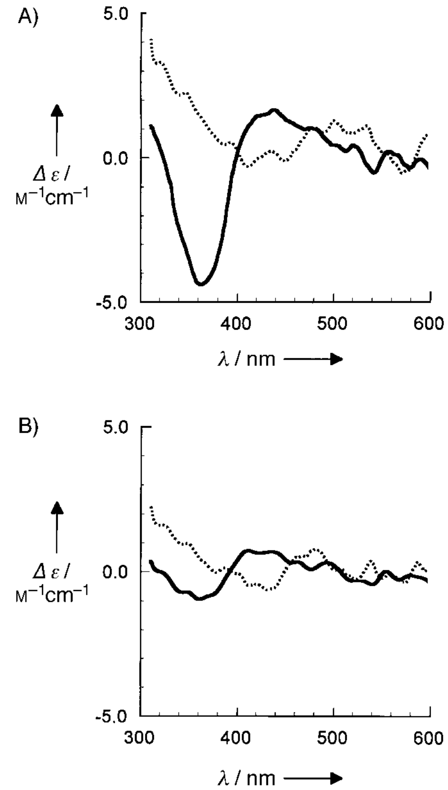

Figure 2. The CD spectra of the solutions containing the [**t**/**a**] duplex and either *trans*-$\mathbf{XT}_{13}$ (A) or *cis*-$\mathbf{XT}_{13}$ (B) at 0 °C (——) and 45 °C (- - - -). The concentrations of the oligonucleotides **t**, **a**, and $\mathbf{XT}_{13}$ are 5.5, 5.0, and 6.0 μM, respectively, and [$MgCl_2$] = 0.1 M.

(which is parallel to the transition moment) is almost parallel to the plane of the A-T base pairs.[6] If the transition moment were to be parallel to the helical axis, the induced CD should be positive and much more intense.[7] This indicates strongly that the *trans*-azobenzene moiety intercalates into the [**t**/**a**] and stabilizes the triple helix. The absorption band of the *trans*-azobenzene shows a bathochromic shift, consistent with the triple-helix formation (Figure 3 A).[8] Upon formation of [*cis*-$\mathbf{XT}_{13}$/**t**/**a**], however, the induced CD is much weaker (the solid line in Figure 2 B). Whereas *trans*-azobenzene is planar, *cis*-azobenzene is nonplanar,[9] and rather than intercalation into the [**t**/**a**], it destabilizes the triple helix by steric repulsion.

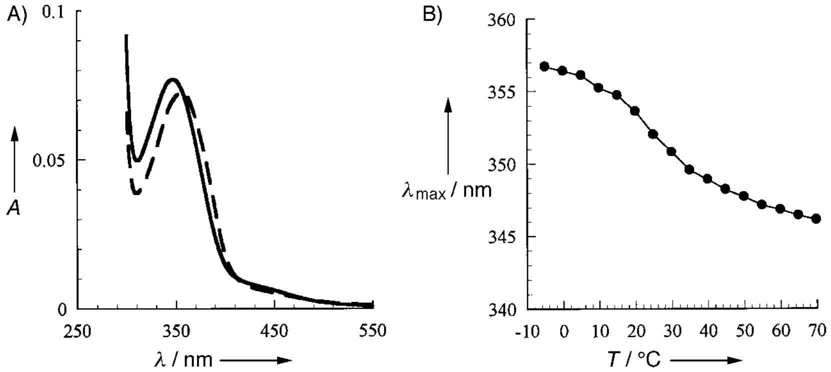

Figure 3. A) Bathochromic shift of λ_{max} for the formation of the *trans*-[$\mathbf{XT}_{13}$/**t**/**a**] triple helix. Spectra were measured at 70 °C (——) (above T_m) and at 0 °C (- - - -) (below T_m). B) Plot of λ_{max} of the *trans*-[$\mathbf{XT}_{13}$/**t**/**a**] system as a function of temperature.

Triple-helix formation is also photoregulated when an azobenzene is included within the oligo(T) block. As shown in Table 1, [*trans*-**TXT$_{10}$**/**t**/**a**] is more stable than [*cis*-**TXT$_{10}$**/**t**/**a**] ($\Delta T_m = 9.2\,^\circ C$). In this case, however, the triple helices (even of the *trans*-isomer) are less stable than either [**T$_{11}$**/**t**/**a**] or [**T$_{12}$**/**t**/**a**]. The intercalation of the *trans*-azobenzene to form the triple helix is less efficient here, mainly because it accompanies partial breakdown of the adjacent Hoogsteen-type base-pairs.

Experimental Section

The modified oligonucleotides (**XT$_{13}$**, **XT$_{11}$**, and **TXT$_{10}$**) were synthesized as described in ref. [3a]. The ratio of the *trans* to the *cis*-isomer in the reaction mixtures was determined by reversed-phase HPLC. In order to isomerize the azobenzene, the solutions were irradiated for 30 min by light from a 150 W xenon lamp through an appropriate filter (UV-D36C and L-42 filters from Asahi Technoglass Corporation for the *trans* → *cis* and *cis* → *trans* isomerization, respectively). The T_m value was determined from the maximum in the first derivative of the melting curve. The absorbance at 280 nm, which is the isosbestic point of the *trans*- and the *cis*-azobenzene, was monitored at pH 7.0 (10 mM 2-[4-(2-hydroxylethyl)-1-piperazinyl] ethanesulfonic acid (HEPES) buffer) on a JASCO model V-530 spectrophotometer equipped with a programmable temperature controller. The temperature ramp was 1.0 °C min^{-1}. The concentrations of **t**, **a**, and the modified oligo(T) were 2.2, 2.0, and 2.4 μM, respectively.[10] In the T_m measurement of the *cis* isomer, intermittent UV irradiation was used in order to suppress the thermal *cis* → *trans* isomerization. The fraction of the *cis* isomer was kept almost constant (at 70%) throughout the measurement.

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[4] For other studies on the introduction of azobenzene to oligonucleotides, see: a) K. Yamana, A. Yoshikawa, H. Nakano, *Tetrahedron Lett.* **1996**, *37*, 637–640; b) K. Yamana, A. Yoshikawa, R. Noda, H. Nakano, *Nucleosides Nucleotides* **1998**, *17*, 233–242.

[5] The modified oligonucleotides **XT$_{13}$**, **XT$_{11}$**, and **TXT$_{10}$** were used as mixtures of the two diastereomers with respect to the chirality of the **X** residue. The attempts to separate these two diastereomers by HPLC have been unsuccessful.

[6] Nordén et al. concretely correlated the sign and magnitude of the CD, induced on the binding of small molecules to DNA, to the manner of the binding: a) M. Kubista, B. Åkerman, B. Nordén, *J. Phys. Chem.* **1988**, *92*, 2352–2356; b) R. Lyng, A. Rodger, B. Nordén, *Biopolymers* **1992**, *32*, 1201–1214; c) P. Pradhan, B. Jernström, A. Seidel, B. Nordén, A. Gräslund, *Biochemistry* **1998**, *37*, 4664–4673.

[7] The rotatory strength of the [*trans*-**XT$_{13}$**/**t**/**a**] triple helix was determined to be −0.15 Debye–Bohr magnetons (DBM). This is in marked contrast with the large positive values for the well-known groove binders dibutylproflavine (+1.77 DBM) and netropsin (+1.31 DBM) (data from ref. [6]).

[8] The middle point of the λ_{max} versus T plot is 25 °C (Figure 3B), which is identical with the T_m of the triple helix, within experimental error.

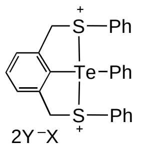
[9] J. M. Robertson, *J. Chem. Soc.* **1939**, 232–236.

[10] The **t**:**a** ratio was kept at 1:1 in order to ensure that there exists no free **a**, which should form a duplex with the modified oligo(T) and perturb the T_m measurement.

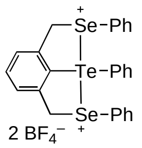
Synthesis of Dicationic Telluranes by Remote Oxidation through a π-Conjugated System[**]

Katsutoshi Kobayashi, Soichi Sato, Ernst Horn, and Naomichi Furukawa[*]

Recently, we synthesized a sulfanyl-substituted tellurium cation as a bis-tetrafluoroborate (**1a**) and a bis-trifluoromethanesulfonate salt (**1b**) and the analogous selenyl-substituted tellurium cation as bis-tetrafluoroborate salt (**2**) by the reaction of tellurides or telluroxides having heteroatoms at the 2,6-positions of the benzene ring with oxidizing agents such as $NOBF_4$ and $NOPF_6$, or with $(CF_3SO_2)_2O$. In these reactions, the tellurium atom should be directly oxidized by the oxidizing agent to form the corresponding dicationic tellurane.[1] Furthermore, we have reported on remote oxygen migration between sulfur atoms in the monooxide of 1,4-bis(methylsulfanyl)benzene in the presence of CF_3CO_2H. This reaction is proposed to proceed not via a quinoid-type intermediate but via the bis(dithia dication) dimer.[2]



1a (X= BF$_4^-$)
1b (X= CF$_3$SO$_3^-$)



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