Photoresponsive double-stranded helices composed of complementary strands†

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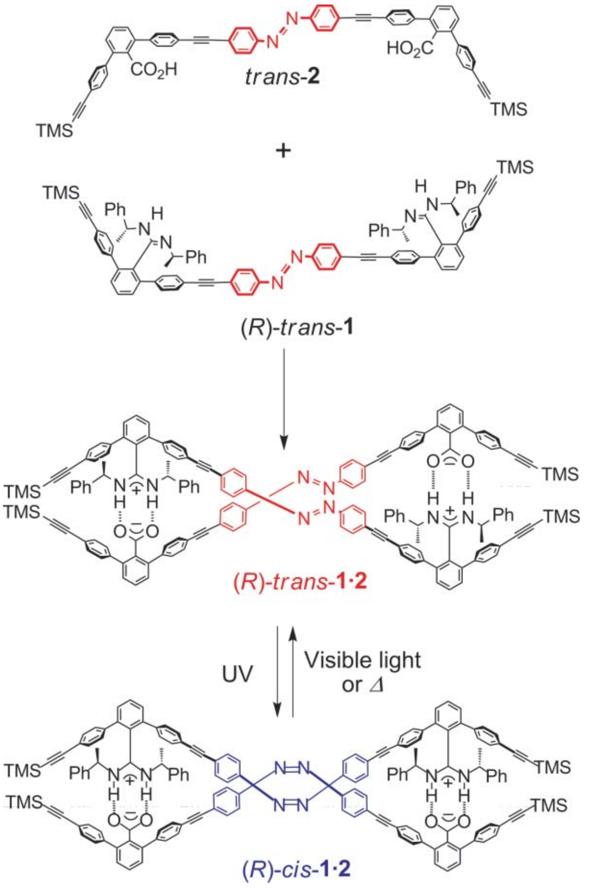
A photoresponsive single-handed double helical supramolecule composed of complementary strands bearing azobenzene moieties underwent a reversible *trans–cis*-isomerization regulated by photoirradiation, resulting in a change in its molecular length.

The double helical structure of DNA has inspired chemists not only by its topological features, but also by its biologically indispensable functions in the preservation and transmission of genetic information. In addition, DNA has recently been proven to provide efficient reaction fields for organic reactions, including enantioselective synthesis, and this discovery suggests the potential of the double helix as a promising molecular discriminating element.[1,2] Therefore, it should be of great interest to create stimulus-responsive double helices that undergo structural changes with some external stimuli since they can be applied to novel photoswitchable functional materials, biomaterials, and liquid crystals, in which their properties are photoregulated.[3] In contrast to the highly developed methodologies for synthesizing molecular strands that fold into a single-stranded helical conformation, the structural motifs available for constructing double helices are limited in number.[4–8] In particular, there are, to the best of our knowledge, no reports on wholly-artificial double helices endowed with photoresponsive properties.[9,10] We now report the synthesis and chiral property of an artificial double helical molecule bearing azobenzene moieties with a controlled helicity that undergoes reversible *trans–cis*-isomerization by photoirradiation, resulting in a change in the molecular length that is derived from the conformational change in the double helix.

The design and synthesis of the optically active photoresponsive double helical molecule bearing azobenzene moieties is based on our recently developed strategy using amidinium–carboxylate salt bridges, which assist in the intertwining of the two complementary molecular strands,[7] as illustrated in Scheme 1. The two complementary molecular strands, (*R*)-*trans*-**1**† and *trans*-**2**†, bear chiral amidine and achiral carboxyl groups, respectively, and the *m*-terphenyl moieties are linked through azobenzene units.

The diamidine strand, (*R*)-*trans*-**1**, was complexed with the complementary dicarboxylic acid strand, *trans*-**2**, through salt bridge formation in $CDCl_3$. The duplex formation was confirmed from electron-spray ionization mass spectrometry (ESI-MS) measurements; the ESI-MS spectrum of a $CDCl_3$ solution of (*R*)-*trans*-**1·2** showed signals at *m*/*z* 2345.8 and 1172.4 corresponding to [(*R*)-*trans*-**1·2** − H]$^-$ and [(*R*)-*trans*-**1·2** − 2H]$^{2-}$, respectively (ESI Fig. S1†). The ^{1}H NMR (500 MHz, $CDCl_3$) spectra of (*R*)-*trans*-**1·2** showed the resonances of the NH protons in the low magnetic field of δ = 13.51 and 13.45 ppm, indicating the salt bridge formation (Fig. S5†). The absorption band at *ca.* 390 nm of the azobenzene moieties of (*R*)-*trans*-**1** and *trans*-**2** exhibited a blue shift of $\Delta\lambda$ = *ca.* 10 nm upon complexation (Fig. 1), probably due to the close twisted alignment of the two azobenzene units, which was supported by molecular mechanics



Scheme 1 Double helix formation and subsequent *trans–cis*-photoisomerization of (*R*)-*trans*-**1·2**.

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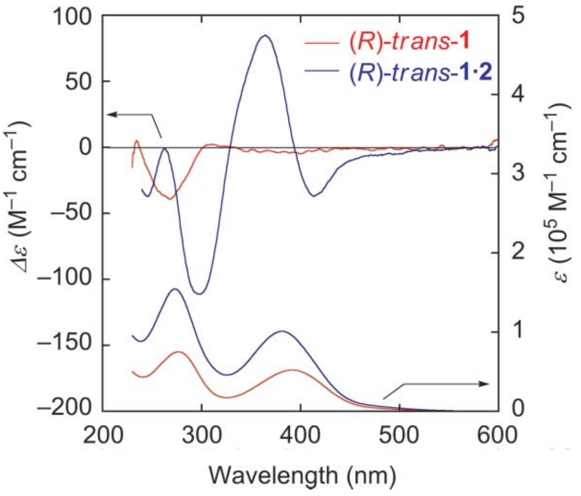

Fig. 1 CD and absorption spectra of (*R*)-*trans*-**1** and (*R*)-*trans*-**1·2** in CDCl$_3$ (0.1 mM) at 25 °C.

(MM) calculations for the duplex (Fig. S2†). The association constant for (*R*)-*trans*-**1** and *trans*-**2** was estimated to be greater than 10^6 M^{-1} in CDCl$_3$ at 25 °C from circular dichroism (CD) and absorption spectroscopies; the CD and absorption spectra exhibited almost no change within the range of 10^{-1} to 10^{-3} mM (Fig. S3†). This value is comparable to that of the analogous diacetylene-linked double helices.[7a]

The CD spectrum of the duplex, (*R*)-*trans*-**1·2**, in CDCl$_3$ showed distinct CD signals, whereas (*R*)-*trans*-**1** exhibited quite weak Cotton effects in the same region (Fig. 1). The significant enhancement in the Cotton effects for (*R*)-*trans*-**1·2**, especially in the absorption region of the azobenzene linkages (*ca.* 330–550 nm), indicated that the duplex likely adopts an excess one-handed double helical structure induced by the chiral amidine groups. The (*R*)-*trans*-**1·2** may have a right-handed double helix on the basis of the X-ray structure of an analogous diacetylene-linked double helical molecule[7a] and the MM-calculation results (Fig. S2†). The Cotton effect intensities of (*R*)-*trans*-**1·2** in CDCl$_3$ showed almost no temperature dependency between 25 and −45 °C (Fig. S4†). In addition, all the ^{1}H NMR signals of (*R*)-*trans*-**1·2** did not show any chemical shift changes nor any splits due to the diastereomeric pairs within the temperature range of 55 to −60 °C (Fig. S5†), and thereby it is not possible to quantify the diastereomeric excesses of the chiral helices.

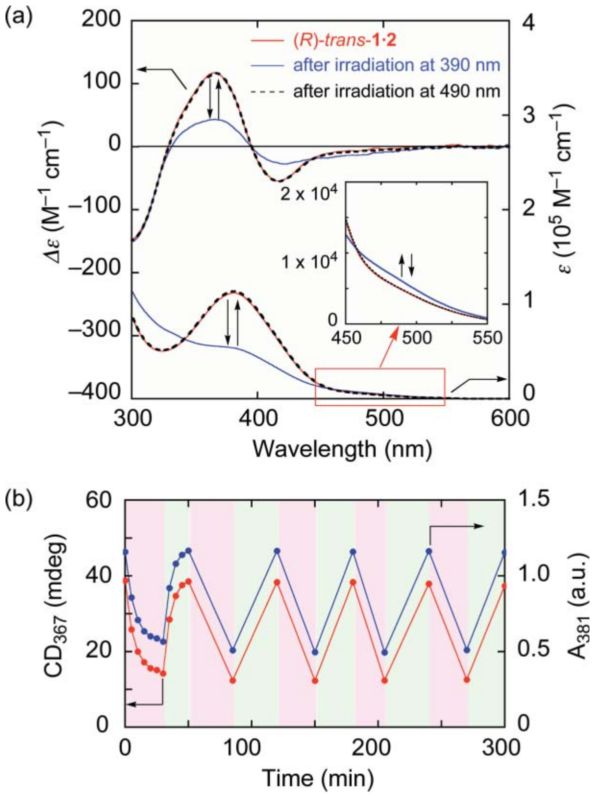

Fig. 2 (a) CD and absorption spectra of (*R*)-*trans*-**1·2** before (solid red line) and after (solid blue line) irradiation at 390 nm for 30 min, and after further irradiation at 490 nm for 20 min (dotted black line) in toluene (0.1 mM) at 25 °C. Inset shows the expanded absorption spectra in the 450–550 nm region. (b) CD and absorption intensity changes in (*R*)-*trans*-**1·2** at 367 and 381 nm, respectively, upon alternating irradiation of UV light (λ = 390 nm, pink regions) and visible light (λ = 490 nm, light green regions).

When (*R*)-*trans*-**1·2** in CDCl$_3$ was irradiated with UV light (390 nm) for 30 min at 25 °C, the intensity of the absorption band at *ca.* 390 nm, attributable to the π–π* transition of the azobenzene moieties, significantly decreased, while that of the absorption band at *ca.* 490 nm, due to the n–π* transition, increased (Fig. 2a). The ^{1}H NMR spectrum of (*R*)-*trans*-**1·2** just after the irradiation showed a new set of signals attributable to the *cis*-isomer (*R*)-*cis*-**1·2** (Fig. S6†). These spectral changes are typical for the *trans*-to-*cis*-isomerization of azobenzene derivatives (Scheme 1), and the maximum *cis*-content in the photostationary state was estimated to be 48% based on the absorbance at 390 nm.[11] In addition, the Cotton effect intensity due to the π–π* transition region (*ca.* 330–450 nm) decreased, while that arising from the n–π* transition (*ca.* 450–550 nm) slightly increased. On the other hand, irradiation with visible light (490 nm) for 20 min at 25 °C caused the complete recovery of (*R*)-*trans*-**1·2** *via* backward isomerization, as evidenced from the absorption, CD, and ^{1}H NMR spectra. Thus, the azobenzene units in (*R*)-**1·2** can reversibly isomerize in response to UV and visible light. This cycle could be repeated several times by sequential UV and visible light irradiations in an alternating manner, as shown in Fig. 2b. The distance between the two salt bridges was estimated roughly from the MM-calculation study to be *ca.* 2.6 and *ca.* 2.2 nm for (*R*)-*trans*-**1·2** and (*R*)-*cis*-**1·2**, respectively. Thus, (*R*)-**1·2** changes the molecular length by *ca.* 15% though the *trans*–*cis*-photoisomerization (Fig. S2†); therefore, this double helix can be considered as a photoresponsive molecular muscle.[12]

The kinetics of the thermal *cis*-to-*trans*-isomerization of (*R*)-*cis*-**1·2** was then investigated in order to obtain information on the conformational dynamics during the isomerization, and this was done by following the changes in the absorption spectra of (*R*)-*cis*-**1·2**. Kinetic analysis of the data at 25 °C in CDCl$_3$ provided the apparent first-order rate constants of 9.71×10^{-5}, 5.75×10^{-4}, and 8.42×10^{-5} s^{-1} for the amidine strand (*R*)-**1**, the carboxylic acid strand **2**, and the double helix (*R*)-**1·2**, respectively (Table 1). These values are typical for the thermal isomerization of azobenzene derivatives in solution.[13] Of particular note is that the first-order rate constant for (*R*)-**1·2** was virtually the same as that for (*R*)-**1**, while the thermal isomerization rate of the

Table 1 The first-order rate constants for the thermal *cis*-to-*trans*-isomerization in $CDCl_3$ and toluene at 25 °C

	k_{298} in $CDCl_3$/s^{-1}	k_{298} in toluene/s^{-1}
(*R*)-**1**	$(9.71 \pm 0.01) \times 10^{-5}$	$(1.07 \pm 0.01) \times 10^{-4}$
2	$(5.75 \pm 0.01) \times 10^{-4}$	—[a]
(*R*)-**1·2**	$(8.42 \pm 0.01) \times 10^{-5}$	$(8.98 \pm 0.01) \times 10^{-5}$

[a] Insoluble in toluene.

carboxylic acid strand **2** significantly decreased by a factor of *ca.* 6 in the presence of the amidine strand. Similar isomerization rate constants for (*R*)-**1** and (*R*)-**1·2** were also obtained in toluene (Table 1). Taking these results together with the high association constant for (*R*)-**1·2** into consideration, it seems probable that the *cis*-to-*trans*-isomerization of the azobenzene residues in (*R*)-**1·2** synchronously proceeds at once in the form of the duplex without dissociation into each single strand in solution.

In summary, we have designed and synthesized the first optically active double helical supramolecule bearing photoresponsive azobenzene moieties, which undergoes a reversible *trans–cis*-isomerization regulated by photoirradiation. The present strategy may provide new approaches for the rational design of switchable helical architectures[14] *via* the reversible photoinduced inversion of helicity[9] in double helices. Work along this line is now in progress in our laboratory.

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