Ultimate diastereoselectivity in the ring closure of photochromic diarylethene possessing facial chirality†

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A bisthienylethene with hitherto unprecedented facial chirality imposed by a triethyleneglycol bridge on a thiophene ring was synthesized and its photochromic ring closure was shown to occur with 100% diastereoselectivity upon UV-light irradiation.

Among the photochromic compounds, diarylethenes[1] are one of the most investigated families due to their high durability, simple synthetic pathways to specifically designed molecules, and an attractive feature of a modifiable conjugation system spread all over the molecule which can be switched by photochemical ring-closure and ring-opening reactions. Recent research into this third property has led to the development of switches for: (1) the reactivity of the central ethene moiety,[2] (2) the conjugation/deconjugation of the π-conjugated systems attached to the end of the hexatriene,[3] (3) the conjugation path around the central ethene moiety,[4] (4) communication between the functional groups on both ends of the aryl groups,[5,6] and (5) the hybridization mode of the carbon atoms involved in the ring closure between sp^2 and sp^3.[7] The hybridization switch of the carbon atoms induces the generation of a pair of stereogenic centers upon photocyclization which results in the generation of a pair of isomeric molecules—enantiomers, if there are no other chiral units.[7]

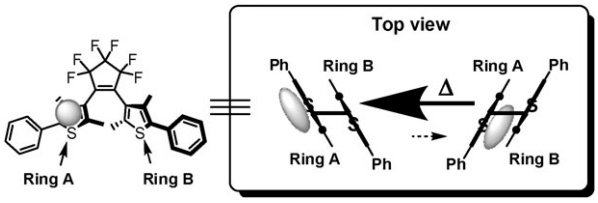
Our group[8] and others[9–12] have been interested in the research of how to control the absolute stereochemistry of these newly generated sp^3 carbon atoms not only for its scientific significance but also for its potential application to biological materials,[13] elaboration of functional materials such as liquid crystals[14–16] and supramolecular systems,[10] and other applications requiring stereoselectivity.[17] Most of the previous work adopted a diastereoselective protocol in which one or two inherent chiral units were introduced into a molecule in order to induce an asymmetric ring-closing reaction.

Loosely classified, there are three categories of asymmetry:[18] asymmetric carbon atoms, axial chirality, and facial chirality. We have so far proposed the use of asymmetric carbon atoms[8] and axial chirality[19] to induce a high diastereoselectivity for the photochromic ring closure of diarylethenes and fulgides which both exhibit thermally irreversible photochromic 6π-electrocyclizations. Similar to the case of axial chirality, facially chiral compounds do not have asymmetric carbon atoms. In fact, facial chirality has been successfully introduced to thermally reversible photochromic azobenzenes.[20] We report here on the use of this third chirality, *i.e.*, facial chirality, on a diarylethene to induce 100% diastereoselectivity of photochromic ring closure in various solvents, and the concept is shown in Scheme 1. If one of the two surfaces of an aromatic ring (ring **A**) is occupied by a bulky attachment, ring closure is possible when the other aromatic ring (ring **B**) approaches from the back of ring **A**. Perfect control of the diastereoselectivity during ring closure could, thus, be realized.

Our molecular design and the expected photochromic reaction pathways are shown in Scheme 2. The target open form **1*O*** has a bridge across the surface of thiophene ring **A** which prevents access of the other thiophene **B** to the side of the bridge. Therefore, this molecule can take only one antiparallel (cyclizable) conformation. We chose the C2 and C4 carbon atoms to span the bridge because C3 is used to connect with hexafluorocyclopentene while C5 is useful in attaching to a functional substituent. We decided to introduce a phenyl group on C5 as a typical example. As the bridge, we chose triethylene glycol (TEG) which is long enough to connect the methylene carbon atoms on C2 and C4, yet short enough to prohibit isomerization of the facial chirality with the rope-jumping action of the TEG bridge over a substituent, such as the phenyl group, on C5.

Thus, a bisthienylethene **1*O*** possessing a facial chirality which generates only one diastereomer of the closed form (**1*C***-real) upon photoirradiation was designed. First, we carried out DFT calculations[21] which proved that one of the two possible antiparallel conformers (**1*O***-major) in which the other thiophene (**B**) is located at the back side of the bridge is more stable by 32.8 kJ mol^{-1} than the other (**1*O***-minor). If the population at 25 °C is calculated from the difference in heat-of-formation (ΔH_f) by disregarding the entropy term, the ratio is 564 800/1. In addition, ΔH_f of the two closed-ring C-forms (**1*C***-real and **1*C***-imaginary) is 194.1 kJ mol^{-1}, which is too large to be imaginable.

Encouraged by the calculation results, we undertook the synthesis of **1*O***. The synthetic route is shown in Scheme 3. Starting from 2,5-dibromothiophene, 2,4-dibromo-3,5-bis(chloromethyl)-thiophene (**2**)[22] was obtained in 49% yield. Interestingly, regioselective partial Suzuki coupling on C5 of **2** to introduce a



Scheme 1 Molecular modelling concept of facially chiral diarylethenes.

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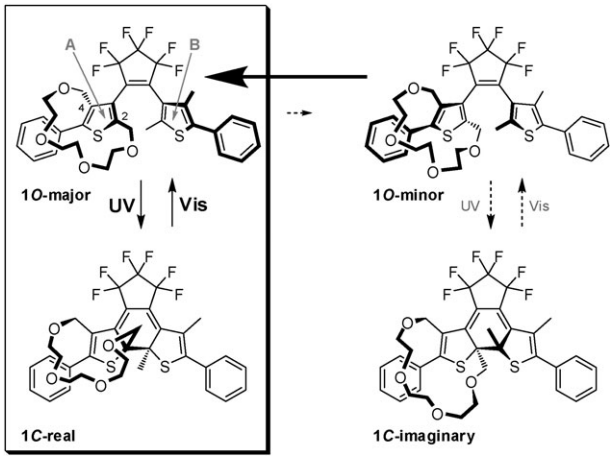
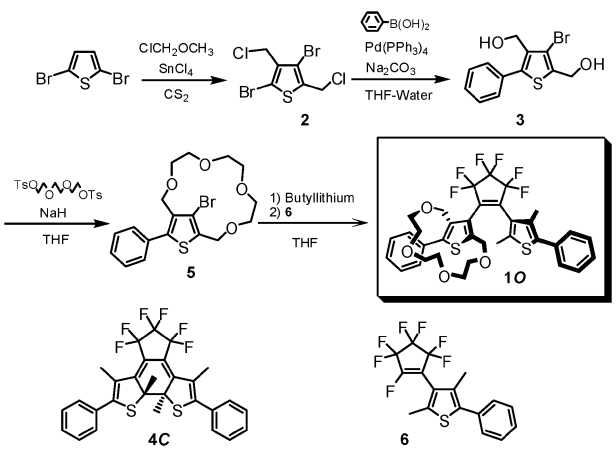


Scheme 2 Molecular design and photochromic reactions of **1**.

phenyl group generated 3-bromo-2,4-bis(hydroxymethyl)-5-phenylthiophene (**3**) with a 57% yield. This may be the result of solvolysis of the benzylic chlorides under aqueous basic conditions. The position where the phenyl was introduced was envisaged by the difference in reactivity and steric hindrance, the NOE experiments on **3** showing only one of the methylene protons exhibiting NOE signals,[23] and ultimately determined by the absorption maximum wavelength of the final bisthienylethene **1*C*** (559 nm in hexane) which is similar to the value of 1,2-bis(2,4-dimethyl-5-phenyl-3-thienyl)hexafluorocyclopentene **4C** (562 nm),[24] whereas the corresponding 2-thienyl compounds are known to have absorption bands at shorter wavelengths than the 3-thienyl compounds.[25] Bridging of the C2 and C4 hydroxymethyl groups by a TEG chain by reacting **3** with triethylene glycol bis(4-toluenesulfonate) in THF in the presence of NaH under high-dilution conditions afforded the bridged thiophene **5**, though the yield was merely 3%. Introduction of **5** to 1-(2,4-dimethyl-5-phenyl-3-thienyl)heptafluorocyclopentene **6**[26] gave the desired **1*O*** with a 44% yield after purification with silica gel column chromatography.[23]

Photochromic reactions of **1*O*** were carried out in hexane, toluene, and ethyl acetate. A change in the absorption spectra during the ring-closing reaction of **1*O*** in (hexane) with 313 nm light irradiation until the photostationary state (pss) was



Scheme 3 Synthetic pathway to **1*O***.

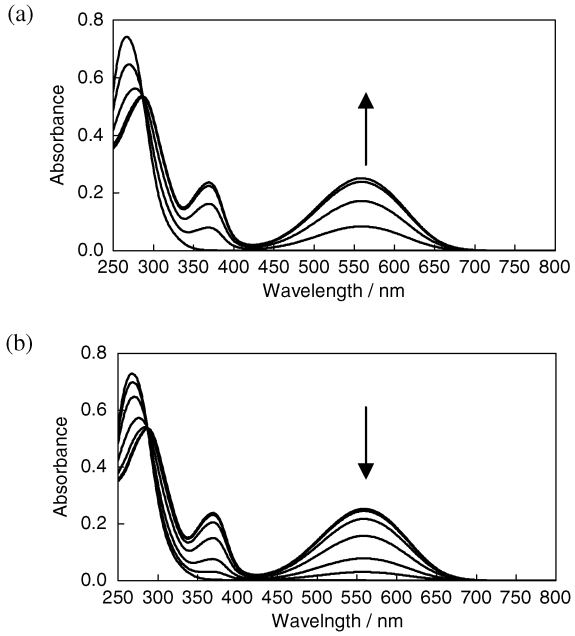


Fig. 1 Absorption spectral changes of **1** in hexane. (a) **1*O*** to pss. 313 nm (0.71 mW cm^{-2}). 0 to 15 min. (b) Pss to **1*O***. 512 nm (1.24 mW cm^{-2}). 0 to 150 min.

achieved and the ring-opening reaction upon 512 nm light irradiation to the pss solution are shown in Fig. 1. A clear isosbestic point (287 nm) was observed.

The components existing at the pss were examined thoroughly by HPLC with three different columns and three different solvent systems. A typical HPLC chromatogram of **1** at pss in hexane detected at a wavelength of 559 nm is shown in Fig. 2. ^{1}H NMR analysis of the compounds was also carried out, however, not even any slight evidence of the formation of the minor C-form was observed. From these results obtained along with the calculation results, it was concluded that **1*O*** showed ultimate diastereoselectivity within the detection limit of the minor diastereomer upon photochromic ring closure under any of the reaction conditions carried out. The spectroscopic data as well as quantum yields of the photoreactions in the three solvents used are described in Table 1.

Subsequently, **1*O*** was resolved into enantiomers by an HPLC equipped with a chiral column (Daicel Co. Chiralpak IA with $CHCl_3$–hexane = 4.5 : 95.5 as the eluent) to investigate

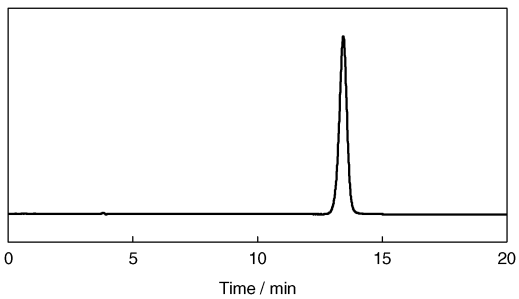


Fig. 2 Detection of diastereomers at the pss of 313 nm irradiation of **1*O*** in hexane. Column: Wakosil 5SIL, Eluant: 33% v/v ethyl acetate–hexane. Flow rate: 0.5 mL min^{-1}. Detection wavelength: 559 nm.

Table 1 Absorption spectroscopic data and quantum yields of the photoreactions of **1**

Solvent	Hexane	Toluene	Ethyl acetate
λ_{max}**1O**/nm (ε^a)	267 (24 400)	—[b]	268 (2500)
λ_{max} **1O**/nm (ε^a)	559 (9630)	567 (9840)	563 (9610)
Φ_{OC}(313)	0.30	0.31	0.33
Φ_{CO}(313)	0.017	0.015	0.019
Φ_{CO}(512)	0.0030	0.0033	0.0036
CR[c](%)	86	88	86

[a] Molar absorption coefficient/cm^{-1} mol^{-1} dm^3. [b] No absorption maximum was observed due to solvent absorption. [c] Conversion ratio to the coloured form at pss.

its chiroptical properties and racemization possibility upon thermal treatment.

The two enantiomers obtained (**1O$_f$**: moving faster on HPLC and **1O$_s$**: moving slower, 50 : 50 ratio) showed a pair of mirror-image CD spectra.[23] At pss, a new CD band appeared in the visible region due to the absorption of the C-form.

One of the enantiomers (**1O$_f$**) was refluxed in toluene (bp 110 °C) for 5 h and its racemization behavior was monitored by HPLC with a chiral column. As anticipated, no evidence of racemization of **1O$_f$** was observed, showing the phenyl group at C5 of the thiophene (ring **A**) is sufficiently large enough to prohibit the jump-rope-like motion of the TEG bridge which causes the racemization.

In conclusion, we have succeeded in synthesizing a bisthienylethene with hitherto unprecedented facial chirality imposed by a TEG bridge on a thiophene ring and it showed photochromic ring closure with 100% diastereoselectivity upon UV irradiation.

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