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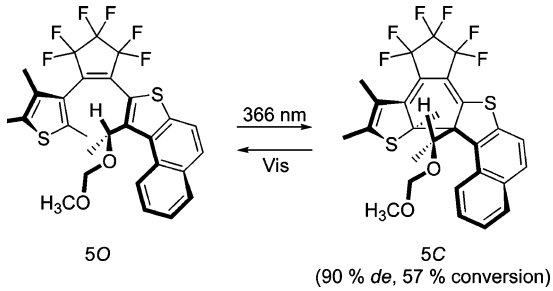
Chiral Helicenoid Diarylethene with Highly Diastereoselective Photocyclization[1]

Yutaka Tani,[†] Takashi Ubukata, Yayoi Yokoyama,[‡] and Yasushi Yokoyama*

Department of Advanced Materials Chemistry, Graduate School of Engineering, Yokohama National University, Hodogaya, Yokohama, 240-8501, Japan, and Department of Home Economics, Tokyo Kasei Gakuin University, Aiharacho, Machida, Tokyo, 194-0292, Japan

yyokoyam@ynu.ac.jp

Received September 30, 2006



A novel photochromic helicenoid diarylethene (*R*)-1-[1-(1-methoxymethoxyethyl)-2-naphtho[2,1-*b*]thienyl]-2-(2,4,5-trimethyl-3-thienyl)hexafluorocyclopentene was synthesized enantioselectively. It showed highly diastereoselective photocyclization (90% de) and a large change (950°) in the specific optical rotation value at 633 nm upon UV light irradiation in ethyl acetate.

Introduction

In the preceding paper,[2] we reported a chiral helicenoid diarylethene **1*O***/**1*C*** (Figure 1), which showed a large change in specific optical rotation by photochromism. However, **1*O*** exhibited only moderate diastereoselectivity (47% de). The concept to attain high selectivity should be originated from the combination of (1) allylic 1,3-strain[3]-controlled conformation around the stereogenic center and (2) preference of one of the two antiparallel conformations, having smaller steric as well as electronic repulsions.

This concept has best been realized in **2*O*** and related compounds (Figure 1).[4] Because of the allylic 1,3-strain,[3] the smallest substituent on the stereogenic center, i.e., hydrogen in the case of **2*O***, is forced to face the sterically congested direction, i.e., to face the perfluorocyclopentene. One of the other substituents, a methoxymethoxyl (MOMO) group, worked as

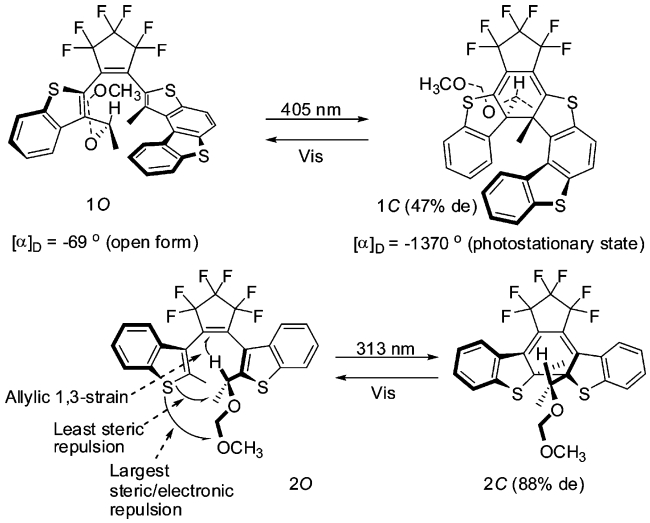


FIGURE 1. Helicenoid diarylethene **1*O***/**1*C*** in the preceding paper and the allylic 1,3-strain working on a diarylethene **2*O***.

* To whom correspondence should be addressed. Phone/Fax: +81-45-339-3934.
† JSPS Research Fellow.
‡ Tokyo Kasei Gakuin University.

(1) Studies on Helicenoid Diarylethenes, Part 2. For Part 1, see ref 2.
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10.1021/jo062022v CCC: $37.00
Published on Web 02/08/2007

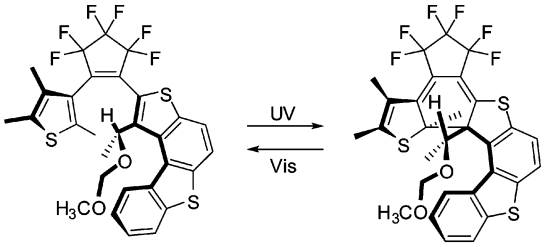

FIGURE 2. Helicenoid diarylethene **3*O***/**3*C***.

the sterically and electronically more repulsive substituent with the other benzothiophene group compared with the methyl group on the stereogenic center. However, in **1*O***, although the steric repulsion worked as well, the electronic repulsion did not seem to work well because of the larger distance between the oxygen atoms and the relevant sulfur atom compared with that in **2*O***. In this paper, our efforts and success in overcoming the lack of electronic repulsion in **1*O*** are described.

Results and Discussion

Molecular Design and Synthesis. To restore the electronic repulsion between the oxygen atoms on the MOMO group and the sulfur atom on the other aromatic group, the longer helicene wing should possess the stereogenic carbon atom with a MOMO group, and the shorter wing should be a thiophene group (or another heteroaromatic ring) that is connected to the perfluorocyclopentene at C-3. If the aromatic group is connected to the perfluorocyclopentene at C-2, the distances between its sulfur atom and the MOMO oxygen atoms become larger. If a benzothiophene instead of thiophene is connected to the perfluorocyclopentene at C-3, the colored form generated by photocyclization can no longer maintain the helicenoid structure. Instead, it would take an S-shaped structure. Therefore, the following structural requirements are inevitable: (1) the longer wing should possess the methoxymethoxyethyl group, and (2) the other wing should be a thiophene that is connected to perfluorocyclopentene at C-3. We first designed **3*O*** (Figure 2), by taking advantage of the common structure of the longer wing of **1**.[2]

However, the synthesis of **3*O*** was not successful, despite our execution of several possible methods as shown in Scheme 1. The reason why we could not obtain **3*O*** is the sterically severe situation around the chiral substituent. The phenyl group on the end of the longer wing of **3*O*** (**4**) gives severe steric pressure to the chiral substituent, almost colliding with it. Therefore **4** takes the conformation shown in Figure 3. In this conformation, hydrogen, the smallest substituent, is forced to face the phenyl group, so that the methyl and MOMO groups will come close to C-2. Similar observations of the conformation of a chiral auxiliary attached to the terminal of helical oligoamide foldamers has been described.[5] Therefore, the C−C coupling reaction between the carbanion, generated from **4** and butyllithium, and perfluorocyclopentene is almost impossible because of the steric hindrance caused by the methyl and MOMO groups.

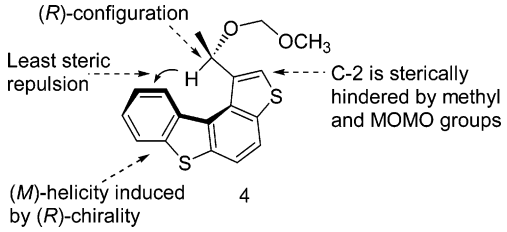

FIGURE 3. Most stable conformation of **4**.

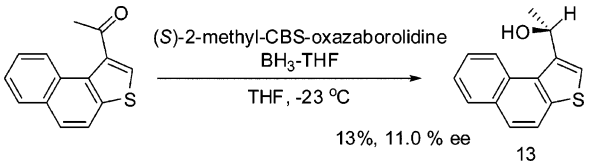

FIGURE 4. Catalytic asymmetric reduction of 1-acetylnaphthothiophene.

We then designed **5** by shortening the longer wing of **3**. In **5**, the steric repulsion that the chiral substituent suffers from the end phenyl group was not so large. The synthetic route of **5*O*** we have carried out is shown in Scheme 2.

Although the enantioselective reduction of 1-acetylnaphthothiophene with borane catalyzed by (*S*)-2-methyl-CBS-oxazaborolidine[6] proceeded to give **13** with only 11% ee and 13% chemical yield (Figure 4), reduction of 3-acetylthiophene with the same reaction conditions successfully yielded the (*R*)-3-(1-hydroxyethyl)thiophene (**7**) in 96.0% ee[7] with quantitative chemical yield. The ee values were determined on their acetates (**8**) by chiral HPLC, based on the behavior of the racemic compounds.

The absolute configuration of the alcohol **7** was determined to be *R*, because (*S*)-2-methyl-CBS-oxazaborolidine catalyzed borane reduction of arylmethylketones had been known to give (*R*)-alcohols.[6] In addition, the specific optical rotation value ($[\alpha]_D$) of the alcohol **7** was +20° (ethyl acetate; 6.4×10^{-4} g/mL, 19 °C), the sign of which is the same as those of the known (*R*)-alcohols.[6] As the enantioselective reduction was done at the first stage of the whole synthesis, all successive reactions were done on chiral materials.

Introduction of the formyl group to C-5 of (*R*)-3-(1-hydroxyethyl)thiophene **7** was done after the protection of the hydroxyl group with the bulky *tert*-butyldiphenylsilyl group. Other smaller protecting groups such as *tert*-butyldimethylsilyl group gave a mixture of aldehydes in which a formyl group was introduced at C-2 or C-5. When the hydroxyl group was protected with a methoxymethyl group, which had been used in **1** and **2**, introduction of the formyl group occurred on C-2 predominantly because of the favorable chelation to the C-2 lithium cation by the MOMO group.

At the last step of the synthesis, introducing trimethylthiophene, an unidentified and non-photochromic byproduct was produced, which was inseparable from **5*O*** by column chromatography. Although the byproduct was produced in a considerable amount in THF, it was greatly reduced when the reaction was carried out in ether.

In order to get rid of the byproduct, the mixture was irradiated with 366-nm light in ethyl acetate to produce **5*C***, and **5*C*** was

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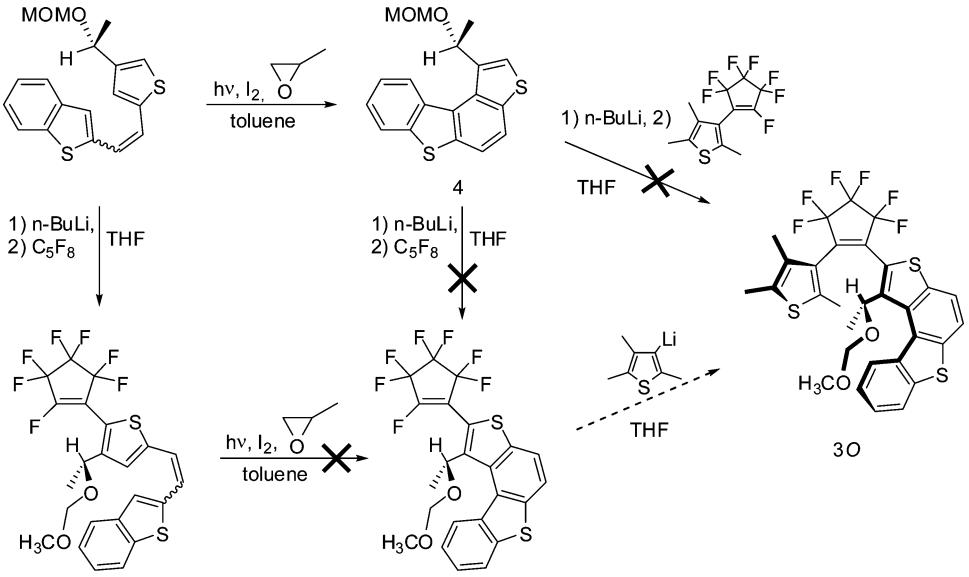
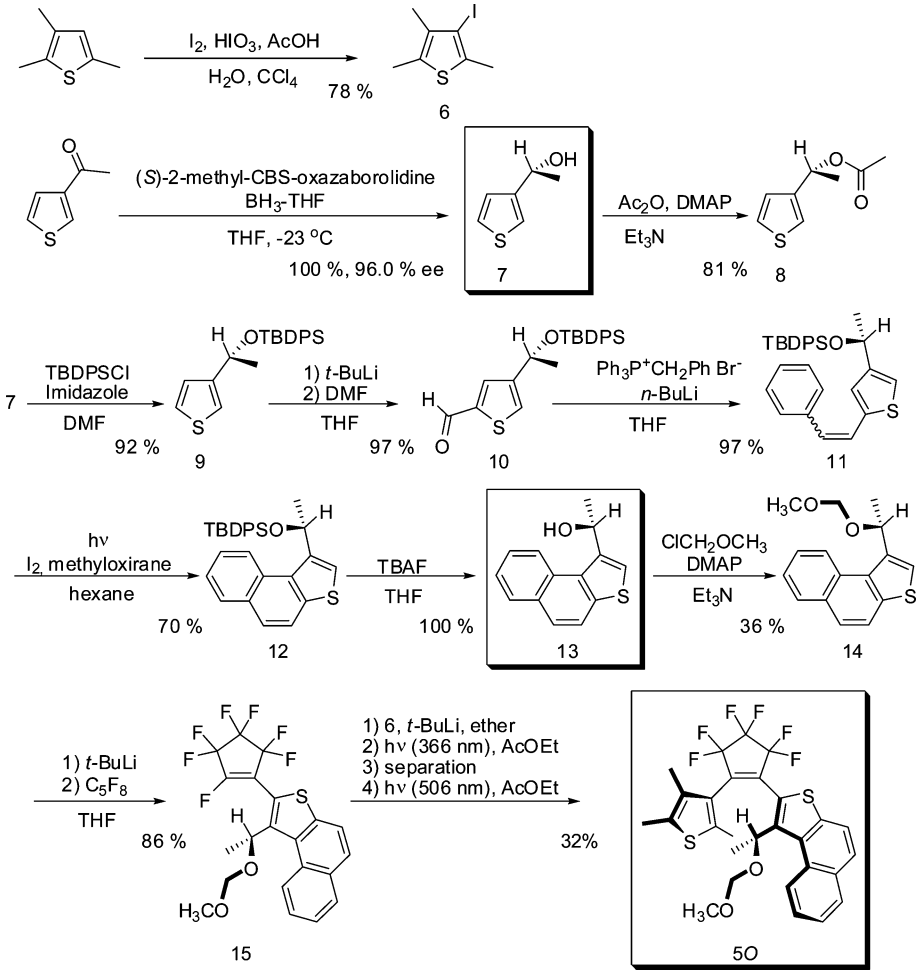
(7) See Supporting Information.

SCHEME 1. Synthetic Trials of 3*O*



SCHEME 2. Synthetic Route to 5*O*



successfully separated from the byproduct by column chromatography. Pure **5*O*** was obtained by irradiation of an ethyl acetate solution of **5*C*** with visible light.

^{1}H NMR Analysis. It is known that although the antiparallel conformation[8] (cyclizable upon UV irradiation) and the parallel conformation[8] (cyclization impossible upon UV irradiation) of the bisbenzothienylethenes connected to perfluorocyclopentene at C-2 have not been observed separately by ^{1}H NMR at room temperature because of the quick interconversion between them, these conformations in which both aromatic rings are connected to perfluorocyclopentene at C-3 can be observed. For example, the simplest C-2-connecting bisbenzothienylethene **16** shows

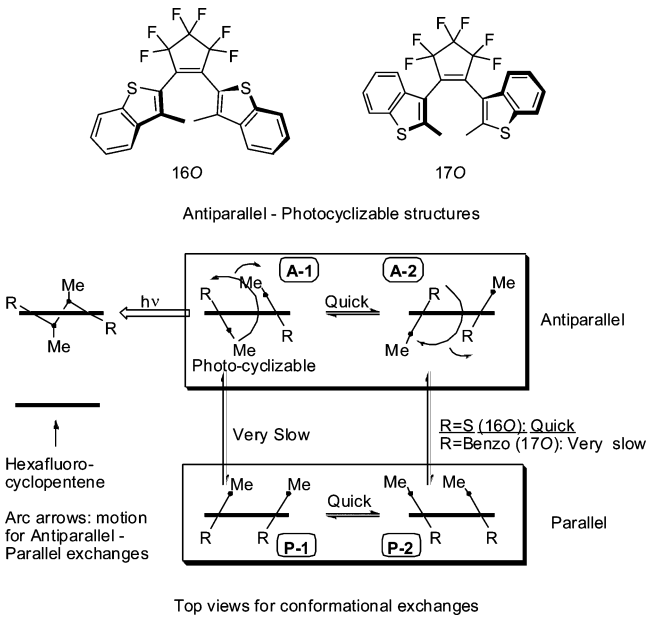


FIGURE 5. Structures and top views of conformational exchanges of diarylethenes **16*O*** and **17*O***.

the methyl signal at δ 1.98 (6H, s).[9] To the contrary, C-3-connecting bisbenzothienylperfluorocyclopentene **17** shows two singlet peaks at δ 2.21 (antiparallel) and 2.49 (parallel) in the ratio of 65:35 in $CDCl_3$.[8d] The difference in the exchange rate between antiparallel and parallel conformations should be caused by the steric interference of the rotation of the C−C single bonds between the perfluorocyclopentene ring and the aromatic rings. The single bond in **17** is surrounded by a neighboring C-2 methyl substituent and the benzo-annulation on the thiophene ring. On the other hand, the neighboring groups in **16** are a methyl group on C-3 and a sulfur atom; the latter is not a substituent but is located in the ring. Therefore the energy barrier of the rotation of the single bond to exchange the antiparallel/parallel conformations for **16** (no more than 180° rotation is necessary when the sulfur atom faces the other ring during the exchanging rotation) should be much smaller than that for **17** (Figure 5).[10]

The anticipated frictions at the hexatriene part (inner) and between the hexafluorocyclopentene and the heteroaromatic ring (outer) during the antiparallel/parallel interconversion for **16*O*** and **17*O*** are summarized in Table 1.

For the conformation exchange through the A-1/P-1 route, the inner frictions for **16*O*** and **17*O*** are the same (methyl group versus surface of the other benzothiophene ring) while the outer frictions are electronically (**16*O***; sulfur atom versus fluorine atoms of hexafluorocyclopentene) and sterically (**17*O***; phenyl ring versus hexafluorocyclopentene) considerable, respectively. For the conformation exchange through the A-2/P-2 route, the outer frictions for **16*O*** and **17*O*** are the same (methyl group versus fluorine atoms of hexafluorocyclopentene). As for the inner friction for **16*O*** (sulfur atom versus surface of the other benzothiophene ring), it is considerably smaller than that for **17*O*** (benzene ring versus surface of the other benzothiophene ring). Therefore the conformation exchange for **16*O*** occurs mainly by way of the A-2/P-2 route quickly, so that the ^{1}H NMR spectrum exhibits the average signals of all of the conformers, while that for **17*O*** is so slow that the A-1/A-2 (antiparallel) and P-1/P-2 (parallel) conformational isomers can be observed separately by ^{1}H NMR.

TABLE 1. Possible Frictions during Conformation Exchange in Diarylethenes 16*O* and 17*O*

conformation exchange	frictions	**16*O***	**17*O***
A-1/P-1	inner (vs surface of the other ring)	CH_3	CH_3
	outer (vs F atoms of hexafluoro-cyclopentene)	S atom	phenyl
A-2/P-2	inner (vs surface of the other ring)	S atom	phenyl
	outer (vs F atoms of hexafluoro-cyclopentene)	CH_3	CH_3

In the case of **5*O***, there can be four conformational isomers (the combination of (1) antiparallel/parallel conformers and (2) the conformers with smaller/larger repulsive interaction between two wings (i.e., more-stable/less-stable conformers)), each composed of two easily exchangeable conformers by the synchronous swinging of the aromatic groups (Figure 6). However, the ^{1}H NMR spectrum of **5*O*** showed only two sets of signals. For example, two doublet peaks (major δ 1.10 (3H, d, J/Hz = 6.8), minor δ 1.03 (3H, d, J/Hz = 6.8)) corresponding to the methyl group on the stereogenic carbon atom, in the ratio of 52/48, were observed. As the longer wing of **5*O*** is connected to the perfluorocyclopentene at C-2 of the thiophene end in a similar manner to **16*O***, it can rotate (less than 180°) easily by facing the sulfur atom to the flat surface of the trimethylthiophene hanging down on the other side of the double bond, resulting in the quick exchange of antiparallel/parallel conformations. The other diastereomeric conformational group would show an averaged signal at a different chemical shift.

Although two signals were observed separately, the ratio of more stable and less stable photocyclizable antiparallel conformations that is responsible for the diastereomer excess value was unknown, because the information of the ratio of them in each ^{1}H NMR-detectable group is included inseparably in each averaged signal; the ratio of antiparallel/parallel conformers is not explicitly obtained from the ^{1}H NMR signals.

Photochromism of 5. The photochromic reactions between **5*O*** and **5*C*** were examined. The ethyl acetate solution of **5*C*** (1.4×10^{-4} mol dm^{-3}) was irradiated by 506-nm light. The change in absorption spectra is shown in Figure 7a.

The coloration reaction was subsequently carried out on the resulting solution of **5*O*** with 366-nm light. Conversion of **5*O*** to **5*C*** in ethyl acetate by 366-nm light irradiation was 57% at the photostationary state (PSS) (Figure 7b). The diastereomer excess was determined by ^{1}H NMR spectrum of **5*C*** of the independent experiment. The signals corresponding to the methyl groups on the MOMO moiety of the diastereomers (major δ 3.30, minor δ 3.25; ratio 95.2/4.8) showed the diastereoselectivity clearly, and the diastereomer excess was 90%. Most of major signals are also accompanied by the minor signals whose ratios to the major peaks also gave the diastereomer excess values of approximately 90%.

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(10) The discussion with regard to the calculated activation energy values of conformational exchange and the ^{1}H NMR behavior of **16*O*** and **17*O*** will be reported in due course.

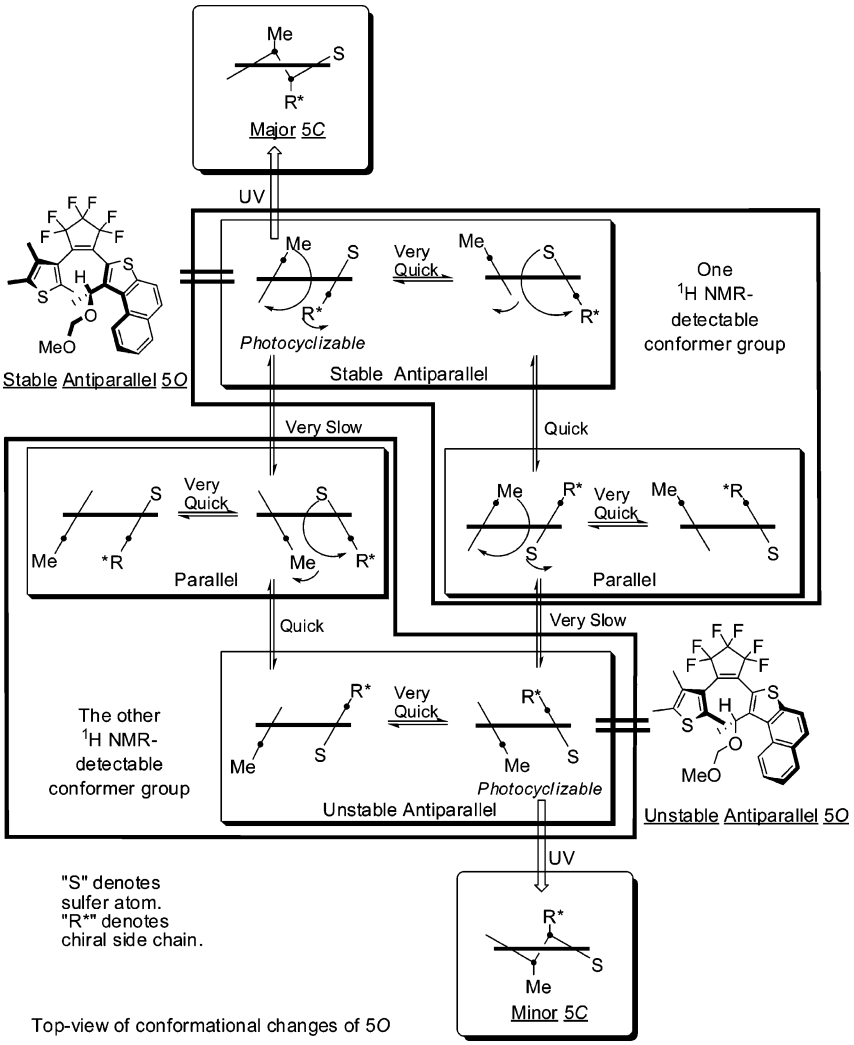

FIGURE 6. Top views of conformational exchanges of diarylethene **5*O***.

The spectroscopic data and the quantum yields of the photoreactions were determined from the change in absorption spectra, with the assumption that the diastereomeric *C*-forms behave as one compound. The quantum yield values are listed in Table 2.

Specific Optical Rotation. The change in specific optical rotation values of **5** during the photochromic reactions measured at 633 nm (He−Ne laser) where the isomers do not have absorption was determined. They are listed in Table 3, together with the values of **1** at 589 nm.

The specific rotation values of **5*C*** and **5*O*** were −1610° and +48°, respectively, and that at PSS with 366-nm light irradiation was −905°. The last value reflects the conversion ratio of 57% to **5*C***. The value of **5** at PSS (−905°) was considerably smaller than that of **1** at PSS (−1370°), although the diastereoselectivity was much higher (47% de for **1** versus 90% de for **5**) and the conversion ratio to the C-form at PSS (64% for **1** versus 57% for **5**) was comparable. It is probably because of the reduction of the number of the aromatic rings comprising of the helicenoid structure. The number of aromatic rings (including one dihydroaromatic ring at the ring-closing position) is seven for **1*C***, whereas the number is five for **5*C***. It was reported that an increase in the number of the aromatic rings in helicene increases the magnitude of the specific optical rotation value.[11]

In regard to the sign of the specific rotation values of the helicenes, it has been reported that *M* (minus, left-handed screw) helicenes show minus rotation values, and *P* (plus, right-handed screw) helicenes show plus values.[12] Because the optical rotation value of **5*C*** (90% de) including the sign is −1610°, its helicity is judged to be *M*. As the chirality of **5*C*** reflects the conformation of **5*O***, which is controlled by the chirality of the stereogenic center, it is in accordance with the borane-CBS reduction of the 3-acetylthiophene. This reaction produced (*R*)-3-hydroxyethylthiophene **7**, which was finally converted to the (*R*)-diarylethene. The most stable antiparallel conformation of **5*O*** derived from **7** is shown in Figure 6. Photocyclization of this species will give *M*-helicenoid **5*C***.

The value of optical rotation can be detected by linearly polarized light at the wavelength where the molar absorption coefficient is null, although the value is larger when measured at a wavelength closer to the absorption. In order to know the feasibility whether the optical rotation can be used as the nondestructive readout of the record, we measured the ORD

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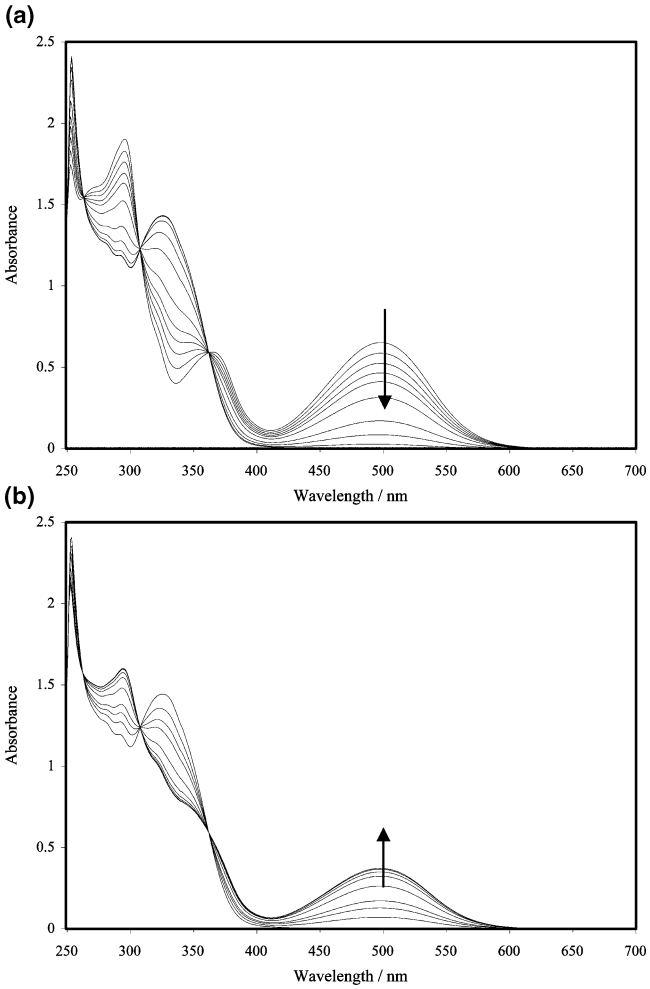

FIGURE 7. UV−vis spectral change of **5** (1.4×10^{-4} mol dm^{-3}, cell length 1 cm) in ethyl acetate. (a) 506-nm irradiation to **5*C***. Irradiation time (min): 0 to 30. (b) 366-nm irradiation to **5*O***. Irradiation time (min): 0 to 20.

TABLE 2. Spectroscopic Data and Quantum Yields of Photoreactions of 5*O* and 5*C*

λ_{max}/nm (ϵ_{max}/mol^{-1} dm^3 cm^{-1})		quantum yield			conversion ratio
		366 nm		506 nm	
5*O*	**5*C***	Φ_{OC}	Φ_{CO}	Φ_{CO}	C/O at PSS
326 (10590)	498 (4840)	0.32	0.21	0.11	57/43

TABLE 3. Specific Optical Rotation Values[a] ([α]$_\lambda$, deg) of 5 and 1 in Ethyl Acetate

	O-form	C-form[b]	at PSS
5	+48	−1610 (−9190)	−905
1	−69	−4680 (−30380)	−1370

[a] Measurement conditions: 633 nm at 35 °C for **5**, 589 nm at 25−29 °C for **1**. [b] In the parentheses: molar optical rotation values [Φ]$_\lambda$.

spectra of **5*O*** and **5*C***, which are shown in Figure 8. While the absorbance of **5*C*** becomes almost zero at 600 nm, the optical rotation has the certain value in the visible region longer than 600 nm. Therefore the memory can be read by the linearly polarized 658-nm diode laser light for DVD recording system. However, if the molecular modification to **5** would result in pushing the absorption band to the longer wavelength region,

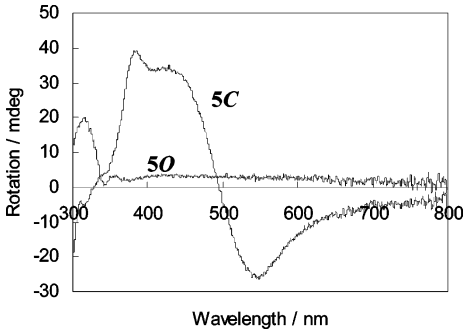

FIGURE 8. ORD spectra of **5*O*** and **5*C*** in ethyl acetate. Concentration: 1.01×10^{-4} mol dm^{-3}. Cell length: 1 cm.

the diode-laser light may cause the destruction of the memory. The absorption band should lie in the shorter region, but the change in optical rotation should be larger.

Conclusion

The enantioselective synthesis of **5*O*** possessing one stereogenic carbon atom was successfully carried out. The diastereoselectivity and the conversion to the colored and helicenoid **5*C*** proceeded in 90% de and 57%, respectively. The optical rotation values of **5*O***, **5*C***, and PSS by UV irradiation in ethyl acetate are +48°, −1610°, and −905°, respectively.

Experimental Section

Details of synthesis, purification, and structure identification including measurement of optical rotation of compounds are described in Supporting Information.

Photochemical reactions of **5** at 366 nm in ethyl acetate (1.4×10^{-4} M) were carried out in a 10 mm path length quartz cell, using a 500 W high-pressure mercury lamp that was separated by filters (a 5 cm water filter, a 5 cm aqueous $CuSO_4 \cdot 5H_2O$ solution, a UV-35 glass filter, and a UV-D35 glass filter), and those at 506 nm were carried out using 500 W xenon lamp that was separated by filters (a 5 cm water filter, a Pyrex glass filter, a Y-47 glass filter, and a KL-50 interference glass filter). During the photoreaction, solutions in the cell were stirred continuously.

Change in component concentration as a function of irradiation time during photoreaction was followed by the change in absorption spectra of **5** in ethyl acetate.

Acknowledgment. The authors thank Zeon Corp. for the generous gift of octafluorocyclopentene. This work was supported by a Grant-in-Aid for Scientific Research (A) (no. 16205025) from the Ministry of Education, Culture, Sports, Science, and Technology (MEXT) of the Japanese Government. Y.T. thanks Japan Society of Promotion of Science (JSPS) for the research aid through a Grant-in-Aid for JSPS Fellows (no. 17-5424). The authors thank the Analytical Instrument Center of Yokohama National University for the use of ^{1}H NMR and MS facilities and JASCO Co. for the measurement of ORD spectra.

Supporting Information Available: Experimental details of synthetic procedures, ^{1}H NMR spectra, characterization data of all new compounds, change in absorption spectra of **5** upon photoirradiation, and chiral HPLC chromatograms of the acetate of **7** (**8**). This material is available free of charge via the Internet at http://pubs.acs.org.

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