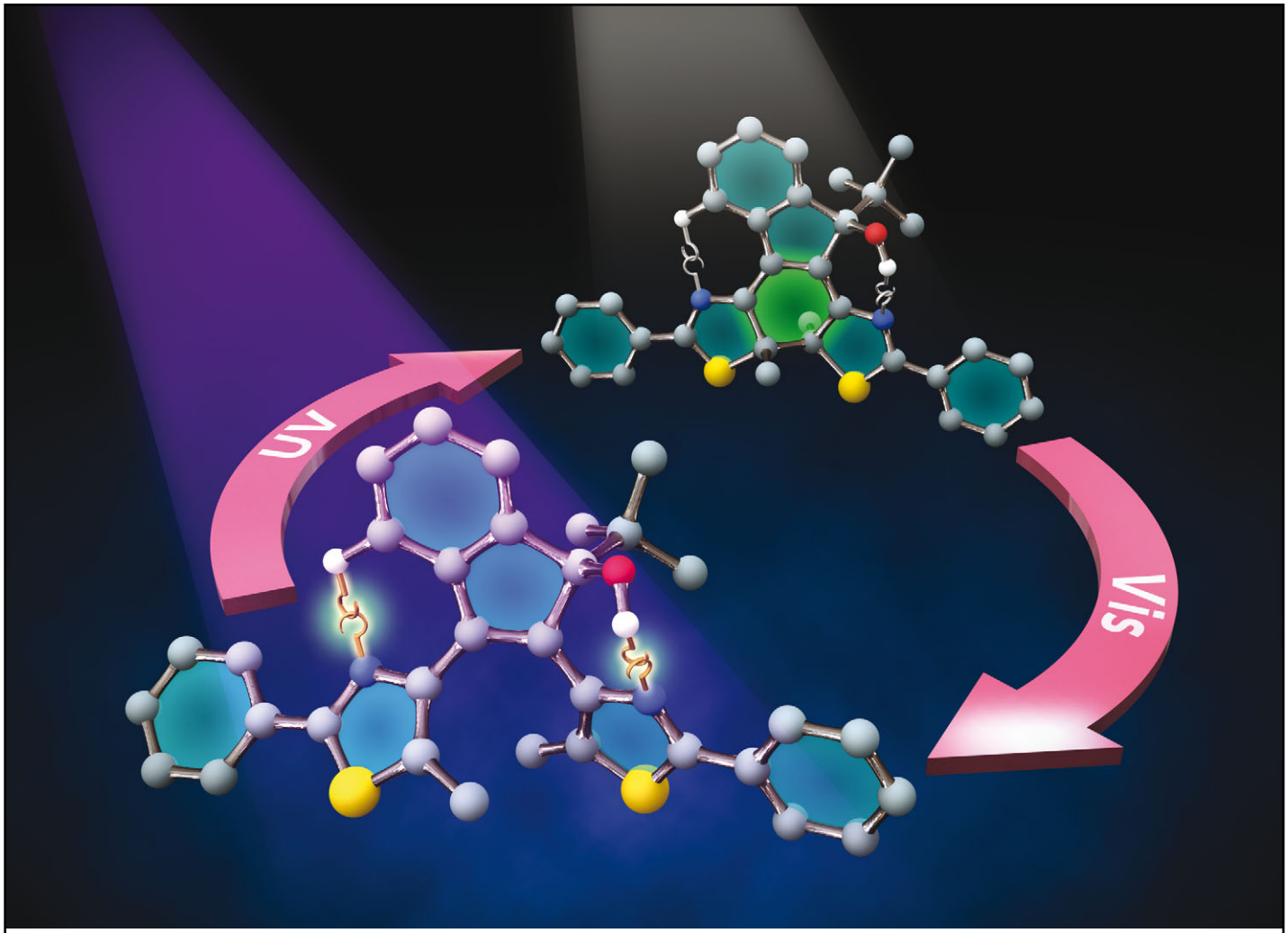

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Bisarylindenols: fixation of conformation leads to exceptional properties of photochromism based on 6π-electrocyclization

Photochromic 1-t-butyl-2,3-bisthiazolyl-1-indenol was synthesized. Upon 313-nm light irradiation in hexane, it showed 98% conversion to the closed form with 100% diastereoselectivity as well as a ring-closing quantum yield of 85%. The collaborative interaction between two sets of intramolecular hydrogen bonds and the steric restriction of a t-butyl group worked efficiently to fix its conformation in favor of cyclization in a diastereoselective manner.

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COMMUNICATION

Bisarylindenols: fixation of conformation leads to exceptional properties of photochromism based on 6π-electrocyclization†

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Thermally irreversible photochromic 1-*tert*-butyl-substituted 2,3-bisthiazolylindenol has been synthesized. It showed perfect diastereoselectivity and high ring-closing quantum yield with high conversion ratio to the closed form. The collaborative interaction of two intramolecular hydrogen bonds and the steric restriction fixed the conformation in favour of cyclization in a highly diastereoselective manner.

In contrast to ground-state synthetic organic reactions,[1] it is not easy to lead a photochemical reaction to one of several possible stereoisomers without undergoing other incidents such as emission of fluorescence, intersystem crossing, or thermal de-excitation, since they proceed by way of excited states having substantially higher energy. Photochemical reactions are, thus, less controllable than the corresponding ground-state reactions.[2]

High photon economy (large quantum yield) as well as the high stereoselectivity are required when photoreactions occur in biological systems[3] since a large quantum yield saves the living cells from prolonged exposure to light, and the high stereoselectivity creates a simple system with regard to the different interactions of the photo-generated isomers of the molecules and the biological chiral environment.

We have been carrying out investigations on photochromism based on 6π-electrocyclization such as in fulgides[4] and diarylethenes.[5] There are several important properties for photochromic compounds that the compounds should possess, such as high fatigue durability,[6] facile modulation of the absorption spectra by accessible structural modifications,[7] high stereoselectivity for photochemical ring closure,[8,9] and high photoreaction quantum yields.[10,11] As 6π-electrocyclization reactions of diarylethenes obey Woodward–Hoffmann rules to proceed in a conrotatory manner with an *s-cis–cis–s-cis* configuration of the hexatriene moiety to yield a cyclohexadiene skeleton with two stereogenic sp^3 carbon atoms, it is a good template to attain high stereoselectivity as well as high efficiency of the photochemical reactions. We have already achieved high stereoselectivity of up to 100% in cyclization reactions with several diarylethenes[8j–l] with the aim of avoiding ground-state conformation of the compound which would generate a minor stereoisomer. A high quantum yield for the photocyclizations has also been achieved on a different but related system by fixing the molecular conformation in favor of cyclization.[10b] We report here that fixation of the conformation can induce not only a high quantum yield for photocyclization but also high stereoselectivity.

We have recently synthesized **1**,[10b] an ethylene acetal of 2,3-bisthiazolylindenone **2**, which showed a thermally irreversible photochromic reaction to give its closed form **1C** with a cyclization quantum yield of 0.81. In the most stable conformation of **1** as obtained by DFT calculations, we found that two sets of CH–N interactions between two hydrogen atoms on the indenone acetal part and two nitrogen atoms on the thiazole rings fix the molecule in antiparallel conformation,[12] which favors photocyclization. As these interactions are obviously weak, we considered the introduction of a stronger interaction in this photochromic system to enhance the controlling ability of the conformation. As **2** has a carbonyl group, nucleophilic alkylation will generate the tertiary hydroxy group which can form a strong hydrogen bond with the nitrogen atom on the nearest thiazole ring (**3**). In addition, as the carbon atom bearing the hydroxy group in **3** is now stereogenic, the photochemical ring closure of **3** to give **3C** will generate a pair of diastereomers. Judging from the close proximity of the hydroxy group and the nitrogen atom, the most favorable conformation will predominantly generate one of the diastereomers ($\mathbf{3C_{major}}$) (Scheme 1).

With these expectations in mind, we have synthesized four bisthiazolylindenols, **3a–3d**, and examined their diastereoselectivity and quantum yields for photocyclization.

Synthesis of bisthiazolylindenols **3a–3d** was carried out by nucleophilic addition of the corresponding alkyl- or phenyllithium reagents to bisthiazolylindenone **2**.[10b] Fortunately, X-ray crystallographic analysis of **3b** successfully revealed its structure in the crystalline state (see ESI†). The notable characteristics are the existence of a hydrogen bond between the hydroxy group and

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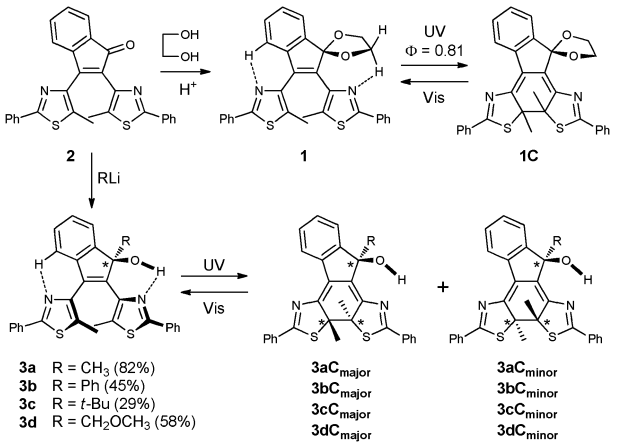
† Electronic supplementary information (ESI) available: Synthesis, analysis of photoreactions by HPLC, ^{1}H and ^{13}C NMR spectra of bisarylindenols, X-ray crystallographic analysis of **3b** and DFT calculation results of **3b**. CCDC 882504. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc35793c



Scheme 1 Synthesis of the indenol family and their conformation-controlled photochromism.

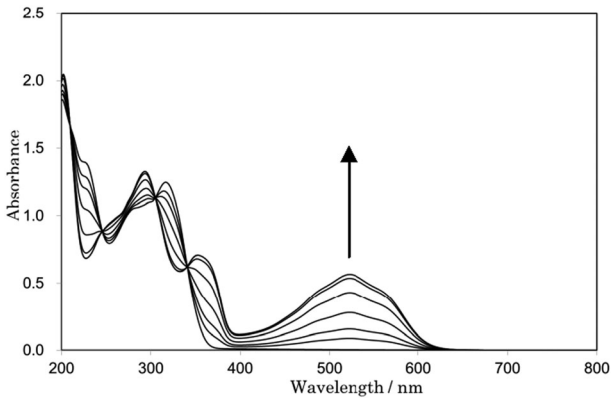


Fig. 1 The change in absorption spectra of **3c** by 313 nm light irradiation in hexane. Concentration/mol dm^{-3}: 0.450×10^{-4} (hexane). Light intensity/mW cm^{-2}: 0.153. Irradiation time/min: 0, 0.25, 0.5, 1, 2, 4, 8, 16.

Table 1 Diastereomer ratio, conversion ratio to the closed form, and quantum yields of photocyclization of indenols in solution[a]

Indenol	**3a** (Me)	**3b** (Ph)	**3c** (*t*-Bu)	**3d** (MOM)
Hexane	94.9/5.1	99.1/0.9	>99.9/<0.1	90.8/9.2
	97.6%	96.6%	97.9%	98.4%
	0.74	0.78	0.85	0.56
Diethyl ether	75.8/24.2	92.0/8.0	99.8/0.2	74.6/25.4
	97.6%	97.3%	97.0%	97.2%
	0.65	0.70	0.75	0.43
CH_3CN	71.6/28.4	86.7/13.3	99.7/0.3	75.6/24.4
	93.0%	92.9%	94.9%	96.2%
	0.49	0.60	0.64	0.44

[a] Upper numbers: ratio of diastereomers. Middle numbers: conversion percentage to the closed form at the photostationary state of 313 nm light irradiation. Lower numbers: quantum yield for major closed form generation by 313 nm light irradiation.

the nitrogen atom (OH–N distance: 215.7 pm), and a positive hydrogen bond-like interaction between the phenyl hydrogen on the indenol moiety and the other nitrogen atom (C(indenol Ph)-H–N distance: 274.3 pm). These two interactions fix the conformation of **3b** in favor of cyclization.

The presence of two conformers, hydrogen bonding and non-hydrogen bonding, for **3b** and **3c** may be verifiable from ^{1}H NMR. However, they showed only one set of signals in several deuterated solvents (cyclohexane-d_{12}, tetrahydrofuran-d_8 and acetonitrile-d_3; corresponding to the solvents used for the photoreactions) at room temperature. IR data of the broad OH stretching vibrations also did not provide any evidence of multiple conformations.

The indenols were then subjected to photochromic reactions by irradiation with 313 and 514 nm light in hexane, diethyl ether and acetonitrile (with different polarities) to see the effect of the intramolecular hydrogen bonds. Typical absorption spectral changes of **3c** in hexane upon irradiation of 313 nm light are shown in Fig. 1, and the diastereoselectivities, conversion ratios to the closed form and quantum yields of the photocyclization of **3a–3d** are summarized in Table 1.

The diastereoselectivity,[13] shown in Table 1, is apparently higher when the alkyl/aryl substituent is larger. This is because the steric repulsion is enhanced for the less stable conformation when the substituent is large. This effect is the largest for **3c** with a *t*-Bu group. When the photoreaction was carried out in hexane, the minor diastereomer was not observed, although tiny amounts were detected in diethyl ether and acetonitrile. This is because the solvent molecules did not interfere with the intramolecular hydrogen bond in hexane. As for **3d** possessing a methoxymethyl (MOM) group, it exhibited lower diastereoselectivity than **3a** having a methyl group, although the MOM group is larger than the methyl group. This is interpreted in terms of a partial replacement of the hydrogen bond (OH–N) by the other hydrogen bond (OH–OMe) forming a five-membered ring. The latter hydrogen bond enables the rotation of the single bond between the "right" thiazole ring and the indenol part so that diastereoselectivity is significantly lowered.

Among the three solvents employed, hexane always led to the highest diastereoselectivity. In ether or acetonitrile, heteroatoms with the lone pair on the solvent molecules interfered with the formation of intramolecular OH–N hydrogen bonds so that the fixation of the conformation was not so complete.

For **3c**, the influence of the difference in solvent polarity is the smallest (practically 100/0 in hexane, 99.8/0.2 and 99.7/0.3 in ether and acetonitrile, respectively) since the bulky *t*-Bu group prevented **3c** from adopting the less stable conformation, irrespective of the solvent polarity. And yet, the least polar hexane gave the highest diastereoselectivity.

Similar tendencies were observed for the cyclization quantum yield of the indenols (Table 1). As the alkyl/aryl substituent becomes larger, the cyclization quantum yield to form the major closed form becomes larger. For **3c** possessing a *t*-Bu group, it showed the largest quantum yield of $\mathbf{3cC_{major}}$ generation. In contrast, **3d**, possessing a functional group capable of forming another hydrogen bond, showed rather low cyclization quantum yields. These results can be interpreted as follows: the replacement of the OH–N hydrogen bond with the OH–OMe hydrogen bond increases the amount of molecules with parallel conformation[12] which cannot cyclize in a conrotatory manner upon light irradiation.

It should be noted that the conversion ratios of the open forms to the closed forms upon 313 nm light irradiation are exceptionally high for all of the indenols examined (Table 1)

due to the large ring-closing quantum yields. As their ring-opening reactions proceed entirely upon 514 nm light irradiation, photochromism of the indenol family is a highly efficient system in light of the switching of the molecular structure.

Judging from the three properties, *i.e.*, the diastereoselectivity, quantum yield of photocyclization, and conversion ratio to the closed form, **3c** having a *t*-Bu group can be considered the best among all the compounds examined. With the collaboration between the intramolecular OH–N and CH–N hydrogen bonds and the sterically demanding *t*-Bu group, generation of the less stable conformation was almost entirely prevented and the molecules were fixed in the more stable antiparallel conformation, which led to high diastereoselectivity. In addition, fixation of the conformation also resulted in an increase in the cyclization quantum yield to the highest level (≥ 0.8) for 6π-electrocyclization of thermally irreversible photochromic compounds in solution known so far.[10,11] The stereogenic carbon atom on the indenol part of **3c** induced the helically chiral arrangement of two thiazolyl groups by the two sets of hydrogen bonds. Upon UV irradiation, when $\mathbf{3cC_{major}}$ is produced, two new stereogenic carbon atoms are formed. As the nature of photochromic compounds, the conversion between the helical chirality and the point chirality of **3c** can be repeated on demand with the alternate irradiation of UV- and visible-light.

In conclusion, we have synthesized **3c**, a fascinating compound which shows both perfect diastereoselectivity and an extremely high ring-closing quantum yield with a high conversion ratio to the closed form in hexane. In this compound, the collaborative interaction between two sets of intramolecular hydrogen bonds and the steric restriction of a *t*-Bu group worked very efficiently to fix its conformation in favor of cyclization in a diastereoselective manner. These properties are highly beneficial when photochromic compounds are applied to biological systems for the switching of organic functions, or as probes for material flow within cells.

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