Optical Resolution of a Thermally Irreversible Photochromic Indolylfulgide

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The first optical resolution of a photochromic fulgide is performed for a thermally irreversible indolylfulgide to give a pair of enantiomers of helical chirality, and their optical properties and photochemical and thermal enantiotopomerization processes are investigated.

As an optically active photochromic compound can change its chiroptical properties according to the photochromic reaction, it can send more information than optically inactive (either racemic or non-chiral) photochromic compounds, *i.e.* in addition to the reversible changes of properties associated with the change of structure, such as the absorption spectra, reversible changes of chiroptical properties as well.

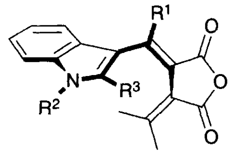
We are interested in thermally irreversible photochromic systems with optical activity,[1,2] and have already reported the elucidation of the enantiotopomerization process of a helically chiral furylfulgide **1**.[3] The enantiotopomerization of **1** occurs when the 4-H of the furan ring passes by the *E*-methyl of the isopropylidene group (Fig. 1). This finding prompted us to synthesize and resolve the helically chiral fulgides which hardly enantiotopomerize. Here we report the first optical resolution of a conformationally enantiomeric fulgide.

To prevent the enantiotopomerization of fulgides, three things must be considered: (i) the aromatic ring must have a large substituent on C-4 (such as 4,5-benzoannulation), so that the major enantiotopomerization process observed for **1** should be avoided; (ii) it is preferable that the isopropylidene group and/or the 2-methyl group of the aromatic ring are substituted with larger groups, in order to prevent the minor pathway of enantiotopomerization of **1**, *i.e.* passing of the 2-methyl of the aromatic ring by the *E*-methyl of the isopropylidene group; (iii) as the Z-isomer might enantiotopomerize easily, the photochromic system should not involve the *E*–*Z* isomerization process.[4] With these requirements in mind, we synthesized indolylfulgides **2**[5]–**7**, and carried out optical resolution of them.

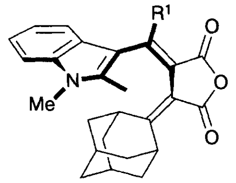
Details of the synthesis and photochromism of indolylfulgides **3**–**7** will be reported separately. The possibility of separation of enantiomers of each indolylfulgide was examined by an HPLC apparatus. Among the chiral columns used, only the one with cellulose tris(3,5-dimethylphenylcarbamate) (Daicel Chem. Ind., Ltd., CHIRALCEL® OD-H) could resolve a few of the fulgides when a 10:90 (*v*/*v*) mixture of propan-2-ol–hexane was used as eluent. Although the *E*-forms of fulgides **2*E***–**5*E*** showed two well-resolved peaks, **6*E*** and **7*E*** showed ill-resolved peaks. Therefore indolylfulgides with an adamantylidene group were found to be unsuitable for optical resolution.

Among the resolution-amenable indolylfulgides, only **4*E*** did not enantiotopomerize in solution at room temperature. Furthermore, UV irradiation of the isopropyl indolylfulgide **4*E***‡ did not afford any detectable amount of **4*Z*** during photoirradiation, similarly the corresponding furylfulgide **1*E*** did not afford **1*Z***. Thus, optical resolution of **4*E*** with HPLC was carried out.

The resolution was successful to give **4*E*$_f$** (99.8% e.e.; the enantiomer moving faster in the chiral column) and **4*E*$_s$** (92.7%



	R^1	R^2	R^3
2*E*	Me	Me	Me
3*E*	Me	Et	Me
4*E*	Pr^i	Me	Me
5*E*	Me	Me	Et



	R^1
6*E*	Me
7*E*	Pr^i

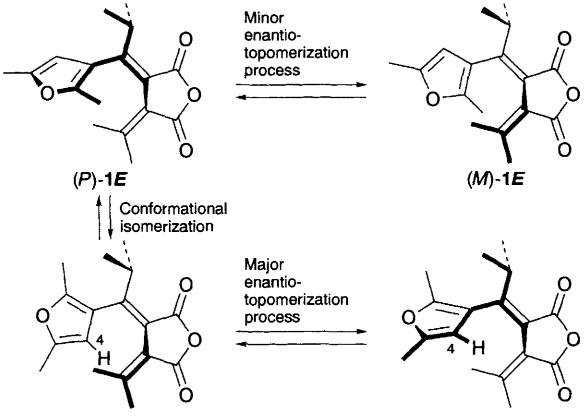


Fig. 1 Major enantiotopomerization process of furylfulgide **1**

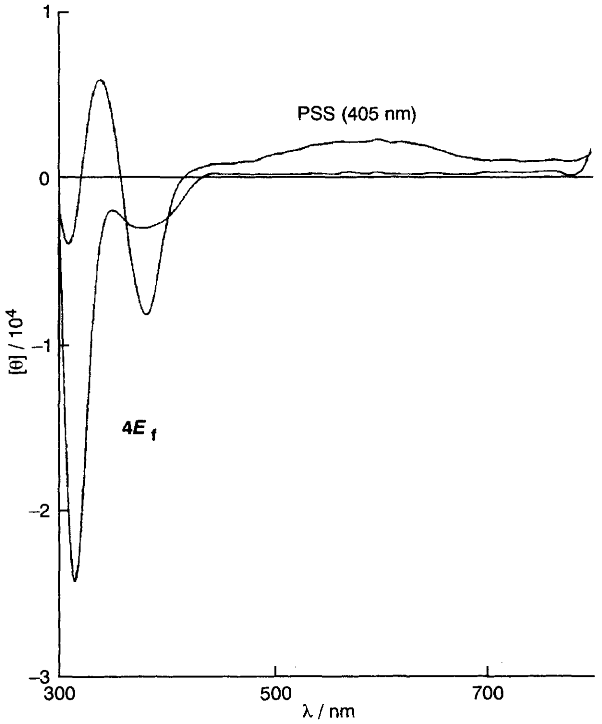


Fig. 2 CD spectra of **4*E*$_f$** and the photostationary state of 366 nm light irradiation of **4*E*$_f$** (**4*E*$_f$**:**4C** = 19:81) in toluene (c 2.1 × 10^{-4} mol dm^{-3})

e.e.; moving slower). Irradiation with 405 nm light of a toluene solution of $\mathbf{4}E_s$ gave the photostationary state (PSS) (**4***E* : **4**C = 19:81). Irradiation with visible light (>580 nm) of the PSS mixture reproduced $\mathbf{4}E_s$, whose optical purity remained unchanged. CD spectra of $\mathbf{4}E_f$ and the PSS produced by 405 nm light irradiation in toluene are shown in Fig. 2.

In order to assess the resistivity towards enantiotopomerization of **4***E*, thermal and photochemical treatments were examined. Solutions of $\mathbf{4}E_f$ in toluene [110.6 (reflux) and 56.3 °C (temperature of toluene in the reaction vessel surrounded by refluxing acetone)] or in benzene [80.1 °C (reflux)] were kept at constant temperature and the change in enantiomeric purity as a function of heating time was monitored by HPLC. The rate constants of enantiotopomerization at the temperature examined were calculated to be 33.9×10^{-1} (384 K), 24.4×10^{-2} (353 K) and 13.1×10^{-3} (329 K) h^{-1}, respectively. The Arrhenius activation energy of enantiotopomerization of **4***E* in the aromatic hydrocarbon obtained from the plot of ln *k* as a function of T^{-1} was 107 kJ mol^{-1}. By analogy with the enantiotopomerization of furylfulgide **1**, the enantiotopomerization is supposed to occur when the 2-methyl group of the indole ring passes by the *E*-methyl of the isopropylidene group. AM1 molecular orbital calculations[6] supported this result: the activation enthalpy of the above process was calculated to be 113 kJ mol^{-1}.§

Enantiotopomerization of **4***E* during UV irradiation was next examined. The toluene solution of a PSS of $\mathbf{4}E_f$ (*c* 1.47×10^{-4} mol dm^{-3}, optical purity 93.7% e.e.) was continuously irradiated with 405 nm light (light intensity: 0.694 mW cm^{-2}), and the change of the ratio of enantiomers of **4***E* was monitored by HPLC. The optical purity decreased to 75.0% e.e. after 7 h irradiation. Because thermal enantiotopomerization is negligible at room temperature, the isomerization might have occurred at the scarcely detectable *Z*-form. As AM1 calculations predicted the activation enthalpy of enantiotopomerization of the *Z*-form to be 21 kJ mol^{-1},§ *Z*-form molecules, once produced from *E*-form molecules, are considered to enantiotopomerize quite easily.

In summary, we have succeeded in the optical resolution of an indolylfulgide **4***E*. Although **4***E* showed photochromic reaction with retention of chirality, prolonged irradiation with 405 nm light of the photostationary state or thermal treatment resulted in gradual enantiotopomerization. A project to determine the absolute stereochemistry of the resolved enantiomers is under way.

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Footnotes

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‡ **4***E*: λ_{max} 385 nm (ε_{max} 4790 mol^{-1} dm^3 cm^{-1}, toluene). **4**C: λ_{max} 574 nm (ε_{max} 6180 mol^{-1} dm^3 cm^{-1}, toluene).

§ AM1 molecular orbital calculations were done on a CAChe system. The transition-state geometries obtained by AM1 calculations assured that only one of the frequencies was negative. For optimized ground-state conformations, all the frequencies were positive. Neither abnormal atom distances nor bond angles were observed.

References

1 For a review on asymmetric photochemical reactions, see Y. Inoue, *Chem. Rev.*, 1992, **92**, 741. However, this article does not include examples of asymmetric *photochromic* reactions.

2 For examples of optical resolution of photochromic compounds, see (*a*) highly substituted stilbenes: B. L. Feringa, W. F. Jager and B. de Lange, *J. Am. Chem. Soc.*, 1991, **113**, 5468; *J. Chem. Soc., Chem. Commun.*, 1993, 288; (*b*) spiropyran derivatives: B. Stephan, A. Mannschreck, N. A. Voloshin, N. V. Volbushko and V. I. Minkin, *Tetrahedron Lett.*, 1990, **31**, 6335.

3 Y. Yokoyama, T. Iwai, Y. Yokoyama and Y. Kurita, *Chem. Lett.*, 1994, 225.

4 Y. Yokoyama, T. Goto, T. Inoue, M. Yokoyama and Y. Kurita, *Chem. Lett.*, 1988, 1049; Y. Yokoyama, T. Iwai, N. Kera, I. Hitomi and Y. Kurita, *Chem. Lett.*, 1990, 263.

5 A. Kaneko, A. Tomoda, M. Ishizuka and R. Matsushima, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 3569; Y. Yokoyama, T. Tanaka, T. Yamane and Y. Kurita, *Chem. Lett.*, 1991, 1125.

6 M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902.