ORGANIC
LETTERS

2011
Vol. 13, No. 7
1856–1859

Enantiodifferentiating Photoisomerization of (*Z*,*Z*)-1,3-Cyclooctadiene Included and Sensitized by Naphthoyl-Curdlan

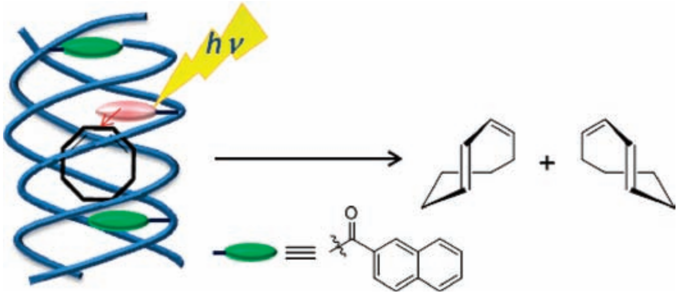
Gaku Fukuhara,* Mami Imai, Cheng Yang, Tadashi Mori, and Yoshihisa Inoue*

Department of Applied Chemistry, Osaka University, 2-1 Yamada-oka, Suita 565-0871, Japan

gaku@chem.eng.osaka-u.ac.jp; inoue@chem.eng.osaka-u.ac.jp

Received February 8, 2011

ABSTRACT

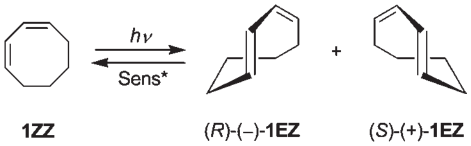


6-*O*-(2-Naphthoyl)curdlan was newly synthesized as a sensitizing polysaccharide host to examine the chiroptical properties, supramolecular complexation, and photochirogenic behavior with (*Z*,*Z*)-1,3-cyclooctadiene (1ZZ). The enantiodifferentiating photoisomerization of 1ZZ included and sensitized by this polysaccharide host gave a highly strained chiral (*E*,*Z*)-isomer in up to 8.7% enantiomeric excess (ee) in solution and 11.7% ee in the solid state, which are the highest values ever reported for a supramolecular photochirogenesis of 1EZ.

Photochirogenesis,[1] which opens a channel to optically active compounds via thermally forbidden routes, is one of the most challenging goals in current photochemistry. A supramolecular approach to photochirogenesis is advantageous due to the dual stereocontrol in both ground and excited states, and is also intriguing from an entropic point of view, as the enantiodifferentiation occurs in an inherently low entropic (well-organized) environment.[1b,c,2]

In a nonsupramolecular regime, the enantiodifferentiating photoisomerization of (*Z*,*Z*)-1,3-cyclooctadiene (**1ZZ**) (Scheme 1) sensitized by optically active arene(poly)carboxylates was examined to give chiral (*E*,*Z*)-isomer (**1EZ**) in modest enantiomeric excess (ee) of 17.6% with (−)-menthyl mellitate and 1.2% with di-(−)-menthyl 1,4-naphthalenedicarboxylate.[3] These are highly contrasting to the much higher ee values reported for cycloheptene[4] and cyclooctene,[5] proving the difficulty of achieving high ee for **1EZ** and the necessity to invent a new methodology.

Scheme 1. Enantiodifferentiating Photoisomerization of (*Z*,*Z*)-1,3-Cyclooctadiene



---

[1] For reviews, see: (a) Griesbeck, A. G.; Meierhenrich, U. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3147. (b) Inoue, Y.; Ramamurthy, V., Eds. *Chiral Photochemistry*; Marcel Dekker: New York, 2004. (c) Müller, C.; Bach, T. *Aust. J. Chem.* **2008**, *61*, 557. (d) Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052.

[2] For representative papers, see: (a) Bach, T.; Bergmann, H.; Grosch, B.; Harms, K. *J. Am. Chem. Soc.* **2002**, *124*, 7982. (b) Fukuhara, G.; Mori, T.; Wada, T.; Inoue, Y. *J. Org. Chem.* **2006**, *71*, 8233. (c) Fukuhara, G.; Mori, T.; Inoue, Y. *J. Org. Chem.* **2009**, *74*, 6714. (d) Albrecht, D.; Vogt, F.; Bach, T. *Chem.−Eur. J.* **2010**, *16*, 4284.

[3] Inoue, Y.; Tsuneishi, H.; Hakushi, T.; Tai, A. *J. Am. Chem. Soc.* **1997**, *119*, 472.

[4] Hoffmann, R.; Inoue, Y. *J. Am. Chem. Soc.* **1999**, *121*, 10702.

[5] Inoue, Y.; Ikeda, H.; Kaneda, M.; Sumimura, T.; Everitt, S. R. L.; Wada, T. *J. Am. Chem. Soc.* **2000**, *122*, 406.

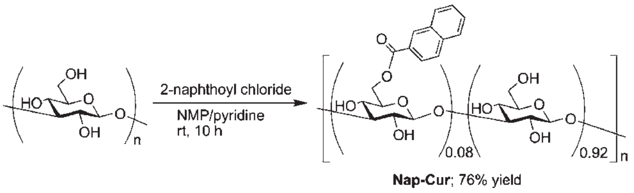
10.1021/ol2003644 © 2011 American Chemical Society
Published on Web 03/01/2011

More recently, supramolecular approaches were applied to this photochirogenic reaction. Thus, the photoisomerization of **1ZZ** was mediated by chiral sensitizing hosts, naphthalene-appended molecular clips,[6] and cyclodextrins,[7] to give **1EZ** in low 0.7% and 4.6% ee, respectively. These results revealed that achieving high ee for **1EZ** is an equally difficult task even in supramolecular photochirogenesis. Nevertheless, this approach is worth expanding from such simple clips and macrocycles to polymeric biomolecules, where the host structures are anticipated to be more dynamically manipulated by various environmental factors.

Curdlan (Cur) is a linear glucan composed of (1→3)-linked *β*-D-glucose units and is known to form a triple helical structure.[8] The most intriguing feature of Cur is the ability to reversibly denature/renature by simply changing the solvent from water or aqueous acidic solution to DMSO or aqueous alkaline solution.[8,9] Thus, Cur host is expected to provide an induced chiral environment fitted to the size and shape of the target guest through reversible complexation equilibrium with dynamic conformational changes.

In this study, we newly synthesized a sensitizer-appended Cur, 6-*O*-(2-naphthoyl)Curdlan (**Nap-Cur**), as a sensitizing host, elucidated its chiroptical properties and complexation behavior with **1ZZ**, and then investigated the enantiodifferentiating photoisomerization of **1ZZ** included and sensitized by **Nap-Cur**.

Scheme 2. Synthesis of 6-*O*-(2-Naphthoyl)curdlan (**Nap-Cur**)



By using the synthetic procedure similar to that employed previously,[10] **Nap-Cur** was prepared in 76% yield in the reaction of 2-naphthoyl chloride with commercially available native Cur, which was swollen overnight in *N*-methyl-2-pyrrolidinone at 130 °C prior to the reaction (Scheme 2). The degree of substitution of **Nap-Cur** obtained was determined as 0.08 from the integrated areas of aromatic versus sugar proton signals in the ^{1}H NMR spectrum; see Figure S1 in the Supporting Information (SI).

The chiroptical properties of **Nap-Cur** were examined in DMSO and aqueous solutions. The CD spectrum of **Nap-Cur** measured in DMSO showed an extremely weak negative Cotton effect at the ^1L_a band of Nap centered at 280 nm (Figure 1, black line; the wavelength region < 260 nm was masked by the DMSO absorption), suggesting that the Cur host is uncoiled to a single strand. In an aqueous solution containing 10% DMSO, the negative Cotton effects at the ^1B_b and ^1L_a bands were greatly enhanced, while the ^1L_a and ^1L_b peaks were diffused with appreciable bathochromic shifts (Figure 1, red line). The large negative CD extremum observed at 246 nm is likely to be the first half of a negative couplet caused by the exciton coupling interaction of the adjacent Nap groups introduced to Cur. This is because a clear bisignate CD pattern was observed for a 5% DMSO solution of **Nap-Cur** in a thinner 1-mm cell, and its crossover wavelength was very close to the peak top (237 nm) of the ^1B_b band of methyl 2-naphthoate used as a reference compound. According to the exciton chirality theory,[11] the negative couplet observed for **Nap-Cur** indicates that the Nap chromophores are helically arranged in a counterclockwise (left-handed) fashion on the triple helical Cur backbone. Such a dramatic chiroptical property change in DMSO versus aqueous solution indicates that the original feature of Cur to reversibly denature/renature in the two solvents is preserved even after the Nap modification. It is of particular interest that the hydrophobic Nap moieties in **Nap-Cur** are incorporated in the right-handed helical triplex Cur to give the

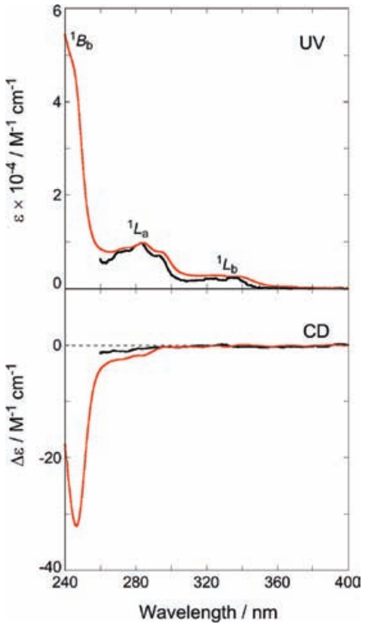


Figure 1. UV/vis (top) and CD (bottom) spectra of 7.5 *μ*M (in chromophore unit) solutions of **Nap-Cur** in DMSO (black) and in 1:9 (v/v) DMSO−H$_2$O (red), both measured in a 1-cm cell at 25 °C. Note that the molar extinction coefficient (*ε*) and molar ellipticity (Δ*ε*) were calculated by using the chromophore concentration (not monomer unit).

---

(6) Fukuhara, G.; Klärner, F.-G.; Mori, T.; Wada, T.; Inoue, Y. *Photochem. Photobiol. Sci.* **2008**, 1493.

(7) Yang, C.; Mori, T.; Wada, T.; Inoue, Y. *New J. Chem.* **2007**, *31*, 697.

(8) For reviews, see: (a) Sakurai, K.; Uezu, K.; Numata, M.; Hasegawa, T.; Li, C.; Kaneko, K.; Shinkai, S. *Chem. Commun.* **2005**, 4383. (b) Numata, M.; Shinkai, S. *Adv. Polym. Sci.* **2008**, *220*, 65.

(9) (a) Yanaki, T.; Norisuye, T.; Fujita, H. *Macromolecules* **1980**, *13*, 1462. (b) Deslandes, Y.; Marchessault, R. H.; Sarko, A. *Macromolecules* **1980**, *13*, 1466.

(10) Fukuhara, G.; Inoue, Y. *Chem. Commun.* **2010**, *46*, 9128.

left-handed helical arrangement, which is consistent with the CD spectral behavior of the other chromophore-modified Cur reported previously.[10]

The complexation behavior of **1ZZ** with **Nap-Cur** was examined in a 3:7 DMSO−H_2O mixture by UV and CD spectroscopy.[12] As shown in Figure 2, the addition of **1ZZ** augmented the UV absorption in the **1ZZ**-absorbing region (240−270 nm), but decreased the intensity of the negative CD signal at 246 nm. The CD spectral change, a smaller negative peak, may be attributed to a positive Cotton effect induced to the π−π^* transition of **1ZZ** at 240−270 nm and/or a reduced couplet amplitude of the ^1B_b band of **Nap-Cur** due to the conformational changes upon inclusion of **1ZZ**.[13] The latter effect seems dominant, since the CD intensity change is not seen over the entire **1ZZ**-absorbing region but restricted to the Nap's ^1B_b band and the addition of **1ZZ** to native Cur induced only negative CD signals in a control experiment.

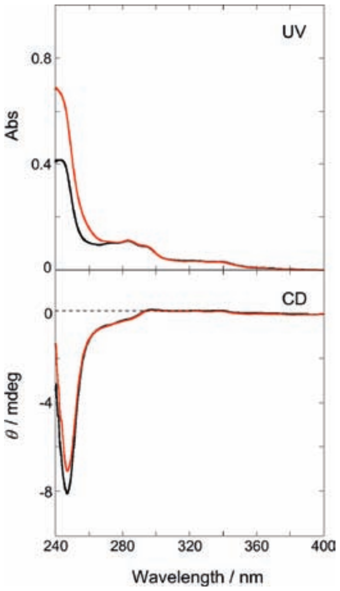


Figure 2. UV/vis (top) and CD (bottom) spectra of 0.75 mM (in monomer unit) solutions of **Nap-Cur** in the presence (red) and absence (black) of 0.5 mM **1ZZ** in 3:7 (v/v) DMSO−H_2O, measured in a 2-mm cell at 25 °C.

The fluorescence spectral behavior of **Nap-Cur** was examined in the presence and absence of **1ZZ** in DMSO−H_2O (Figure S4 and Table S1 in the SI). **Nap-Cur** fluorescence was red-shifted and band-broadened compared to that of methyl 2-naphthoate (used as a reference), suggesting incorporation of excimer fluorescence, which was revealed indeed by the lifetime measurement. Thus, the fluorescence decay profile of **Nap-Cur** was essentially multicomponent in all examined cases, but could be tentatively analyzed as a sum of two exponential functions ($\chi^2 = 1.2$) to give "representative" lifetimes of ca. 6 and 14 ns when measured at 380 nm (the peak top). When measured at 480 nm (the low-energy end), the decay became single-exponential to give a longer lifetime of 24 ns ($\chi^2 = 1.3$), which may be assigned to an excimer. However, the **Nap-Cur** solutions were slightly opaque and light-scattering (Figure S4a, SI), and hence the quantitative fluorescence quenching experiment was not feasible. Nevertheless, upon addition of 2.5 mM **1ZZ**, the fluorescence was appreciably quenched (Figure S4b, SI), but the lifetime did not change (Table S1, SI), suggesting possible operation of the static quenching of excited Nap by **1ZZ** in a host cavity.

The enantiodifferentiating photoisomerization of **1ZZ** sensitized by **Nap-Cur** was performed in DMSO and 3:7 DMSO−H_2O solutions, as well as in the solid state, at various temperatures (Table 1). The ee of **1EZ** obtained was a critical function of solvent, temperature, irradiation time, guest concentration, and phase. Upon irradiation in DMSO at 25 °C, almost racemic **1EZ** (0.7% ee) was produced with a low *E*/*Z* ratio of 0.012, while the use of a 3:7 DMSO−H_2O mixture as solvent led to much better 6.9% ee and *E*/*Z* ratio of 0.110 under comparable irradiation conditions. This contrasting result is compatible with the fact that **Nap-Cur** exists as a single strand in DMSO but forms a triple helix to include **1ZZ** in DMSO−H_2O (Figure 2), and hence indicates that the photosensitization by single-stranded **Nap-Cur** gives only poor ee and *E*/*Z* ratio, whereas the supramolecular photosensitization by triple-helical **Nap-Cur** affords much better ee and *E*/*Z* ratio, most probably due to the inclusion of **1EZ** in the triple-helical host.

Table 1. Enantiodifferentiating Photoisomerization of **1ZZ** Sensitized by 6-*O*-(2-Naphthoyl)curdlan (**Nap-Cur**) in Aqueous DMSO Solution and Solid State[a]

medium	**1ZZ** /mM	temp /°C	irrad time /min	*E*/*Z* ratio	% ee[d]
100% DMSO[b]	2.5	25	5	0.012	0.7
30% DMSO[b]	0.5	25	5	0.065	3.7
	2.5	35	5	0.042	4.5
		25	5	0.110	6.9
		15	5	0.070	5.4
		5	5	0.069	3.8
		−5	5	0.058	2.5
	2.5	25	0.5	0.013	8.7
			1	0.021	7.3
			15	0.185	4.0
			30	0.221	3.1
			60	0.226	2.1
solid state[c]	–[c]	25	60	0.100	2.6
		−50	60	0.088	4.8
		−100	60	0.029	7.1
		−160	60	<0.001	11.7

[a] Irradiated under N_2 with an ultra-high-pressure Hg lamp (500 W) fitted with a UV-29 glass filter. [b] [**Nap-Cur**] = 0.5 mM (in monomer unit). [c] The concentration of **Nap-Cur** and **1ZZ** was not determined. [d] Error in ee < 0.4%.

---

(11) Berova, N.; Bari, L. D.; Pescitelli, G. *Chem. Soc. Rev*. **2007**, *36*, 914.

(12) For the procedures for sample preparation, see the Supporting Information.

(13) Qualitative analysis of the titration data to determine the association constant was not feasible due to the partial spectral overlap of **1ZZ** with **Nap-Cur**.

However, the product's ee was reduced at lower guest concentration or temperature and by extending irradiation time, and the highest ee of 8.7% was reached upon 0.5 min irradiation of 2.5 mM **1ZZ** in DMSO$-$H$_2$O at 25 °C (Table 1). The irregular decrease of ee at 35 °C may be attributed to the decomplexation of **1ZZ** (which was revealed by the recovery of CD intensity at 35 °C shown in Figure S5 in the SI).

The effects of irradiation period on the ee and *E*/*Z* ratio were investigated in further detail. As shown in Figure 3, the *E*/*Z* ratio smoothly increased with increasing irradiation time to reach a plateau after 30 min, from which we determined the *E*/*Z* ratio at the photostationary state, $(E/Z)_{\text{pss}}$, as 0.23. Prolonged irradiations led to the clear deterioration of ee from 8.7% at 0.5 min to 2.1% at 60 min, indicating that the reverse photoreaction is also enantiodifferentiating with a preference for the same enantiomer produced in the forward reaction, as was the case with the supramolecular photoisomerization of cyclooctene included and sensitized by modified cyclodextrin hosts.[2b] Thus, experimentally the shortest irradiation (0.5 min) gave the highest ee of 8.7% and a further extrapolation afforded a hypothetical ee of 13.4% at 0 min.

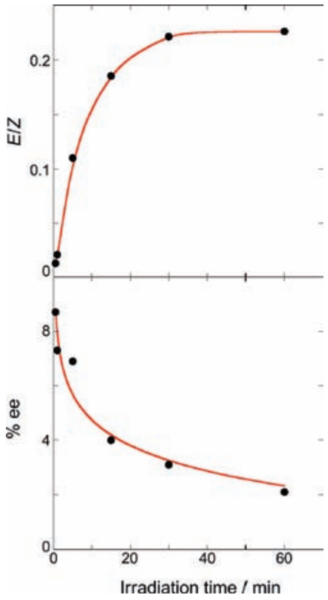


Figure 3. *E*/*Z* ratio and ee values obtained upon enantiodifferentiating photoisomerization of **1ZZ** by **Nap-Cur** in 30% DMSO at 25 °C as a function of irradiation time.

Interestingly, the inclusion complex of **1ZZ** with **Nap-Cur**, prepared as precipitates by gradually adding water to a DMSO solution of both components (see the SI), also gave **1EZ** upon irradiation.[12] This may not be very surprising, since the quenching of Nap singlet by **1ZZ** appears to be static, as shown in the fluorescence lifetime study. In keen contrast to the solution-phase photolysis, the ee was gradually enhanced by lowering the temperature to reach the highest 11.7% ee at -160 °C. The Eyring analysis of the ee values obtained at different temperatures gave a good straight line (Figure S6 in the SI), indicating operation of a single enantiodifferentiation mechanism. From the slope and intercept of the plot, the differential activation parameters were calculated as $\Delta\Delta H^{\ddagger}_{\text{S-R}} = -0.3$ kJ mol^{-1} and $\Delta\Delta S^{\ddagger}_{\text{S-R}} = -0.5$ J mol^{-1} K^{-1}.[14] These fairly small values may reflect the restricted conformational freedoms of the complex in the solid state.

In this first supramolecular photochirogenesis mediated by sensitizer-modified polysaccharide host **Nap-Cur**, we have demonstrated that the product's ee can be controlled by optimizing the irradiation time, solvent or phase, temperature, and guest concentration. The highest ee values obtained were not very high at 8.7% in solution and at 11.7% in the solid state, but the methodologies employed in this study for controlling the product's ee should be applicable to other supramolecular photochirogenic systems. Studies along this line are currently in progress with other substrates.

Acknowledgment. G.F. is grateful for the generous support by a Grant-in-Aid for Young Scientists (start-up) (No. 20850023) from JSPS and a research grant from The Ogasawara Foundation for the Promotion of Science & Engineering. Y.I. thanks the support of this work by a Grant-in-Aid for Scientific Research (A) (No. 21245011) from JSPS.

Supporting Information Available. General experimental methods and the spectroscopic data for **Nap-Cur** and methyl 2-naphthoate. This material is available free of charge via the Internet at http://pubs.acs.org.

---

(14) Eyring analysis of the obtained ee values in the solution phase was not attempted, since the product's ee was highly dependent on the irradiation time (Figure 3) and we did not have enough ee data to extrapolate to the zero conversion at all the examined temperatures.