Supramolecular Photochirogenesis with Novel Cyclic Tetrasaccharide: Enantiodifferentiating Photoisomerization of (*Z*)-Cyclooctene with Cyclic Nigerosylnigerose-Based Sensitizers

CHENG YANG,[1,2]* WENTING LIANG,[2] MASAKI NISHIJIMA,[3] GAKU FUKUHARA,[2] TADASHI MORI,[2] HIROYUKI HIRAMATSU,[4] YASUFUMI DAN-OH,[4] KAZUO TSUJIMOTO,[4] AND YOSHIHISA INOUE[2]**

[1]*Precursory Research for Embryonic Science and Technology (PRESTO), Japan Science and Technology Agency (JST), 4-1-8 Honcho Kawaguchi, Saitama 332-0012, Japan*

[2]*Department of Applied Chemistry, Osaka University, Suita 565-0871, Japan*

[3]*Office for University-Industry Collaboration, Osaka University, Suita 565-0871, Japan*

[4]*Hayashibara Co., Ltd., Okayama 700-0907, Japan*

ABSTRACT Isophthalic and terephthalic acid monoesters of cyclic nigerosyl-(1→6)-nigerose (CNN), a cyclic tetrasaccharide composed of four D-glucopyranosyl residues connected by alternating α-1,3- and α-1,6-linkages, were synthesized as novel chiral supramolecular sensitizers for enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**) to planar chiral (*E*)-isomer (**1E**). Despite the saucer-shaped shallow cavity of CNN that does not immediately guarantee strong ground-state interactions with **1Z**, the sensitizer-appended CNNs afforded optically active **1E** in such enantiomeric excesses that are much improved than those obtained with an α-cyclodextrin analog and comparable with those obtained with a β-cyclodextrin analog. Interestingly, the enantiomeric excess values obtained were a critical function of temperature and solvent to show an inversion of the product chirality by changing the environmental variants. Nevertheless, all of the differential activation parameters calculated from the temperature-dependent enantiomeric excesses gave an excellent compensatory enthalpy–entropy relationship, indicating an operation of a single enantiodifferentiating mechanism in the present chiral photosensitization with modified CNNs. *Chirality 00:000–000, 2012.* © 2012 Wiley Periodicals, Inc.

KEY WORDS: chiral photochemistry; enantiodifferentiating photoisomerization; planar chirality; cyclooctene; cyclic nigerosylnigerose; supramolecular chemistry

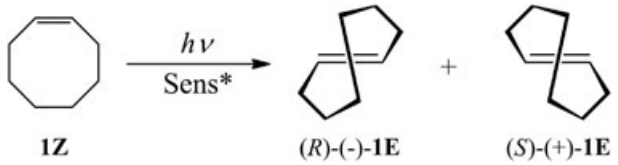
INTRODUCTION

Achieving efficient chirality transfer and amplification is one of the most intriguing topics in current chemistry. In contrast to the significant success in thermal asymmetric synthesis achieved in recent decades, there still remain substantial barriers in realizing efficient chirality transfer in the electronically excited state.[1–4] Chiral photochemistry possesses unique and attractive features, providing a direct access to highly strained compounds and a much wider temperature range expanded in particular to the lower side. At the same time, weak and short-lived chiral interactions in the excited state are difficult in general to precisely manipulate. Nevertheless, foregoing studies have revealed the critical roles of chiral source used as auxiliary or supramolecular host[5–10] and maneuverable environmental variants, such as temperature, solvent, and pressure,[11–16] as well as irradiation wavelength.[17] Thus, seeking chiral sources suitable for a specific photochirogenic system is often the most crucial and demanding task, along with the subsequent optimization of environmental variants.

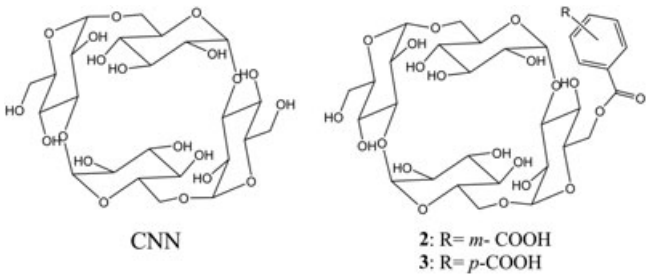
We have been employing the enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**) to planar chiral (*E*)-isomer (**1E**) (Scheme 1) as a benchmark test for evaluating the performance of a wide variety of chiral sources attached to a sensitizing chromophore.[12–14,18–23] The chiral sensitizers hitherto examined may be classified into two categories by the mode of interaction with substrate molecule; thus, a conventional molecular sensitizer uses the diastereomeric interactions in an exciplex intermediate with substrate, whereas a supramolecular sensitizer utilizes the diastereomeric interactions both in the ground and excited states to enhance the stereochemical outcomes.

In the present study, we employed a new class of cyclic tetrasaccharide (Scheme 2), *cyclo*-{→6)-α-D-Glc*p*-(1→3)-α-D-Glc*p*-(1→6)-α-D-Glc*p*-(1→3)-α-D-Glc*p*-(1→} or cyclic nigerosyl-(1→6)-nigerose (CNN),[24,25] as a chiral source. CNN was enzymatically produced from starch relatively recently, and so far, only the production, purification, and degradation behaviors have been investigated intensively.[26–28] The X-ray crystallographic analysis revealed that this tetrasaccharide possesses only a shallow saucer-like shape with a small concave at the center.[29] As a supramolecular host, CNN is known to interact with ethanol,[30] whereas a dicarboxylic acid derivative of CNN can selectively chelate some cations.[31]

Contract grant sponsor: Japan Science and Technology Agency (CY and YI).
Contract grant sponsor: Japan Society for the Promotion of Science (GF, TM, and YI).
Contract grant sponsor: Sumitomo Foundation (CY and TM).
Contract grant sponsor: Iwatani Naoji Foundation (GF).
Contract grant sponsor: Mitsubishi Chemical Corporation Fund (TM).
*Correspondence to: Y. Inoue, Department of Applied Chemistry, Osaka University, Yamada-oka, Suita 565-0871, Japan. E-mail: inoue@chem.eng.osaka-u.ac.jp; C. Yang, Department of Applied Chemistry, Osaka University, Yamada-oka, Suita 565-0871, Japan. E-mail: c.yang@chem.eng.osaka-u.ac.jp
Received for publication 22 October 2011; Accepted 12 January 2012
DOI: 10.1002/chir.22014
Published online in Wiley Online Library (wileyonlinelibrary.com).



Scheme 1. Enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**) to planar chiral (*E*)-isomer (**1E**).



Scheme 2. Chemical structure of cyclic nigerosyl-(1→6)-nigerose (CNN) and its hydrogen isophthalate and terephthalate (**2** and **3**).

We became interested in the use of CNN as a potential supramolecular host for the enantiodifferentiating photoisomerization of **1Z** because of its inherent chirality and unique chemical structure with a shallow cavity. CNN is the smallest cyclic gluco-oligosaccharide that has some similarities with the well-known analog, cyclodextrin (CD). Both are composed of the same building blocks but differ in linkage connecting the adjacent glucose units and also in shape and cavity size: shallow saucer versus truncated hollow corn. To assess the ability of CNN as a chiral source for enantiodifferentiating photosensitization, we introduced an isophthalate or terephthalate moiety to one of the CNN's 6-hydroxyl groups and investigated the enantiodifferentiating photoisomerization of **1Z** sensitized by these CNN derivatives.

EXPERIMENTAL

Instruments

Ultraviolet–visible (UV–vis) and circular dichroism spectra were measured on JASCO (Tokyo, Japan) V-560 spectrophotometer and JASCO (Tokyo, Japan) J-810 spectropolarimeter, respectively. Fast atom bombardment mass spectra were recorded on a JEOL (Tokyo, Japan) JMS-DX303 mass spectrometer. Hydrogen-1 (^{1}H) and carbon-13 (^{13}C) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DRX-600 spectrometer (Germany).

Materials

Cyclic nigerosyl-(1→6)-nigerose was obtained from Hayashibara Co., Ltd. (Okayama, Japan). Terephthaloyl chloride, isophthaloyl chloride, and other chemicals were purchased from Tokyo Chemical Industries and used without further purification.

Synthesis and Characterization of 2 and 3

Cyclic nigerosyl-(1→6)-nigerose (648 mg, 1.0 mmol), dried in vacuo at 100 °C overnight, was dissolved in dry pyridine (30 ml). To the solution was added isophthaloyl or terephthaloyl chloride (240 mg, 1.2 mmol) at 0 °C, and the resulting mixture was stirred for 2 h at 0 °C and then quenched with 5 ml of water. After removal of the solvent in vacuo, the residue obtained was dissolved in 5 ml of DMF, and the solution was poured into 30 ml of acetone to give white precipitates, which were collected by filtration and dissolved in water. The aqueous solution was subjected to reverse-phase liquid chromatography ((octadecylsily1)silica gel, 26 × 300 mm) with a gradient of 3%–30% EtOH to give pure **2** in 8% yield or **3** in 12% yield as white solid.

2: ^{1}H NMR (600 MHz, D_2O), δ (ppm): 8.31 (1H, dd, J_1 = 1.4 Hz, J_2 = 1.4 Hz), 8.00 (1H, dd, J_1 = 1.8 Hz, J_2 = 1.5 Hz), 7.99 (1H, dd, J_1 = 1.8 Hz, J_2 = 1.5 Hz), 7.44 (t, J = 10.8 Hz), 5.44 (1H, d, J = 4.0 Hz), 5.22 (1H, d, J = 4.0 Hz), 4.74 (1H, d, J = 3.6 Hz), 4.72 (1H, d, J = 3.6 Hz), 4.14–4.01 (2H, m), 3.92–3.81 (2H,m), 3.65–3.36 (18H, m), 3.08 (2H, m). ^{13}C NMR (151 MHz, D_2O), δ (ppm): 175.17, 174.15, 136.86, 133.89, 131.24, 128.78, 98.31, 97.76, 96.97, 96.46, 74.38, 73.66, 73.43, 72.58, 72.23, 71.53, 71.37, 71.28, 71.24, 70.76, 70.50, 70.03, 69.92, 69.76, 69.17, 67.34, 63.66, 59.99. High-resolution mass spectra: *m/z* calculated for $C_{32}H_{44}KO_{23}$ 835.191, found: 835.192.

3: ^{1}H NMR (600 MHz, 1:1 D_2O-DMSO-d_6): δ/ppm 8.07 (2H, d, J = 8.0 Hz), 8.02 (2H, d, J = 8.0 Hz), 5.62 (1H, d, J = 4.0 Hz), 5.34 (1H, d, J = 4.0 Hz), 4.71 (1H, d, J = 3.6 Hz), 4.66 (1H, d, J = 3.6 Hz), 4.56 (1H, dd, J_1 = 9.8 Hz, J_2 = 9.0 Hz), 4.42 (1H, dd, J_1 = 9.8 Hz, J_2 = 9.0 Hz), 3.87–3.79 (2H, m), 3.62–3.30 (16H, m), 3.23 (1H, dd, J_1 = 9.8 Hz, J_2 = 3.6 Hz), 3.16 (1H, dd, J_1 = 9.6, J_2 = 9.0 Hz), 3.10 (1H, dd, J_1 = 9.8, J_2 = 9.0 Hz), 2.90 (1H, dd, J_1 = 9.8, J_2 = 9.0 Hz). ^{13}C NMR (150 MHz), δ (ppm): 174.6, 167.8, 141.3, 130.9, 129.5, 128.6, 98.5, 98.2, 96.6, 96.4, 75.9, 74.7,74.4,74.3, 74.2, 73.9, 72.6, 71.4, 70.8, 70.5, 70.2, 69.9, 69.8, 69.7, 68.7, 67.2, 60.0. High-resolution mass spectra: *m/z* calculated for $C_{32}H_{44}NaO_{23}$ 819.217, found: 819.217.

Photoreaction

An aqueous or organic solution (3 mL) of **1Z** (1.5 mM) and sensitizer-modified CNN **2** or **3** (0.5 mM) in a quartz cell was placed in a Unisoku USP-203 cryostat (Osaka, Japan) with a quartz window for irradiation, purged with nitrogen gas, kept at a given temperature, and irradiated at 254 nm under a nitrogen atmosphere with a 30-W low pressure mercury lamp (Eikosha, Osaka, Japan) or a MAX-301 light source (a 300-W xenon lamp fitted with a band-pass filter; Asahi Spectra Co., Tokyo, Japan). An aliquot of the irradiated organic solution was analyzed by gas chromatography (GC) on a Shimadzu (Kyoto, Japan) CBP-20 (PEG) column for *E/Z* ratio. In the case of aqueous samples, the irradiated solution was extracted with pentane, and the pentane extract was subjected to the gas chromatography analysis. To determine the enantiomeric excess (ee) value, a 20% aqueous silver nitrate solution was added to the irradiated solution at 0–5 °C to form a stable Ag^+ complex with **1E**. The aqueous solution containing [Ag^+•**1E**] complex was washed with pentane and then added with stirring to a 28% aqueous ammonia solution at 0 °C to liberate **1E**, which was extracted with pentane, and the pentane extract was subjected to chiral gas chromatography analysis on a Supelco β-DEX120 column (Bellefonte, USA).

Preparation of CNN Isophthalate and Terephthalate 2 and 3

Sensitizer-appended CNNs **2** and **3** (Scheme 2) were prepared by reacting isophthaloyl or terephthaloyl chloride with CNN in pyridine under a typical reaction condition employed for the synthesis of primary rim-modified CDs.[20,22,23] However, the target compounds **2** and **3** were obtained only in low yields (<10%) after separation by reverse-phase liquid chromatography, along with small amounts of side products. Thin-layer chromatography analyses of the side products suggested formation of CNN isophthalates or terephthalates esterified at one of the secondary hydroxyl groups (with R_f similar to those of **2** and **3**) as well as bridged CNN dimers (with R_f smaller than that of native CNN. After full characterization (see the Supporting Information), the isolated CNN monoesters **2** and **3** were directly used as chiral sensitizers for photoisomerization of **1Z**.

RESULTS AND DISCUSSIONS

Enantiodifferentiating Photoisomerization of 1Z

In the previous studies,[12,13,18–20,32–34] we systematically investigated the enantiodifferentiating photoisomerization of **1Z** using a wide variety of chiral sensitizers to reveal a significant correlation between the sensitizer structure and the ee of **1E** produced. In general, aromatic sensitizers multiply substituted by bulky chiral auxiliaries with the stereogenic center located closer to the chromophore are more advantageous in inducing high enantioselectivity, presumably as a result of the congested arrangement of chiral auxiliaries around the sensitizing aromatic moiety.[34] External factors, such as temperature, solvent, and pressure, also affect the enantioselectivity.[13,15,32]

Intriguingly, the supramolecular enantiodifferentiating photoisomerization of **1Z** included and sensitized by benzoate-appended CDs in aqueous solution behaves very differently from the conventional photosensitization in organic solvents.[19,22,23] Thus, the CD derivatives bind **1Z** in the hydrophobic cavity to form the corresponding inclusion complexes in the ground state, which allows efficient chirality transfer in the subsequent photoisomerization even when the aromatic sensitizer possesses only one CD as a chiral substituent.

Supramolecular Interactions

Direct examination of the ground-state complexation of **1Z** with CNN was not feasible due to the inherently weak Cotton effects observed for **2** and **3** (*vide infra*). Indeed, the addition of **1Z** of up to 1 mM to an aqueous solution of **2** did not cause any significant change in circular dichroism spectrum. Nevertheless, the expectation that saucer-shaped CNN may form a weak complex with **1Z** prompted us to run the photosensitization with **2** and **3** in aqueous solutions at 0–40 °C to give **1E** in modest 1%–5% ee (Table 1). These ee values are comparable with or slightly better than those (1%–3% ee) obtained upon photosensitization with α-CD benzoate[20] and therefore do not immediately exclude the possibility of supramolecular photosensitization with CNN isophthalate and terephthalate.

To better understand the result, the structure of **2** was optimized by the molecular mechanics. As shown in Figure 1, the CNN moiety preserves its original saucer-like structure despite the esterification of the primary hydroxyl group. The concave is obviously too small to fully accommodate **1Z** but appears to form partial hydrophobic contacts with **1Z** in water, as evidenced by the appreciable up-field shifts and line broadening of guest proton signals upon addition of host **2** in ^{1}H NMR spectrum. As shown in Figure 2, the olefinic (H-1) and allylic (H-2) protons of **1Z** were shifted up-field by 0.14 and 0.04 ppm, respectively, upon addition of **2**, indicating loose confinement and/or π–π interactions of **1Z** with **2** in the ground state. On the other hand, the aromatic moiety, tethered to the six position of glucoside, is relatively flexible and not closely located to the stereogenic centers of CNN. These two structural features would be jointly responsible to the observed low enantioselectivity.

Experimentally, the existence of weak supramolecular interaction of CNN derivatives with **1Z** was confirmed by the very rapid photoisomerization in aqueous solutions and the appreciable decrease of ee in 10% methanol and also in methanol and ethanol (Table 1). These results may be accounted for in terms of the reduced hydrophobic interaction in polar alcoholic solvents, which is compatible with the

TABLE 1. Enantiodifferentiating photoisomerization of 1Z sensitized by cyclic nigerosyl-(1→6)-nigerose isophthalate 2 and terephthalate 3 in some solvents[1]

Sensitizer	Solvent	Temperature/°C	Irradiation time/min	*E/Z*	% ee
2	H_2O	0.5	3	0.03	−1.6
		15	3	0.03	+0.8
		30	3	0.05	+2.9
		40	3	0.06	+4.6
	10% MeOH	0.5	3	0.03	−1.1
		15	3	0.04	+0.3
		30	3	0.06	+2.2
	MeOH	−5	10	0.06	+0.3
	EtOH	−40	60	0.03	+0.6[2]
	1-Butanol	−5	10	0.13	−1.4
	Ethyl ether	−40	60	0.002	+9.3[2]
		−5	10	0.002	+5.5
		10	10	0.005	+3.1
		20	10	0.006	+2.3
	Pentane	−40	60	*c*	+0.6[2]
3	H_2O	0.5	3	0.05	+3.3
		15	3	0.06	+2.4
		30	3	0.05	+1.5
		40	3	0.08	+1.1
	10% MeOH	0.5	3	0.03	+1.3
		15	3	0.09	+0.5
		30	3	0.24	−0.3
	MeOH	−5	10	0.03	+0.9
	EtOH	−40	60	0.02	+0.9[2]
		−5	60	0.05	0.0[2]
		25	60	0.04	−0.6[2]
	1-Butanol	−5	20	*c*	−2.9
	Ethyl ether	−30	30	0.006	−7.2[2]
		−5	10	0.002	−3.4
		20	30	0.01	+0.3[2]
	Pentane	−40	60	*c*	0.0[2]

ee, enantiomeric excess.
[1][**1Z**] = 1.5 mM, [**2**] = 0.05 mM, [**3**] = 0.05 mM; Irradiated at 254 nm in a quartz cell placed in a USP-203 cryostat (Unisoku) with a 30-W low-pressure mercury lamp (Eikosha), unless noted otherwise.
[2]Irradiated at 254 nm with a MAX-301 (Asahi Spectra, a 300-W xenon lamp fitted with a band-path filter).
[3]Not determined.

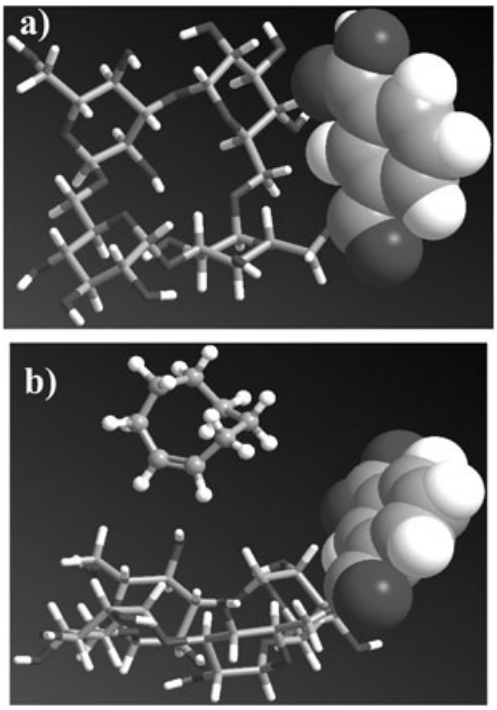


Fig. 1. (**a**) Top view of **2** and (**b**) side view of [**2**•**1Z**] complex optimized by the MM2 program; the aromatic part is emphasized as a space-filling model.

less dramatic reduction of ee in less polar butanol. Hence, we cannot rigorously rule out the minor contribution of the hydrophobic interaction in the chirality transfer process, probably in the ground and/or excited state.

Isophthalate versus Terephthalate Sensitization

Somewhat unexpectedly, the seemingly small difference in the position of the hydroxycarbonyl substituent turned out to have significant influences on the stereochemical outcomes to afford antipodal **1E** upon sensitization with CNN isophthalate **2** versus terephthalate **3**. Thus, in aqueous solution at 0.5 °C, CNN isophthalate **2** gave (−)-**1E** in 1.6% ee, whereas terephthalate **3** afforded antipodal (+)-**1E** in 3.3% ee at 0.5 °C. Also, in diethyl ether at −40 °C, isophthalate **2** gave (+)-**1E** in 9.3% ee, whereas terephthalate **3** afforded antipodal (−)-**1E** in 7.2% ee at −40 °C. It is to note that **2** and **3** share the same chiral source, CNN, but differ in substitution pattern, that is, meta versus para. Because the hydroxycarbonyl substituent at different position is not likely to sterically influence the chirality transfer process in an exciplex, we deduce that the opposite product chirality would be related to the difference in electronic structure between isophthalate and terephthalate.

Solvent Effects

The product's ee was significantly affected by the solvent properties. As mentioned earlier, sensitizer **2** gave modest enantiomeric excesses (ee's) of −1.6% to +4.6% in water but much decreased ee's upon addition of 10% methanol (Table 1). This solvent-induced ee change prompted us to further explore the solvent effects on this enantiodifferentiating photoisomerization by using organic solvents such as methanol, ethanol, butanol, ethyl ether, and pentane. The photoisomerization in polar alcoholic and nonpolar hydrocarbon solvents gave **1E** in low ee (0%–2%), irrespective of the sensitizer used (**2** or **3**). However, the use of diethyl ether as a solvent led to the formation of antipodal **1E** in the highest ee's of +9.3% and −7.2% at −40 °C upon sensitization with **2** and **3**, respectively (Table 1).

To elucidate the effects of solvent on the structure of CNN sensitizers, UV–vis and circular dichroism spectra of **2** were measured in some of the solvents used earlier. As can be seen from the UV–vis spectra of **2** (Fig. 3), the ^1L_a band at 240–250 nm is red-shifted, whereas the ^1L_b band at 280–300 nm blue-shifted by altering the solvent from butanol and ether to water and ethanol. This suggests a greater contribution of the carboxylate rather than carboxylic acid form of iso/terephthalate in more polar solvents. In contrast, the circular dichroism spectra are less informative (Fig. 4), displaying only very weak Cotton effects of similar profiles with $\Delta\varepsilon < 1.0\,M^{-1}cm^{-1}$ for both ^1L_a and ^1L_b bands. This result seems reasonable in view of the

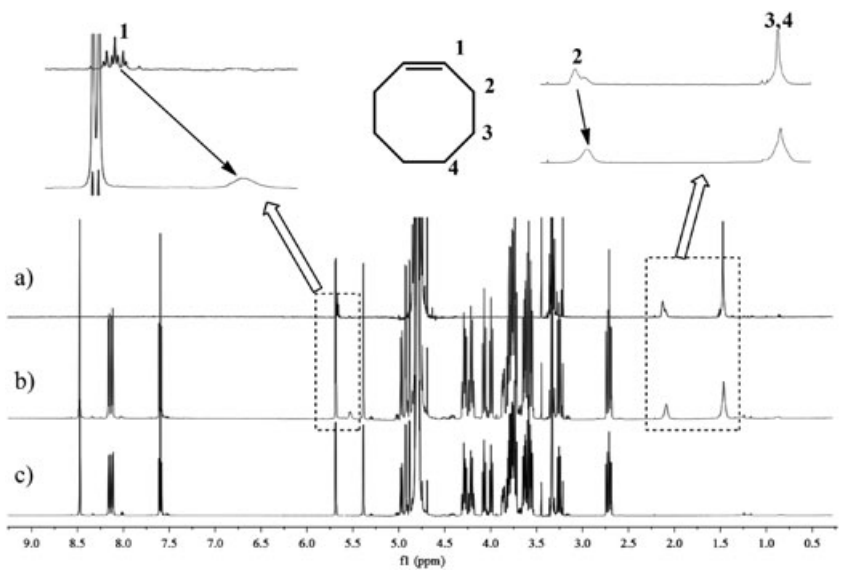


Fig. 2. Hydrogen-1 nuclear magnetic resonance spectra of (**a**) **1Z** (1.0 mM), (**b**) a mixture of **1Z** (1.0 mM) and **2** (8.0 mM), and (**c**) **2** (8.0 mM) in D_2O at 20 °C; the enlargements (top) show clear up-field shifts of olefinic H-1 and allylic H-2 proton signals, accompanied by the line broadening of all protons in the mixture (**b**).

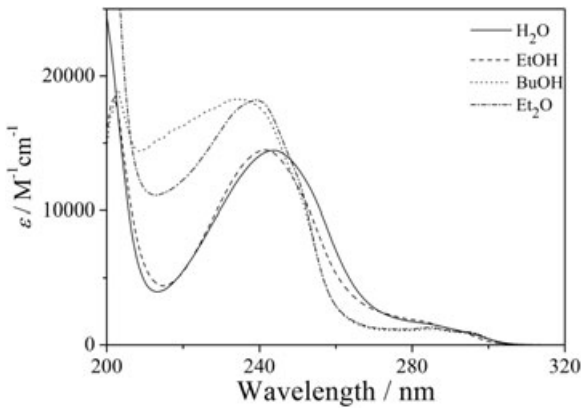


Fig. 3. Ultraviolet–visible spectra of **2** measured in water (solid line), ethanol (dashed line), butanol (dotted line), and ethyl ether (dash-dotted line) at 20 °C.

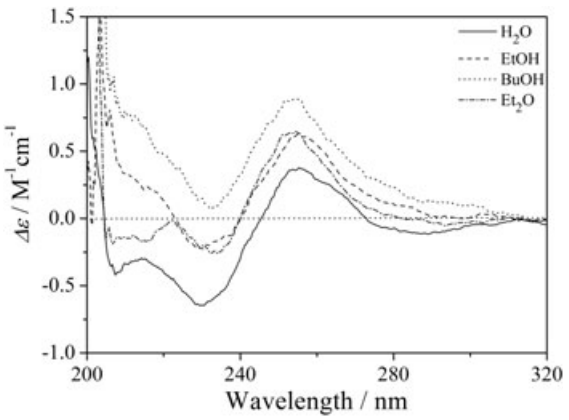


Fig. 4. Circular dichroism spectra of **2** measured in water (solid line), ethanol (dashed line), butanol (dotted line), and ethyl ether (dash-dotted line) at 20 °C.

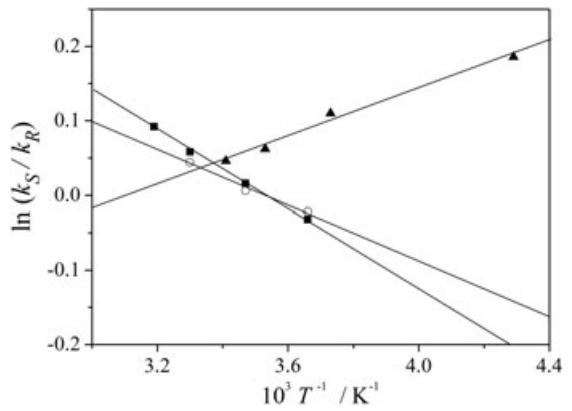


Fig. 5. Eyring plots for the enantiodifferentiating photoisomerization of 1Z sensitized by 2 in H_2O (■), 10% aqueous MeOH (○), and Et2O (▲).

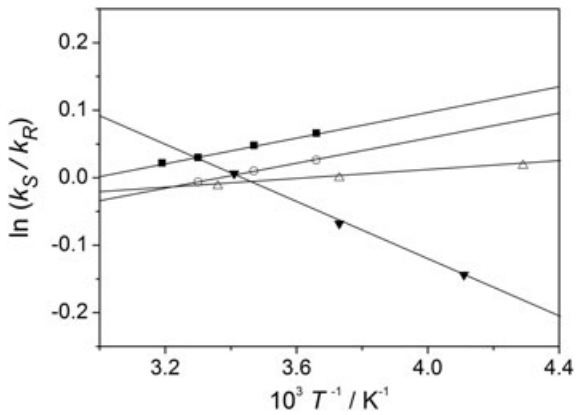


Fig. 6. Eyring plots for the enantiodifferentiating photoisomerization of 1Z sensitized by 3 in H_2O (■), 10% aqueous MeOH (○), EtOH (△), and Et2O (▼).

relatively distant position of the nearest stereogenic center from the aromatic chromophore in **2**.

Temperature Dependence Studies

As was the case in the conventional enantiodifferentiating photosensitization of **1Z** reported earlier,[12,13,18] the product's ee was a critical function of the reaction temperature, occasionally leading to an inversion of the product chirality, as shown in Table 1. To quantitatively elucidate the enantiodifferentiating mechanism, we plotted the logarithm of the relative rate constant for giving (*S*)- and (*R*)-**1E**, that is, $\ln(k_S/k_R)$ or $\ln[(100+\%ee)/(100-\%ee)]$, as a function of reciprocal temperature to obtain excellent straight lines in all the examined cases (listed in Table 1), as illustrated in Figures 5 and 6. The good straight line indicates that the enantiodifferentiation mechanism does not change at least in the temperature range employed.

To more quantitatively and globally discuss the factors and mechanism controlling the enantiodifferentiation process, we calculated the differential activation enthalpy ($\Delta\Delta H^{\ddagger}$) and entropy ($\Delta\Delta S^{\ddagger}$) from the slope and intercept of the regression line by using the established procedures.[12,33] The activation parameters obtained are listed in Table 2. It is remarkable that, although the activation parameters obtained are dynamic functions of the sensitizer and solvent used, the $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values consistently share the same sign, and the $\Delta\Delta H^{\ddagger}$ and $T\Delta\Delta S^{\ddagger}$ values are comparable in magnitude at $T = 298$ K for all the sensitizer/solvent systems. The former fact suggests the existence of equipodal temperature (T_0) at which the enthalpic gain/loss is canceled out by the entropic loss/gain, whereas the latter accounts for the very low ee's obtained at ambient temperatures. Because $\Delta\Delta G^{\ddagger} = \Delta\Delta H^{\ddagger} - T\Delta\Delta S^{\ddagger}$, the product's ee can be enhanced to the opposite direction to form the antipodal products by performing the photosensitization at temperatures lower or higher than T_0, provided that $\Delta\Delta S^{\ddagger} \neq 0$. Because of the relatively large activation parameters and

TABLE 2. Differential activation entropy ($\Delta\Delta S^{\ddagger}$) and enthalpy ($\Delta\Delta H^{\ddagger}$) changes for the formation of enantiomeric 1E in photoisomerization of 1Z mediated by 2 and 3[1]

Sensitizer	Solvent	$\Delta\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta\Delta S^{\ddagger}$/J mol^{-1} K^{-1}	$T\Delta\Delta S^{\ddagger}$[2]/kJ mol^{-1}
2	H_2O	2.2	7.8	2.3
	10%MeOH	1.5	5.4	1.6
	Et_2O	−1.3	−4.2	−1.2
3	H_2O	−0.8	−2.4	−0.7
	10%MeOH	−0.7	−2.5	−0.7
	EtOH	−0.3	−1.0	−0.3
	Et_2O	1.8	6.1	1.8

[1]Differential activation parameters derived from the Eyring plots.
[2]$T = 298$ K.

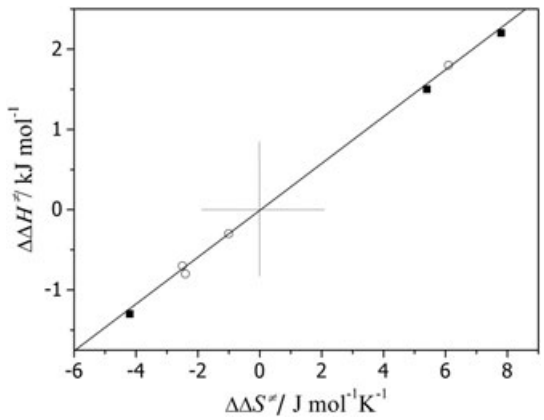


Fig. 7. Enthalpy–entropy compensation plot for the differential activation parameters obtained for the enantiodifferentiating photoisomerization of cyclooctene **1Z** sensitized by **2** (square) and **3** (open circle).

the wide applicable temperature range, the highest ee's of +9.3% and −7.2% were achieved by **2** and **3**, respectively, in ether at −40 °C and −30 °C.

Enthalpy–Entropy Compensation

In conventional enantiodifferentiating photosensitization, the compensatory $\Delta\Delta H^{\ddagger}$–$\Delta\Delta S^{\ddagger}$ relationship is often observed, confirming the mechanistic consistency throughout the reaction conditions employed.[32,35] Hence, we plotted the $\Delta\Delta H^{\ddagger}$ values against the $\Delta\Delta S^{\ddagger}$ values obtained in the present system to obtain an excellent straight line passing through the origin: $\Delta\Delta H^{\ddagger} = 0.29\Delta\Delta S^{\ddagger} - 0.04$ (correlation coefficient 0.99), as illustrated in Figure 7. This suggests that the same enantiodifferentiation mechanism is operative despite the changes in solvent and sensitizer. From the slope, we can determine that the equipodal temperature (T_0) was calculated as 292 K for this enantiodifferentiating photosensitization.

CONCLUSION

In the present study, two new cyclic tetrasaccharide sensitizers **2** and **3** were prepared by introducing a hydrogen isophthalate or terephthalate moiety to the six position of a 1,3-linked glucose unit of CNN. These CNN derivatives were used as chiral supramolecular sensitizers for mediating the enantiodifferentiating photoisomerization of **1Z** to facially chiral **1E**. The photoisomerization of **1Z** sensitized by these two CNN derivatives was appreciably accelerated in aqueous solutions to give antipodal **1E** in modest optical yields (1%–5% ee), which are comparable with those obtained upon supramolecular photosensitization with α-CD benzoate (1%–3% ee), suggesting weak hydrophobic interactions to promote hydrophobic contacts with chiral CNN moiety in the excited state. More interestingly, the photosensitization in ether afforded antipodal **1E** in the highest ee of +9.3% and −7.2%, respectively. Thus, the ee of **1E** was highly sensitive to sensitizer, solvent, and temperature employed, and the product chirality was often switched by altering solvent and temperature. The temperature-driven switching of product chirality was attributed to the nonzero differential activation entropy ($\Delta\Delta S^{\ddagger}$). The differential activation parameters were critical functions of solvent and sensitizer but still obeyed the enthalpy–entropy compensation relationship, suggesting the same enantiodifferentiation mechanism operating irrespective of the sensitizer and solvent used. The present results also demonstrate the enantiodifferentiating photoisomerization of cyclooctene functions as a sensitive benchmark test for assessing chiral auxiliaries and hosts, even in the borderline cases examined in this study.

LITERATURE CITED

1. Inoue Y. Asymmetric photochemical reactions in solution. Chem Rev 1992;92:741–770.
2. Griesbeck AG, Meierhenrich UJ. Asymmetric photochemistry and photochirogenesis. Angew Chem Int Ed 2002;41:3147–3154.
3. Inoue Y, Ramamurthy V, editors. Chiral photochemistry. New York: Marcel Dekker; 2004.
4. Müller C, Bach T. Chirality control in photochemical reactions: enantioselective formation of complex photoproducts in solution. Aust J Chem 2008;61:557–564.
5. Sivaguru J, Natarajan A, Kaanumalle LS, Shailaja J, Uppili S, Joy A, Ramamurthy V. Asymmetric photoreactions within zeolites: role of confinement and alkali metal ions. Acc Chem Res 2003;36:509–521.
6. Bauer A, Westkämper F, Grimme S, Bach T. Catalytic enantioselective reactions driven by photoinduced electron transfer. Nature 2005; 436:1139–1140.
7. Tung CH, Wu LZ, Zhang LP, Chen B. Supramolecular systems as microreactors: control of product selectivity in organic phototransformation. Acc Chem Res 2003;36:39–47.
8. Tung CH, Guan JQ. Remarkable product selectivity in photosensitized oxidation of alkenes within nafion membranes. J Am Chem Soc 1998; 120:11874–11879.
9. Sivaguru J, Poon T, Franz R, Jockusch S, Adam W, Turro NJ. Stereocontrol within confined spaces: enantioselective photooxidation of enecarbamates inside zeolite supercages. J Am Chem Soc 2004; 126:10816–10817.
10. Yang H, Bohne C. Chiral discrimination in the fluorescence quenching of pyrene complexed to β-cyclodextrin. J Photochem Photobiol Chem 1995;86:209–217.
11. Fukuhara G, Mori T, Wada T, Inoue Y. Entropy-controlled supramolecular photochirogenesis: enantiodifferentiating *Z-E* photoisomerization of cyclooctene included and sensitized by permethylated 6-*O*-benzoyl-β-cyclodextrin. Chem Commun 2005;4199–4200.
12. Inoue Y, Matsushima E, Wada T. Pressure and temperature control of product chirality in asymmetric photochemistry. enantiodifferentiating photoisomerization of cyclooctene sensitized by chiral benzenepolycarboxylates. J Am Chem Soc 1998;120:10687–10696.
13. Inoue Y, Yokoyama T, Yamasaki N, Tai A. An optical yield that increases with temperature in a photochemically induced enantiomeric isomerization. Nature 1989;341:225–226.
14. Yang C, Mori T, Wada T, Inoue Y. Supramolecular enantiodifferentiating photoisomerization of (*Z,Z*)-1,3-cyclooctadiene included and sensitized by naphthalene-modified cyclodextrins. New J Chem 2007;31:697–702.
15. Kaneda M, Nakamura A, Asaoka S, Ikeda H, Mori T, Wada T, Inoue Y. Pressure control of enantiodifferentiating photoisomerization of cyclooctenes sensitized by chiral benzenepolycarboxylates. The origin of discontinuous pressure dependence of the optical yield. Org Biomol Chem 2003;1:4435–4440.
16. Inoue Y, Sugahara N, Wada T. Vital role of entropy in photochirogenesis. Pure Appl Chem 2001;73:475–480.
17. Wang Q, Yang C, Ke C, Fukuhara G, Mori T, Liu Y, Inoue Y. Wavelength-controlled supramolecular photocyclodimerization of anthracenecarboxylate mediated by γ-cyclodextrins. Chem Commun 2011;6849–6851.
18. Inoue Y, Yokoyama T, Yamasaki N, Tai A. Temperature switching of product chirality upon photosensitized enantiodifferentiating *cis-trans* isomerization of cyclooctene. J Am Chem Soc 1989;111:6480–6482.
19. Inoue Y, Dong SF, Yamamoto K, Tong L-H, Tsuneishi H, Hakushi T, Tai A. Inclusion-enhanced optical yield and *E/Z* ratio in enantiodifferentiating photoisomerization of cyclooctene included and sensitized by β-cyclodextrin monobenzoate. J Am Chem Soc 1995;117:11033–11034.
20. Inoue Y, Wada T, Sugahara N, Yamamoto K, Kimura K, Tong L-H, Gao X-M, Hou Z-J, Liu Y. Supramolecular photochirogenesis. 2. Enantiodifferentiating photoisomerization of cyclooctene included and sensitized by 6-*O*-modified cyclodextrins. J Org Chem 2000;65:8041–8050.
21. Fukuhara G, Mori T, Wada T, Inoue Y. Entropy-controlled supramolecular photochirogenesis: enantiodifferentiating *Z-E* photoisomerization of

cyclooctene included and sensitized by permethylated 6-*O*-modified β-cyclodextrins. J Org Chem 2006;71:8233–8243.

22. Lu R, Yang C, Cao Y, Tong L, Jiao W, Wada T, Wang Z, Mori T, Inoue Y. Enantiodifferentiating photoisomerization of cyclooctene included and sensitized by aroyl-β-cyclodextrins: a critical enantioselectivity control by substituents. J Org Chem 2008;73:7695–7701.
23. Lu R, Yang C, Cao Y, Wang Z, Wada T, Jiao W, Mori T, Inoue Y. Supramolecular enantiodifferentiating photoisomerization of cyclooctene with modified β-cyclodextrins: critical control by a host structure. Chem Commun 2008;3:374–375.
24. Biely P, Cote GL, Burgess-Cassler A. Purification and properties of alternanase, a novel *endo*-α-1,3-α-1,6-D-glucanase. Eur J Biochem 1994;226:633–639.
25. Cote GL, Biely P. Enzymically produced cyclic α-1,3-linked and α-1,6-linked oligosaccharides of D-glucose. Eur J Biochem 1994;226:641–648.
26. Aga H, Higashiyama T, Watanabe H, Sonoda T, Nishimoto T, Kubota M, Fukuda S, Kurimoto M, Tsujisaka Y. Production of cyclic tetrasaccharide from starch using a novel enzyme system from *Bacillus globisporus* C11. J Biosci Bioeng 2002;94:336–342.
27. Aga H, Nishimoto T, Kuniyoshi M, Maruta K, Yamashita H, Higashiyama T, Nakada T, Kubota M, Fukuda S, Kurimoto M. 6-α-Glucosyltransferase and 3-α-isomaltosyltransferase from *Bacillus globisporus* N75. J Biosci Bioeng 2003;95:215–224.
28. Oku K, Kudou N, Kurose M, Shibuya T, Chaen H, Fukuda S. The crystal properties of cyclic nigerosyl-(1→6)-nigerose (CNN) and powdering of α-tocopherol, cholecalciferol and EPA using CNN. J Jpn Soc Food Sci Technol 2007;54:326–331.
29. Bradbrook GM, Gessler K, Cote GL, Momany F, Biely P, Bordet P, Perez S, Imberty A. X-ray structure determination and modeling of the cyclic tetrasaccharide cyclo-{→6)-α-D-Glc*p*-(1→3)-α-D-Glc*p*-(1→6)-α-D-Glc*p*-(1→3)-α–Glc*p*-(1→}. Carbohydr Res 2000;329:655–665.
30. Funasaki N, Ishikawa S, Hirota S, Neya S, Nishimoto T. Structure and ethanol complexation of cyclic tetrasaccharide in aqueous solution studied by NMR and molecular mechanics. Chem Pharm Bull 2004; 52:708–713.
31. Dunlap CA, Cote GL, Momany FA. Oxidation and metal-ion affinities of a novel cyclic tetrasaccharide. Carbohydr Res 2003;338:2367–2373.
32. Inoue Y, Ikeda H, Kaneda M, Sumimura T, Everitt SRL, Wada T. Entropy-controlled asymmetric photochemistry: switching of product chirality by solvent. J Am Chem Soc 2000;122:406–407.
33. Inoue Y, Yamasaki N, Yokoyama T, Tai A. Enantiodifferentiating *Z-E* photoisomerization of cyclooctene sensitized by chiral polyalkyl benzenepolycarboxylates. J Org Chem 1992;57:1332–1345.
34. Inoue Y, Yamasaki N, Yokoyama T, Tai A. Highly enantiodifferentiating photoisomerization of cyclooctene by congested and/or triplex-forming chiral sensitizers. J Org Chem 1993;58:1011–1018.
35. Hoffmann R, Inoue Y. Trapped optically active (*E*)-cycloheptene generated by enantiodifferentiating *Z-E* photoisomerization of cycloheptene sensitized by chiral aromatic esters. J Am Chem Soc 1999;121:10702–10710.