Trapped Optically Active (*E*)-Cycloheptene Generated by Enantiodifferentiating *Z*−*E* Photoisomerization of Cycloheptene Sensitized by Chiral Aromatic Esters

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Abstract: Highly strained, optically active (*E*)-cycloheptene (**1E**) was prepared for the first time in the enantiodifferentiating geometrical photoisomerization of the (*Z*)-isomer (**1Z**) sensitized by chiral benzenetetracarboxylates at −40 to −80 °C. Low-temperature irradiations of **1Z** in the presence of the chiral sensitizer, and subsequent stereospecific trapping of the optically active photoproduct, **1E**, through a Diels−Alder reaction with 1,3-diphenylisobenzofuran or by oxidation with OsO_4, afforded the cycloadduct or *trans*-1,2-cycloheptanediol, respectively. The enantiomeric excesses (ee's) of the two products were subsequently determined by chiral HPLC or GC. The ee of the product, which was used as a measure of the efficiency of chirality transfer in the excited state, was found to depend critically not only on the chiral sensitizer employed but also on the temperature and solvent employed. Thus, the ee of the product was doubled in an extreme case simply by changing the solvent from dichloromethane to hexane. Furthermore, the product chirality could be switched over a relatively narrow range of temperature as a consequence of the significant contribution of the entropy term in the enantiodifferentiating isomerization within the exciplex intermediate. Sensitization with (−)-bornyl benzenetetracarboxylate in hexane at −80 °C gave an ee value of 77%, which is the highest ee ever obtained for an asymmetric photosensitization. Based on the differential activation enthalpy and entropy for the enantiodifferentiating process and the fluorescence quenching experiments with C_5−C_8 cycloalkenes, the origin of the highly efficient enantiodifferentiation and a detailed mechanism for the enantiodifferentiating photoisomerizations are discussed.

Introduction

Chirality transfer from optically active sensitizers to prochiral substrates in the excited state is an intriguing and attractive process in photochemistry.[1] Thus, the enantiodifferentiating geometrical photoisomerizations of cyclooctene and its derivatives, sensitized by chiral aromatic esters, have been actively investigated in recent years.[2] In these photoisomerizations, the rotational relaxation of the alkene double bond occurring within an exciplex intermediate constitutes the enantiodifferentiating process, producing the constrained chiral (*E*)-isomer in a relatively high enantiomeric excess (ee). Because the chirality of (*E*)-cyclooctene originates from its distorted structure (10 kcal/mol higher in energy than the (*Z*)-isomer), caused by the hindered rope-jumping motion of the methylene chain bridging the double bond, the much more strained substrate (*E*)-cycloheptene (**1E**) (27 kcal/mol higher in energy than the (*Z*)-isomer **1Z**) is quite an interesting target molecule from a mechanistic and synthetic point of view.[3] Compared with its higher homologues, little is known about (*E*)-cycloheptene. **1E** was first generated by Corey et al.[4] in a thermal elimination reaction and subsequently trapped stereospecifically to afford a stable Diels−Alder adduct with *trans*-configuration. After the first photochemical synthesis of **1Z** was achieved by Kropp through triplet photosensitization,[5] Inoue et al.[3,6] investigated the reaction kinetics of **1E** generated by singlet-sensitized photoisomerization in detail and determined the lifetime (τ) of **1E** at low temperatures by trapping the product with acidic methanol. Under these conditions, $\tau = 9.7$ min at 1 °C and 68 min at −15 °C. Squillacote et al. performed an NMR spectroscopic characterization and were able to study the thermal stability of this labile olefin.[7] More recently, Krebs et al. reported the synthesis of (*E*)-1,1,3,3,6,6-hexamethyl-1-sila-4-cycloheptene and its optical resolution by means of chiral gas chromatography.[8] The anomalous stability of this hetero-(*E*)-cycloheptene ($\tau_{1/2} = 5.7$ d at 123 °C) is mainly attributed to the enlarged ring size as a result of the incorporated silicon atom. However, no attempts to prepare optically active (*E*)-cycloheptene have hitherto been made.

In view of the thermal instability of (*E*)-cycloheptene (**1E**) and the relatively high ee values obtained in the enantiodiffer-

(1) (a) Rau, H. *Chem. Rev.* **1983**, *83*, 535. (b) Inoue, Y. *Chem. Rev.* **1992**, *92*, 741. (c) Everitt, S. R. L.; Inoue, Y. In *Organic Molecular Photochemistry*; Ramamurthy, V., Schanze, K., Eds.; Marcel Dekker: New York, 1999; pp 71−130.

(2) (a) Inoue, Y.; Yamasaki, N.; Yokoyama, T.; Tai, A. *J. Org. Chem.* **1992**, *57*, 1332. (b) Inoue, Y.; Yamasaki, N.; Yokoyama, T.; Tai, A. *J. Org. Chem.* **1993**, *58*, 1011. (c) Inoue, Y.; Matsushima, E.; Wada, T. *J. Am. Chem. Soc.* **1998**, *120*, 10687.

(3) Inoue, Y.; Ueoka, T.; Kuroda, T.; Hakushi, T. *J. Chem. Soc., Perkin Trans. 2* **1983**, 983.

(4) Corey, E. J.; Carey, F. A.; Winter, R. A. E. *J. Am. Chem. Soc.* **1965**, *87*, 934.

(5) Kropp, P. J. *J. Am. Chem. Soc.* **1969**, *91*, 5783.

(6) (a) Inoue, Y.; Ueoka, T.; Hakushi, T. *J. Chem. Soc. Perkin Trans. 2* **1984**, 2053. (b) Inoue, Y.; Hagiwara, S.; Daino, Y.; Hakushi, T. *J. Chem. Soc., Chem. Commun.* **1985**, 1307.

(7) Squillacote, M.; Bergman, A.; De Felippis, J. *Tetrahedron Lett.* **1989**, *30*, 6805.

(8) Krebs, A.; Pforr, K.-I.; Raffay, W.; Thölke, B.; König, W. A.; Hardt, I.; Boese, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 159.

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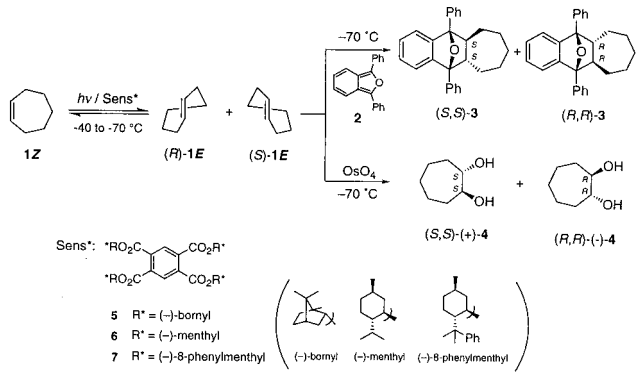
Scheme 1



entiating photoisomerization of (*Z*)-cyclooctene sensitized by chiral benzenepolycarboxylates,[2] the asymmetric photochemical approach is perhaps the most direct and logical choice for the generation and trapping of optically active **1E**. Here we will demonstrate that optically active **1E** can be efficiently generated with high ee's (up to 77%) and can be stereospecifically trapped by a subsequent Diels−Alder reaction with diphenylisobenzofuran or oxidation with OsO_4, as illustrated in Scheme 1. The smaller ring size and higher strain energy of **1E** than those of (*E*)-cyclooctene are thought to be responsible for the much stronger temperature and solvent dependence observed for the ee values of **1E**.

Results

Trapping Experiments and Determination of the Absolute Configurations of the Products. Chromatographic and spectroscopic methods are well established for the direct determination of the optical purity or ee of chiral compounds at ambient and higher temperatures; e.g., the ee of moderately stable (*E*)-cyclooctene has been determined by chiral GC.[2] In the present study, we first planned to separate and preferabaly isolate the enantiomers of (*E*)-cycloheptene by chiral GC or HPLC at a low temperature. However, after discussing the technical problems associated with the low-temperature GC and HPLC with the experts from Shimadzu and Daicel Co., we could not find an appropriate instrument or chiral column which can be operated at temperatures lower than at least −20 °C. At the same time, we tried to solve the problem by using the trapping technique. To preserve the chirality of the photoproduct, an enantiomeric mixture of **1E** produced in the asymmetric photosensitization should be efficiently and stereospecifically converted to the corresponding enantiomers of a thermally stable adduct, the ee of which is then determined by conventional methods and is regarded as being equivalent to that of the photoproduct **1E**. As described below, the Diels−Alder and oxidation reactions proceeded even at low temperatures, leading to the corresponding products in good to excellent yields with stereoretention. Hence, we decided to use the trapping technique for the determination of the enantiomeric excess of the (*E*)-isomer. We notice that this is an indirect method, and certainly the isolation of optically active (*E*)-cycloheptene and the direct measurement of its chiroptical properties are intriguing future targets.

To establish procedures for the photolysis and subsequent trapping at low temperatures, preparative scale irradiations of **1Z** with methyl benzoate as an achiral singlet sensitizer were carried out. The addition of the very reactive diene 1,3-diphenylisobenzofuran (**2**) or OsO_4 to the irradiated solution at −70 °C, followed by gradual warming to room temperature, gave the adduct **3** or the oxidation product **4**, respectively. No significant enantiomeric loss is expected to occur during either trapping procedure, since these reactions are known to proceed stereospecifically and are also carried out at low temperatures. Even in the presence of residual **1Z**, only **1E** was selectively trapped by **2**, affording the adduct **3** as sole product, and **1Z** did not give a Diels−Alder product in an appreciable yield when reacted with **2** under the conditions employed. Similarly, no kinetic resolution in the trapping process is expected to occur in the absence of any specific interaction or complex formation between the trapping agent and chiral sensitizers in the groud state. In fact, all of the temperature dependence experiments gave good straight lines in the Eyring plots, as described below. Such results would not be obtained if the two independent processes, i.e., the enantiodifferentiating *Z*−*E* isomerization in the exciplex and the kinetic resolution in the trapping reaction, were jointly responsible for the determination of the ee.

In contrast, OsO_4 oxidized both **1Z** and **1E** to give the *cis*- and *trans*-1,2-cycloheptanediols, respectively. The enantiomers of the Diels−Alder adducts (*R*,*R*)-**3** and (*S*,*S*)-**3** were satisfactorily separated by chiral HPLC, while the ratio of the *cis*-diol and the enantiomeric *trans*-diols (*S*,*S*)-(+)-**4** and (*R*,*R*)-(−)-**4** were determined by chiral GC.

To assign the absolute configurations of the primary product **1E** and the Diels−Alder adduct **3**, a preparative scale photosensitization of **1Z** with (−)-bornyl 1,2,4,5-benzenetetracarboxylate (**5**) was carried out, and the configuration of **1E** produced was correlated to the known absolute configuration of *trans*-diol **4** by chemical derivatization.[9] Half of the irradiated solution was treated with OsO_4, as above, and the resulting *trans*-diol was separated from the reaction mixture by means of preparative GC on an achiral column. The isolated *trans*-diol was dissolved in dichloromethane and subjected to polarimetric measurement, giving a negative optical rotation ($\alpha = -0.008°$ at 589 nm and $-0.015°$ at 367 nm; error $\pm 0.001°$). This proved the predominant formation of (*R*,*R*)-(−)-**4**, and therefore the excess of (*S*)-**1E** over (*R*)-**1E** in the original photoproduct. The other half of the irradiated solution was treated with **2** to yield the adduct **3**. Based on the absolute configuration of the major photoproduct (*S*)-**1E**, the predominant enantiomer was assigned to be (*R*,*R*)-**3**, which was in turn shown to elute as the first fraction in the chiral HPLC analysis.

Photosensitization and *E*/*Z* Ratio. In previous studies concerning the enantiodifferentiating photoisomerization of cyclooctene and its derivatives,[2,10] a wide variety of optically active polyalkyl benzenepolycarboxylates were employed as chiral singlet sensitizers. Since one of the most interesting aspects of this work is the examination of the effects of the ring size and strain of (*E*)-cycloalkenes on their photochemical and stereochemical behavior, we employed the same chiral sensitizers which have been extensively studied and are known to give satisfactory chemical and optical yields in the cyclooctene case, i.e., (−)-tetrabornyl, (−)-tetramenthyl, and (−)-tetrakis(8-phenylmenthyl) 1,2,4,5-benzenetetracarboxylates (**5**−**7**) (Scheme 1).[2]

The time course of the photoisomerization was examined first. Dichloromethane solutions containing **1Z** (10 mM) and sensitizer **5** or **6** (2 mM) were irradiated for varying periods of time at −70 °C under an argon atmosphere, using a 300-W high-pressure mercury lamp. After a designated period of irradiation,

(9) Posternak, T.; Reymond, D.; Friedli, H. *Helv. Chim. Acta* **1955**, *38*, 205. Mousseron, M.; Richaud, R. *Bull. Soc. Chim. Fr.* **1946**, 643 and 647.

(10) (a) For 1-methylcyclooctene, see: Tsuneishi, H.; Hakushi, T.; Tai, A.; Inoue, Y. *J. Chem. Soc., Perkin Trans. 2* **1995**, 2057. (b) For 1,3-cyclooctadiene, see ref 2b.

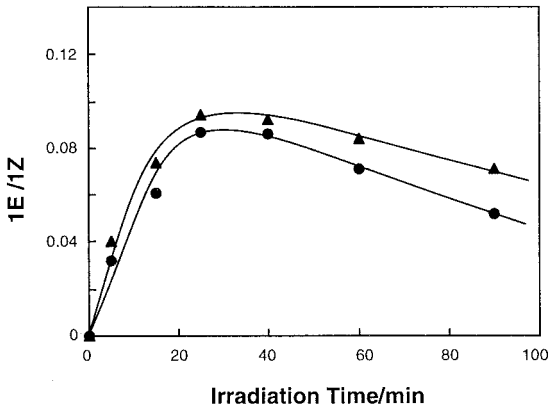


Figure 1. (*E*)- to (*Z*)-cycloheptene ratio (**1E**/**1Z**), as evaluated by **3**/**1Z** ratio, as a function of irradiation time upon sensitization of **1Z** with (−)-bornyl (**5**, ●) and (−)-menthyl (**6**, ▲) 1,2,4,5-benzenetetracarboxylate in dichloromethane.

each solution was poured into dichloromethane containing an excess of trapping agent **2**, cooled to −70 °C. The resultant mixture was left overnight in the bath, gradually warming to room temperature, and then analyzed by chiral GC to give the ratio of adduct **3** and remaining **1Z**. As can be seen from Figure 1, both benzenetetracarboxylate sensitizers **5** and **6** resulted in very similar **3**/**1Z** ratios which rapidly increased with increasing irradiation time, reaching a plateau of 0.1 at 25−40 min, and then gradually decreased upon prolonged irradiations of up to 90 min. The apparent photostationary-state *E*/*Z* ratio, $(E/Z)_{pss}$, of 0.1 is comparable to the corresponding ratio ($(E/Z)_{pss} = 0.10$) reported for cyclooctene at 25 °C,[11] but it is considerably lower than that observed for cyclooctene at −78 °C (0.38).[11] This lower $(E/Z)_{pss}$ ratio at a comparable temperature may be attributed to the higher strain observed for **1E** than for (*E*)-cyclooctene, and the gradual decrease upon prolonged irradiation is ascribed to secondary photoreactions of the highly strained **1E**.

Temperature Dependence of Ee and Activation Parameters. Photochemistry offers an excellent method for conducting experiments over a very wide temperature range without affecting the reaction mechanism. Using this advantage, we have investigated the temperature dependence of the ee of the product in enantiodifferentiating photosensitized Z−E isomerizations of cyclooctene and its derivatives,[2] revealing intriguing behavior over a temperature range from 50 to −90 °C. In the present study, such a wide temperature range could not be applied due to the thermal instability of **1E** at ambient temperatures; e.g., $\tau = 9.7$ min at 1 °C and 45 s at 25 °C.[3] We therefore investigated the temperature dependence of the enantiodifferentiating photoisomerization between −43 and −80 °C, employing the representative benzenetetracarboxylate sensitizers shown in Scheme 1.

In a typical experiment, five quartz tubes containing a solution (10 mL) of **1Z** (10 mM) and sensitizer (2 mM) were placed around a 300-W high-pressure mercury lamp, and the whole system was immersed in a temperature-controlled bath. Photosensitizations were carried out in a variety of solvents with differing polarities, as detailed in Table 1. After irradiation at low temperature and the subsequent trapping procedure with **2**, the ee of adduct **3** produced was determined by HPLC on a Daicel Chiralpak AD column, which afforded a satisfactory separation between the enantiomers.[12] Calibration with racemic **3** indicated that this method gives a small systematic error of 0.5% ee with a standard deviation of ±0.5% ee in favor of (*S*,*S*)-**3**, which eluted second, and each ee value was usually determined by five HPLC runs. Since the standard deviation of the ee determined was also in the range of ±0.5%, the total error can be up to ±1% in a few cases. The irradiation bath temperature was constant within ±0.5 °C. The ee values of **3** produced in the photosensitizations of **1Z** with **5**, **6**, and **7** in some solvents of different polarity at −43 to −80 °C are listed in Table 1.

For a more quantitative treatment of the temperature dependence, the Eyring equations for the formation rate constants (k_S and k_R) of (*S*)- and (*R*)-**1E** were combined to give the expression $\ln(k_S/k_R) = -\Delta\Delta H^{\ddagger}/RT + \Delta\Delta S^{\ddagger}/R$, in which the differential activation enthalpy $\Delta\Delta H^{\ddagger} = \Delta H^{\ddagger}_S - \Delta H^{\ddagger}_R$ and the differential activation entropy $\Delta\Delta S^{\ddagger} = \Delta S^{\ddagger}_S - \Delta S^{\ddagger}_R$. Thus, $\ln(k_S/k_R)$ should give a linear plot against $1/T$. The relative rate constant k_S/k_R is experimentally equal to (100 + %ee)/(100 − %ee). The temperature-dependent ee values obtained in the photosensitization with **5** and **6** in several different solvents were analyzed according to the above kinetic equation to give the plots shown in Figures 2 and 3.

For each sensitizer−solvent combination, a good straight line plot was drawn, indicating that a single enantiodifferentiation mechanism is operating in this temperature range, giving high ee values of up to 77%. It is noted that (*S*)-**1E** is favored at lower temperatures, irrespective of the chiral sensitizer and solvent employed. As is frequently observed in the enantiodifferentiating photoisomerization of cylcooctene,[2] the product chirality was switched from *S* to *R* by raising the temperature upon photosensitization with (−)-menthyl benzenetetracarboxylate **6** (Figure 3). Product chirality is also expected to be inverted at higher temperatures in the case of sensitizer **5** (Figure 2). Beyond this critical point, called the equipodal temperature (which decreases with increasing solvent polarity), the ee of the product increases with increasing temperature, a behavior which is not anticipated in conventional asymmetric syntheses. It is also interesting to note that the slopes of the regression lines for cycloheptene are much steeper than those reported for the photoisomerization of cyclooctene with the same sensitizers.[2]

By changing the solvent from polar dichloromethane to ether and then to nonpolar hexane, the regression line is significantly shifted upward for both sensitizers, favoring the (*S*)-enantiomer. Simultaneously, the slope of the plot increases with decreasing solvent polarity. In an extreme case, as a combined effect of the upward shift and the steeper slope, the ee of the product obtained upon sensitization with **5** is enhanced from 30% in dichloromethane at −75 °C to 77% in hexane at −80 °C (Figure 3). This is the highest ee ever reported for an enantiodifferentiating photosensitized reaction. In contrast, such a marked solvent effect has not been observed for the photosensitized isomerization of cyclooctene or its derivatives.[2]

To investigate the effect of the highly congested, electron-donating chiral ester groups in sensitizer, we studied the photosensitization of **1Z** with (−)-8-phenylmenthyl benzenetetracarboxylate (**7**), which is known to form an intramolecular exciplex with charge-transfer characteristics between the benzenetetracarboxylate core (acceptor) and the 8-phenyl group (donor).[2b] Interestingly, this sensitizer gave very high ee values not only at low temperatures (66% ee at −45 °C and 74% ee at −70 °C) but also at 25 °C (46% ee, extrapolated). Figure 4 illustrates the temperature dependence of the ee obtained with sensitizers **5**, **6**, and **7** in hexane. The menthyl ester **6** gives

(11) Yamasaki, N.; Yokoyama, T.; Inoue, Y.; Tai, A. *J. Photochem. Photobiol., A: Chem.* **1989**, *48*, 465 and unpublished results on photosensitization at low temperatures.

(12) Determination of the ee by chiral GC is not possible. We observed at least partial racemization of **3** upon purification on a preparative GC, which is attributed to a retro[4 + 2] reaction; cf. mass spectra.

Table 1. Temperature and Solvent Effects upon Enatiodifferentiating Photoisomerization of **1Z** Sensitized by (−)-Bornyl (**5**), (−)-Menthyl (**6**), and (−)-8-Phenylmenthyl (**7**) 1,2,4,5-Benzenetetracarboxylates

entry	sensitizer	substrate	solvent	irradiation time/min	temp/°C	% ee	ref
1	**5**	cyclooctene	pentane		25	−9.6	2a
2					−40	7.1	2a
3					−78	21.6	2a
4		**1**	pentane	45	−45	52.1	this work
5				45	−74	67.0	this work
6				45	−80	68.6	this work
7			hexane	45	−43	45.6	this work
8				45	−68	63.8	this work
9				40	−80	76.8	this work
10			ether	45	−43	35.7	this work
11				50	−45	35.8	this work
12				90	−55	44.3	this work
13				45	−68	53.6	this work
14				45	−75	56.2	this work
15				40	−80	58.3	this work
16			dichloromethane	90	−50	16.9	this work
17				90	−65	21.1	this work
18				90	−77	30.8	this work
19			methylcyclohexane	45	−43	46.2	this work
20				45	−55	49.7	this work
21				45	−75	66.9	this work
22	**6**	cyclooctene	pentane		25	11.5	2a
23					−40	27.3	2a
24					−60	30.9	2a
25		**1**	hexane	45	−43	−1.6	this work
26				45	−55	6.3	this work
27				45	−70	28.5	this work
28			ether	50	−45	−16.1	this work
29				60	−55	−6.8	this work
30				45	−76	13.8	this work
31			dichloromethane	90	−50	−14.3	this work
32				90	−65	−0.7	this work
33				90	−75	4.8	this work
34	**7**	cyclooctene	pentane		25	49.5	2b
35					−40	27.3	2b
36					−87	16.1	2b
37		**1**	hexane	45	−45	66.0	this work
38				45	−55	70.3	this work
39				45	−70	74.1	this work

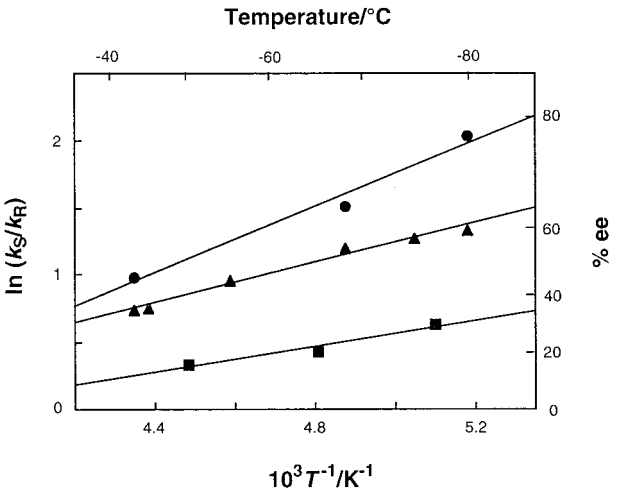


Figure 2. Temperature dependence of enantiomeric excess (ee) of **1E** upon sensitization of **1Z** with (−)-bornyl 1,2,4,5-benzenetetracarboxylate (**5**) in hexane (●), ether (▲), and dichloromethane (■); plots of ln(k_S/k_R), or ln [(100 + % ee)/(100 − %ee)], versus reciprocal temperature.

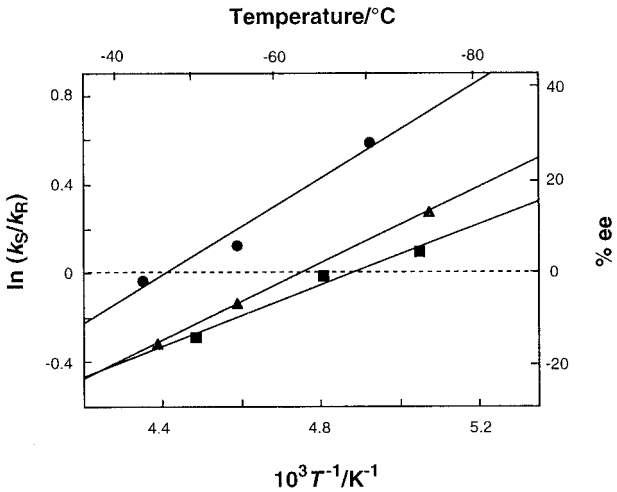


Figure 3. Temperature dependence of enantiomeric excess (ee) of **1E** upon sensitization of **1Z** with (−)-menthyl 1,2,4,5-benzenetetracarboxylate (**6**) in hexane (●), ether (▲), and dichloromethane (■); plots of ln(k_S/k_R), or ln [(100 + % ee)/(100 − %ee)], versus reciprocal temperature.

significantly lower ee's in this temperature range as compared with the bornyl ester **5**, although the slopes for both sensitizers do not differ greatly. In contrast, the use of the 8-phenylmenthyl ester **7** results in much smaller temperature dependence of the ee, probably due to a reduced conformational freedom within the sensitizer. It is reasonable that sensitizers **5** and **6** afford the corresponding (*S*)-enantiomer of (*E*)-cycloalkenes at low temperatures, irrespective of the ring size, although the congested sensitizer **7** is expected to give (*S*)-**1E** but to switch over to give (*R*)-(*E*)-cyclooctene at temperatures below −114 °C (the

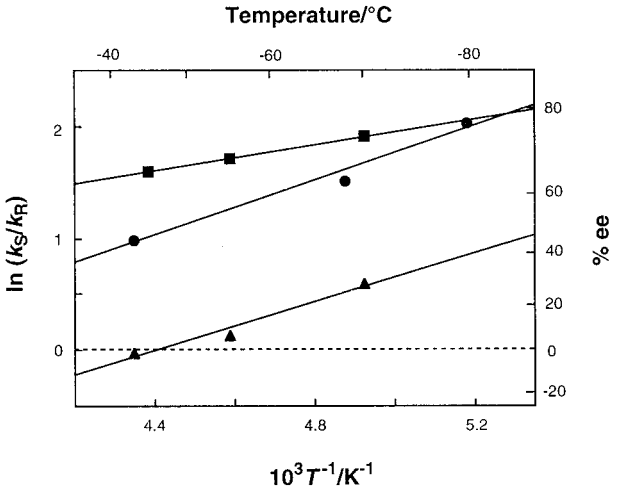


Figure 4. Temperature dependence of enantiomeric excess (ee) of **1E** upon sensitization of **1Z** with (−)-bornyl (**5**, ●), (−)-menthyl (**6**, ▲), and (−)-8-phenylmenthyl (**7**, ■) 1,2,4,5-benzenetetracarboxylates in hexane; plots of $\ln(k_S/k_R)$, or ln [(100 + % ee)/(100 − %ee)], versus reciprocal temperature.

equipodal temperature for the photosensitization of cyclooctene with **7**).[2b]

From the slope and intercept of the regression lines in Figures 2−4, the differential enthalpy and entropy of activation were calculated to give the $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values for each sensitizer−solvent combination. As can be seen from the activation parameters listed in Table 2, the $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values determined for **1** are much larger and depend more on the solvent polarity than the corresponding values reported for cyclooctene.[2a,b]

Fluorescence Quenching. Since sensitizers **5** and **6** emit weak fluorescence in solution, we carried out quantitative fluorescence quenching experiments of **5** and **6** with **1Z** in order to obtain information concerning the quenching process and exciplex formation, and these results can be compared with those for cyclooctene and cyclopentene. As exemplified for menthyl benzenetetracarboxylate **6** in aerated hexane at room temperature, fluorescence at 330 nm was gradually quenched upon the stepwise addition of **1Z**, and a new emission attributable to an exciplex emerged at a longer wavelength, accompanied by an isoemissive point at 385 nm (see Figure 5). The exciplex emission spectrum, shown in the inset of Figure 5, was obtained by subtracting the intensity-normalized original spectrum at [**1Z**] = 0 M from the final spectrum at [**1Z**] = 0.64 M.

According to the conventional Stern−Volmer equation, $F/F_0 = 1 + k_q\tau[\mathbf{1Z}]$, the relative fluorescence intensity (F/F_0) at 330 nm in the presence (F) and absence (F_0) of **1Z** was plotted against the quencher concentration, giving a good straight line, as shown in Figure 6. For comparison purposes, similar quenching experiments were repeated with sensitizers **5** and **6**, using the quencher olefins **1Z** and cyclopentene in several solvents. The Stern−Volmer constant ($k_q\tau$), obtained as the slope of the plot, is listed for each sensitizer−quencher combination in Table 3.

Discussion

Sensitization and Enantiodifferentiation Mechanisms. The similarities observed between the fluorescence quenching parameters, the temperature-dependence profile of ee, and the absolute configuration of the product obtained in the present asymmetric photosensitization of **1Z** and those reported for cyclooctene[2a,b] lead us to the conclusion that essentially the same sensitization and enantiodifferentiation mechanisms are operating in the two systems. The enantiodifferentiating step of the sensitized photoisomerization is believed to be the rotational relaxation of the double bond within the exciplex, formed between the excited chiral sensitizer and cyclooctene.[2] This mechanism, originally proposed for cyclooctene[2a] and later for 1,3-cyclooctadiene[10b] and 1-methylcyclooctene,[10a] can be described as follows. The initial quenching of the singlet-excited sensitizer (^{1}S*) by the substrate **1Z** leads to the formation of an encounter exciplex [**1Z**···^{1}S*]. Rotational relaxation around the double bond of [**1Z**···^{1}S*] gives a relaxed diastereomeric exciplex pair [(*R*)-^1p···S*] and [(*S*)-^1p···S*], which spontaneously fall apart, liberating the corresponding enantiomers of twisted cycloheptene singlet (*R*)-^1p and (*S*)-^1p, which in turn decay stereospecifically to (*R*)-**1E** and (*S*)-**1E** or to **1Z**. Upon prolonged irradiation, the system reaches a photostationary state as a consequence of the concomitant *E*-to-*Z* photoisomerization. In principle, the quenching of the chiral sensitizer by enantiomeric (*E*)-cyclooctene can occur at different rates, but in actuality the quenching process has been demonstrated to be non-enantiodifferentiating as a result of the very fast quenching rate constants which approach diffusion control.[2a] Experimentally, the possibility of enantiodifferentiating quenching can be proved or disproved by examining the dependence of the ee of the product upon conversion, or by using racemic **1E** as the starting material, although the latter check cannot be used in the present study because of its instability. We therefore performed the photosensitization of **1Z** with **5** in ether for different irradiation times (40−90 min) at −43 to −80 °C, giving an excellent linear fit, as shown in Figure 2 (see entries 10−15 in Table 1). Thus, it is shown that the varied irradiation time and extent of conversion do not appreciably affect the ee of the product.

The fluorescence quenching experiments not only support the proposed mechanism, which involves the efficient quenching of an excited singlet sensitizer and the subsequent formation of exciplex intermediate, but also afford quantitative information concerning the quenching kinetics and the properties of the exciplex formed. As shown in Table 3, all of the C_5−C_8 cycloalkenes efficiently quench the fluorescence of sensitizers **5** and **6** at quenching rate constants (k_q) of 10^9−10^{10} M^{-1} s^{-1}. The very large k_q values for (*E*)-cyclooctene, which are close to the diffusion limit, have been attributed to its higher strain and lower singlet energy and are believed to be responsible for non-enantiodifferentiating quenching.[2a] The much weaker exciplex emission observed at longer wavelength for (*E*)-cyclooctene ($\lambda_{max}^{ex} \approx 455$ nm) indicates extensive conformational relaxation of an exciplex which has stronger charge-transfer character.[2a] The Stern−Volmer constants ($k_q\tau$) obtained for **1Z** and cyclopentene in the present study are generally of the same order of magnitude, irrespective of the solvent used. However, a closer examination reveals that the k_q for C_5−C_8 (*Z*)-cycloalkenes gradually increases with decreasing ring size, from (1.1−1.4) × 10^9 M^{-1} s^{-1} for C_8 to (1.8−2.7) × 10^9 M^{-1} s^{-1} for **1Z** and then to (3.1−3.2) × 10^9 M^{-1} s^{-1} for the C_5 cycloalkene. Contrastingly, the exciplex fluorescence maximum (λ_{max}^{ex}) shifts slightly to shorter wavelengths, from 410−415 nm for C_8 to 408−410 nm for **1Z** and then to 395−405 nm for the C_5 cycloalkene, probably reflecting the reduced conformational relaxation for the smaller sized cycloalkenes. More evident bathochromic shifts of λ_{max}^{ex} observed in polar solvents, which vary from 408 nm in hexane, 418 nm in ether, and 435 nm in dichloromethane, unambiguously demonstrate the charge-transfer character of the exciplex. A similar polar solvent-

Table 2. Differential Activation Parameters for Enantiodifferentiating Photoisomerizations of Cyclooctene and Cycloheptene (**1**) Sensitized by (−)-Bornyl (**5**), (−)-Menthyl (**6**), and (−)-8-Phenylmenthyl (**7**) 1,2,4,5-Benzenetetracarboxylates in Some Solvents

			5		**6**		**7**	
substrate	solvent	$E_T(30)^a$/ kcal mol^{-1}	$\Delta\Delta H^{\ddagger}$/ kcal mol^{-1}	$\Delta\Delta S^{\ddagger}$/ cal mol^{-1} K^{-1}	$\Delta\Delta H^{\ddagger}$/ kcal mol^{-1}	$\Delta\Delta S^{\ddagger}$/ cal mol^{-1} K^{-1}	$\Delta\Delta H^{\ddagger}$/ kcal mol^{-1}	$\Delta\Delta S^{\ddagger}$/ cal mol^{-1} K^{-1}
cyclooctene[b]	pentane	31.0	−0.77	−3.00	−0.61	−1.55	0.62	3.90
	ether	34.5	−0.59	−2.28				
1[c]	pentane	31.0	−1.28	−3.26				
	hexane	31.0	−2.43	−8.68	−2.18	−9.62	−1.16	−1.90
	methylcyclohexane	(30.9)[d]	−1.90	−6.36				
	ether	34.5	−1.48	−4.92	−1.72	−8.16		
	dichloromethane	40.7	−0.95	−3.63	−1.37	−6.67		

[a] Solvent polarity parameter; Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH: Weinheim, 1988. [b] References 2a and 2b; revised $\Delta\Delta S^{\ddagger}$ values. [c] This work. [d] E_T for cyclohexane.

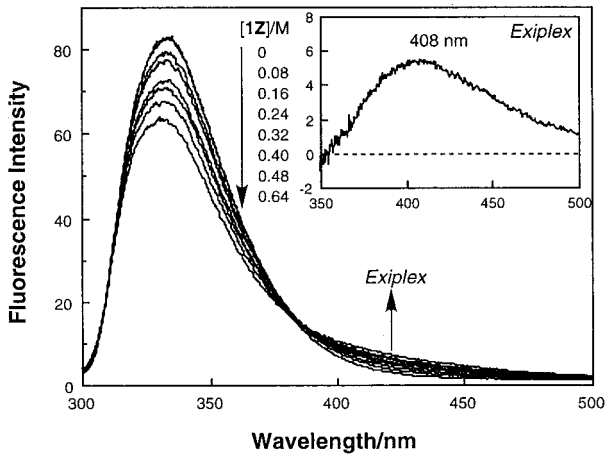


Figure 5. Fluorescence quenching of (−)-menthyl 1,2,4,5-benzenetetracarboxylates **6** with **1Z** in hexane and the exciplex emission (inset) obtained by spectrum subtraction.

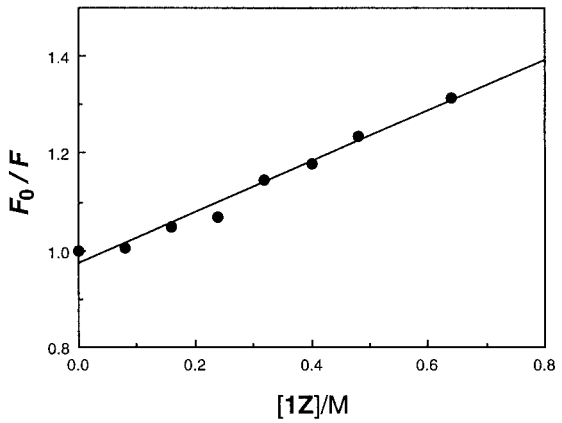


Figure 6. Stern−Volmer plot for the fluorescence quenching of (−)-menthyl 1,2,4,5-benzenetetracarboxylate **6** with **1Z** in hexane.

induced bathochromic shift is also reported for (*Z*)-cyclooctene, which shows a λ_{max}^{ex} of 410 nm in pentane and 445 nm in acetonitrile (Table 3).[2b]

As a logical consequence of the ring size of the quencher, a less hindered approach to the active site of the sensitizer is expected for the smaller substrate, and this was confirmed experimentally by the 2−3 times faster quenching by the smaller-sized cycloalkenes. The smaller ring size of **1Z** enables a closer approach to the chiral sensitizer and the subsequent formation of more intimately interacting exciplex, which should be responsible, at least in part, for the generally higher ee values obtained with **1** than with cyclooctene. In contrast, the ee of the product is significantly reduced by the use of polar solvents. From fluorescence quenching experiments in polar solvents, it is known that the exciplex intervening in this enantiodifferentiating photosensitization has a degree of charge-transfer character. This allows for charge separation between the radical anionic sensitizer and the radical cationic **1Z** in polar solvents, which diminishes chiral recognition in the exciplex intermediate. In conclusion, it should be emphasized that the sensitizer−substrate distance in the exciplex intermediate is critical, and changes that lead to an increased separation remove any enantiodifferentiation in the excited state.

Temperature Switching of Product Chirality. The unusual effect of temperature on the ee of the product is perhaps the most intriguing part of this enantiodifferentiating photoisomerization. In most asymmetric thermal and photochemical reactions, the optical yield is generally believed to be enhanced by lowering the reaction temperature. Indeed, a variety of asymmetric reactions, including some photochemical examples,[13] have been demonstrated to follow this empirical rule, although only relatively narrow ranges of temperature have been employed in the thermal reactions. This widespread belief that the optical yield intrinsically increases at lower temperatures is based on the assumption that the chiral recognition is predominantly governed by the enthalpic term, which is a reflection of the magnitude of steric hindrance of the attacking reagent, and the contribution of the entropy term is simply disregarded in most cases. However, the temperature dependence study of the enantiodifferentiating photoisomerization of cyclooctene has revealed that an unprecedented switching of product chirality can be caused simply by changing the irradiation temperature.[2] This temperature-switching phenomenon can only be interpreted in terms of a significant contribution of the entropy term in the enantiodifferentiating step. Thus, the nonzero $\Delta\Delta S^{\ddagger}$, which possesses the same sign as $\Delta\Delta H^{\ddagger}$, is the origin of their temperature-switching effect. The present study on **1Z** further indicates that such an apparently unusual switching behavior, originally observed for cyclooctene, is not exceptional but is instead a more common phenomenon which should be observed in a wide variety of asymmetric (photo)chemical reactions if a sufficiently wide temperature range is employed. In this respect, photochemical asymmetric synthesis appears to be more promising, since the reaction mechanism does not, in principle, vary over a wide temperature range.

Activation Parameters and Enthalpy−Entropy Compensation. When discussing the mechanism, efficiency, and factors controlling the enantiodifferentiation in the excited state, a global

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Table 3. Fluorescence Quenching of (−)-Bornyl (**5**) and (−)-Menthyl (**6**) 1,2,4,5-Benzenetetracarboxylates with C_5−C_8 Cycloalkenes in Some Solvents at Room Temperature

sensitizer	quencher	solvent	$E_T(30)^a$/kcal mol^{-1}	$k_q\tau^b$/M^{-1}	$k_q{}^c/10^9$ M^{-1} s^{-1}	$\lambda_{max}{}^{ex\,d}$/nm	ref
5	(*E*)-cyclooctene	pentane	31.0	1.80	9.0	∼455	2a
	(*Z*)-cyclooctene	pentane	31.0	0.21	1.1	415	2a
	1Z	hexane	31.0	0.35	1.8	410	this work
	cyclopentene	hexane	31.0	0.62	3.1	395	this work
6	(*E*)-cyclooctene	pentane	31.0	2.08	10.4	∼455	2a
	(*Z*)-cyclooctene	pentane	31.0	0.28	1.4	410	2a
		acetonitrile	45.6	0.83	4.2	445	2b
	1Z	hexane	31.0	0.53	2.7	408	this work
		ether	34.5	0.34	nd[e]	418	this work
		dichloromethane	40.7	0.52	nd	435	this work
	cyclopentene	hexane	31.0	0.63	3.2	405	this work

[a] Solvent polarity parameter; see footnote *a* of Table 2. [b] Stern−Volmer constant. [c] Quenching rate constant, calculated for the hexane solutions by using the same lifetime (τ 0.2 ns) determined for **5** and **6** in pentane (ref 2a). [d] Exciplex fluorescence maximum. [e] Not determined.

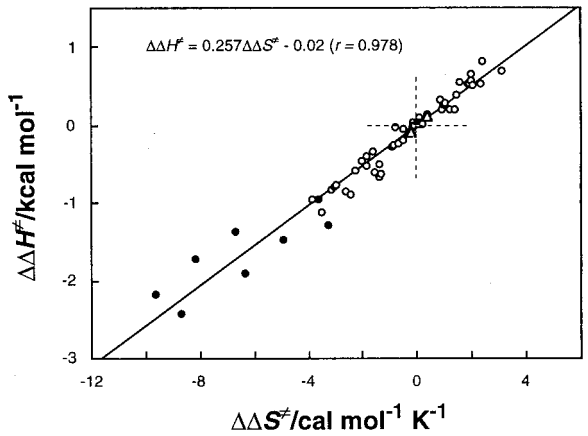

Figure 7. Enthalpy−entropy compensation plot for cycloheptene (**1**) (●), cyclooctene (○), and 1-methylcyclooctene (△).

comparison of the differential activation parameters for cycloheptene **1** and cyclooctene becomes interesting. As can be seen from the data in Table 2, both the $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values obtained for **1** are unexpectedly greater (by a factor of 2−3) than those reported for cyclooctene with the same chiral sensitizers in similar solvents, indicating a much more efficient enantiodifferentiation process for the smaller-sized **1**, which is demonstrated above in the fluorescence quenching experiments. Specifically, the larger $\Delta\Delta S^{\ddagger}$ values may indicate larger conformational changes upon the enantiodifferentiating rotational relaxation of **1** than those experienced by cyclooctene in the corresponding exciplex.

According to the Gibbs−Helmholtz equation, the enthalpy and entropy terms contribute to the differential activation free energy $\Delta\Delta G^{\ddagger}$, and thus to the ee of the product. As a consequence of $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ obtained for **1** and cyclooctene both having the same sign, the regression lines inevitably cross the *x*-axis, as shown in Figures 2 and 3. At this point, which we have called the equipodal temperature and which is characteristic to the specific solvent−sensitizer combination, the enthalpy ($\Delta\Delta H^{\ddagger}$) and entropy ($T\Delta\Delta S^{\ddagger}$) terms cancel each other.

It is interesting to examine the general validity of the compensatory enthalpy−entropy relationship, which was observed for the enantiodifferentiating photoisomerization of cyclooctene. In Figure 7, the $\Delta\Delta S^{\ddagger}$ values obtained in this study and those reported for cyclooctene[2a,b] and 1-methylcyclooctene[10b] are plotted against the $\Delta\Delta H^{\ddagger}$ values. First, it should be pointed out that, compared to the plots for cyclooctene and methylcyclooctene, where the data are accumulated near the origin, the corresponding data points for **1** are located in much more negative regions of $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$, indicating a highly efficient chiral recognition process. Interestingly, while the data points available for **1** are limited in number and rather scattered, the activation parameters obtained with the two cycloalkenes fall essentially on the same regression line, which has a correlation coefficient of 0.978, giving the expression $\Delta\Delta H^{\ddagger} = 0.257\Delta\Delta S^{\ddagger} + 0.02$. It is noted that the data points for the highly congested sensitizers, carrying 8-phenylmenthyl and 8-cyclohexylmenthyl auxiliaries, deviate significantly from the regression line and have not been used in the regression analysis. From the slope of the line, we can calculate an isoenantiodifferentiating temperatures (T_{iso}) of 257 K, at which no enatiodifferentiation takes place. The single regression line for both cycloalkenes unambiguously demonstrates that essentially the same enantiodifferentiation mechanism operates in the asymmetric photosensitization of cycloalkenes even beyond the apparent differences of chiral auxiliary, sensitizer, substrate, and solvent used, while the plots for the congested sensitizers that deviate from this line suggest the operation of a different type of exciplex or a different enantiodifferentiation mechanism.

Conclusions

In the present study, we have revealed several important and novel facts concerning the mechanistic and synthetic aspects of asymmetric photosensitization as well as on the generation, configuration, stability, and reactivity of optically active **1E**. The low-temperature photosensitization of **1Z** with chiral alkyl benzenetetracarboxylates affords optically active **1E** in good chemical and optical yield, which is optically and thermally stable below −40 °C. **1E** can be efficiently and stereospecifically trapped by a Diels−Alder reaction with diphenylisobenzofuran, or by oxidation with osmium tetraoxide, producing the corresponding adduct or oxidation product. As compared with the cyclooctene case, the ee of the product is generally higher under comparable conditions and is more sensitive to both temperature and solvent polarity. These features, which are characteristic for cycloheptene, are totally compatible with the faster quenching rate and the highly solvent polarity-dependent exciplex emission observed in fluorescence quenching experiments. The smaller ring size of **1Z** enables a faster quenching of the chiral sensitizer and the subsequent formation of a more intimately interacting exciplex which has greater charge-transfer character, eventually affording the highest ee values of 70−77% using a conventional chiral sensitizer in nonpolar solvents at −70 to −80 °C. This rather simple strategy for the enhancement of the sensitizer−substrate interaction through a reduction in the steric hindrance is likely not to be restricted to the enantiodifferentiating photosensitization of cycloalkenes but should be widely applicable to the general asymmetric photosensitization systems.

Although there are some dissimilarities between the asymmetric photosensitizations of cycloheptene and cyclooctene (as discussed above), it is crucial to point out similarities between the two systems in order to give an overall picture. Thus, the same chiral sensitizer affords the (*E*)-isomer with the same absolute configuration for both cycloheptene and cyclooctene at low temperature, where the entropic contribution is minimized. The present asymmetric photosensitizing system is yet another example of the temperature-switching behavior of the chirality of the product, which we originally reported for cyclooctene. The different values for the ee and activation parameters obtained for the two cycloalkenes are consolidated by the global fit to the single enthalpy−entropy compensation plot, indicating that the same mechanism is operating in both enantiodifferentiating photoisomerization systems.

Finally, we wish to emphasize that this and previous studies concerning asymmetric photosensitization are gradually revealing a detailed mechanism and factors controlling the enantiodifferentiating step, as well as the chirality and ee of the product, and future work must ultimately lead us to a maximum optical yield.

Experimental Section

General. Melting points were measured with a Yanaco MP-500-D and are uncorrected. Optical rotations were determined by using a Perkin-Elmer Polarimeter 341 with a thermostated 10 cm cell. Mass spectra were recorded by using a GC/MS instrument, HP-5890A/JEOL JMS-DX-303. ^{1}H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively, in $CDCl_3$ or C_6D_6, using a JEOL EX400 spectrometer. Absorption spectra were obtained on a JASCO V-560 spectrophotometer, and fluorescence spectra were recorded on a Hitachi F-4500 spectrofluorimeter. GC analyses were performed on a Shimadzu CBP-1 (25 m × 0.25 mm i.d.) column or a chiral Supelco β-DEX 120 (30 m × 0.25 mm i.d.) column using a Shimadzu GC-14A instrument fitted with a C-R6A integrator. Preparative GC was run on an SE-30 (1 m) column using a GL Sciences GC instrument. HPLC analyses were performed on a Wakosil 5-SIL (4.6 × 150 mm) column or a Daicel Chiralpak AD (4.6 × 250 mm) column using a JASCO HPLC system fitted with UV (254 nm) and RI detectors.

Solvents were dried (over CaH_2, Mg, or KOH) and distilled under an argon atmosphere prior to use. Cycloheptene was fractionally distilled. The sensitizers were synthesized according to a literature procedure from 1,2,4,5-benzenetetracarboxylic chloride and the commercially available optically active alcohols.[14] The trapping agents OsO_4 and 1,3-diphenylisobenzofuran are commercially available and were used without further purification.

Preparative-Scale Irradiation and Trapping of 1E: Formation of (5*RS*,5a*RS*,10a*RS*,11*SR*)-5,11-Epoxy-5a,6,7,8,9,10,10a,11-octahydro-5,11-diphenyl-5*H*-cyclohepta[*b*]naphthalene (3). Ten quartz tubes (10 mm outside diameter) containing a deaerated dichloromethane solution (100 mL in total) of **1Z** (192 mg, 2 mmol) and methyl benzoate (136 mg, 1 mmol) were irradiated for 1 h at −78 °C with a 300-W high-pressure mercury lamp. The irradiated solutions were poured into a precooled flask containing 118 mg (0.44 mmol) of 1,3-diphenylisobenzofuran. The resultant solution was subsequently allowed to warm to room temperature over a period of several hours. After the removal of the solvent and other low-boiling components from the mixture under reduced pressure, the residue was purified on a silica gel column, using a cyclohexanes−ethyl acetate (6:1) eluent, to give 47.2 mg (6% yield based on **1Z** used and 29% based on 1,3-diphenylisobenzofuran) of the Diels−Alder adduct **3** as a colorless solid, mp 148 °C. The TLC (eluent, $R_f = 0.8$) was developed with an oxidizing molybdenum/cerium solution. The ^{1}H NMR spectrum of this compound is in good agreement with the previous report.[15] However, our spectrum is much more resolved, showing a coupling of 12.7 Hz, which is characteristic of the *trans* protons. The ^{13}C NMR gives further support to the proposed structure. **3**: *m*/*z* (70 eV) 270 (M^+ − cycloheptene, retro-Diels−Alder reaction, 100), 207 (50); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.75 (m, 1 H), 1.11 (m, 1 H), 1.4−1.7 (m, 7 H), 1.96 (ddd, J = 3.4/5.9/12.7 Hz, 1 H), 2.04 (m, 1 H), 2.52 (ddd, J = 3.4/5.9/12.7 Hz, 1 H), 7.15−7.25 (m, 4 H), 7.36 (ddd, J = <1/6.8/7.8 Hz, 1 H), 7.42 (ddd, J = <1/6.8/7.8 Hz, 1 H), 7.44−7.54 (m, 4 H), 7.61 (dd, J = <1/7.8 Hz, 2 H), 7.76 (dd, J = <1/7.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 24.64, 28.06, 28.36, 28.81, 29.36, 51.06, 52.04, 89.10, 90.04, 117.11, 121.41, 125.84, 125.98, 126.61, 126.83, 127.15, 127.96, 128.13, 128.30, 129.64, 129.80, 130.33, 132.97, 137.41, 138.29, 144.48, 150.18.

Trapping of 1E by Osmium Tetraoxide:[16] Formation of *trans*-1,2-Cycloheptanediol (4) (Accompanied by the *cis*-Isomer). Except for a change of solvent to diethyl ether, the same irradiation conditions as above were employed in the preparation of **4.** After the irradiation, the solutions were poured into a cooled flask containing OsO_4 (130 mg, 0.51 mmol) and 0.2 mL of pyridine in diethyl ether (10 mL). The resulting mixture was allowed to warm overnight to room temperature. The brown precipitate formed was collected and refluxed for 3 h with 0.7 g of Na_2SO_3 in an ethanol−water mixture. The resultant mixture was poured into water and extracted with ether (4 × 40 mL), and the combined ether extracts were dried over $MgSO_4$. GC analysis indicated that the crude mixture obtained after evaporation of the solvent contained *cis*- and *trans*-1,2-cycloheptanediol with a combined purity of 96%. The isomeric diols showed R_f values of 0.33 and 0.38 upon TLC analysis over silica gel with ethyl acetate as the eluent. The *cis*- and *trans*-isomers were separated by column chromatography on silica gel. The *cis*-diol (13.5 mg, mp 46 °C (lit.[17] mp 48 °C), 21% yield referred to OsO_4) was shown to be pure by NMR, whereas the isolated *trans*-diol **4** (5.6 mg) was still contaminated with the *cis*-isomer (*cis*:*trans* = 1:4). The ^{1}H and ^{13}C NMR spectra of the *trans*-diol **4** prepared photochemically was in good agreement with those of the authentic sample prepared independently by the H_2O_2 oxidation of **1Z**.[18] *cis*-Cycloheptanediol: ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 1.22 (m, 1 H), 1.44 (m, 1 H), 1.53 (m, 1 H), 1.68 (m, 1 H), 1.83 (m, 1 H), 2.2−3.3 (s, broad, 1 H, OH), 3.72 (m, 1 H, C*H*OH); ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 22.10 (2 C), 28.00 (1 C, C-5), 31.11 (2 C), 73.91 (2 C, CHOH). *trans*-Cycloheptanediol **4**: ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 1.27 (m, 2 H), 1.45 (m, 2 H), 1.82 (m, 1 H), 2.9−3.1 (s, broad, 1 H, OH), 3.40 (m, 1 H, C*H*OH); ^{13}C NMR (400 MHz, C_6D_6) δ (ppm) 22.50 (2 C), 26.80 (1 C, C-5), 32.82 (2 C), 78.02 (2 C, CHOH).

Time Dependence of the Formation of 1E. A dichloromethane solution (30 mL), containing **1Z** (35 μL, 0.30 mmol, 9.9 mM) and **5** (49.2 mg, 0.061 mmol, 2.03 mM) or **6** (48.0 mg, 0.059 mmol, 1.96 mM), was prepared. After this stock solution was distributed into six quartz tubes (3 mL each), each solution was irradiated at −70 °C under an argon atmosphere with a 300-W high-pressure mercury lamp for a designated time of 5, 15, 25, 40, 60, or 90 min, and the irradiated solution was poured into a cooled dichloromethane solution (0.5 mL) containing 0.43 mg of dodecane, which was used as an internal standard for the GC analysis, and 1.18 mg (0.0044 mmol) of the trapping agent **2**. The resultant mixture was kept at −70 °C and gradually warmed to room temperature overnight. This was then analyzed by GC. For normalization, the starting concentration of **1Z** relative to dodecane was determined separately by an external standard method.

Standard Procedure for the Analytical-Scale Irradiation. A solution (50 mL), containing **1Z** (10 mM) and chiral sensitizer **5**, **6**, or **7** (2 mM), was distributed into five quartz irradiation tubes (10 mm outside diameter). All tubes were sealed under argon with a septum cap and were fixed near a 300-W high-pressure mercury lamp at a distance of ca. 1 mm from the lamp. The whole system was immersed in a cooling bath filled with methanol, which was stabilized at a desired temperature below −40 °C, after which the solutions were irradiated

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for 45−90 min. To quantitatively trap the **1E** produced, the irradiated solutions were cooled to at least −70 °C and then poured into a cooled flask containing ca. 14 mg (0.05 mmol) of 1,3-diphenylisobenzofuran. When a solvent other than dichloromethane was used for the photolysis, the irradiated solution was poured into a precooled solution of the trapping agent in dichloromethane (50 mL).

Upon completion of the thermal cycloaddition reaction, the resultant mixture containing residual trapping agent was exposed to sunlight until the color of diphenylisobenzofuran disappeared.[19] The solvent was then evaporated under reduced pressure, and the oily residue was separated on a GPC column (Jaigel 1-H and 2-H, Japan Analytical Industry Co.). The cycloadduct **3** was further purified by an additional small-scale liquid chromatography, affording a very pure sample suitable for chiral HPLC (Chiralpak AD, 0.46 × 250 mm). Usually, the enantiomeric excess of **3** was determined as an average of five injections to the chiral HPLC column. From repeated injections, it was shown that a racemic mixture of **3** gave an average ee of 0.5% in favor of the (*S,S*)-isomer, which eluted as the second fraction.

Alternatively, **1E** could be trapped by OsO_4 oxidation. After the oxidation and the subsequent workup described above, the product was analyzed as follows. The *cis*-diol, which always accompanied as the major product from **1Z**, was separated from the *trans*-diol **4** by means of HPLC on a Wakosil 5-SIL column. The pure **4** obtained was then analyzed by chiral GC on a Supelco β-DEX 120 column. Direct chiral GC analysis of the oxidized mixture was not possible on the same chiral GC column, as a result of an overlap of the peaks of the *cis*- and *trans*-diols.

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