

Photosensitized Asymmetric Isomerization and Cycloaddition of Cycloalkenes and Cycloalkadienes

Michael Oelgemöller and Yoshihisa Inoue^{1*}

Bayer CropScience K.K., Japan, 9511-4 Yuki, Yuki-City, Ibaraki 307-0001, Japan

¹Entropy Control Project, ICORP, JST, 4-6-3 Kamishinden, Toyonaka 560-0085, Japan

Recent advances in photosensitized enantiodifferentiating isomerization and cycloaddition reactions of cycloalkenes (other than cyclooctene) and cycloalkadienes are reviewed.

key words: Asymmetric photosensitized Isomerization and cycloaddition of Cycloalkenes, Cycloalkadienes

INTRODUCTION

Photochirogenesis is synonymous with the photochemical induction of molecular chirality *via* the electronically excited state, and thus can be regarded as a unique alternative to existing thermal and enzymatic asymmetric processes. Although a relatively new area in (photo)chemistry, this methodology has attracted growing attention over the last few decades, noticeable by the number of summarizing reviews [1,2,3,4,5]. Among the various strategies for inducing chirality photochemically [1,2], *enantiodifferentiating photosensitization*, which requires only a catalytic amount of a chiral sensitizer has proved to be highly promising. Since the pioneering work on the asymmetric photosensitization of *trans*-1,2-diphenylcyclopropane by Hammond and Cole [6], the enantiodifferentiating *Z-E* photoisomerization of cyclooctene (**1**) has become a major model system in this area (Figure 1) [7,8]. Recently, Inoue and coworkers have shown that the geometrical photoisomerization of **1** sensitized by chiral arenepolycarboxylates gives the optically active (*E*)-isomer (**1E**) in enantiomeric excesses of up to 64%. Furthermore, the product chirality was found to be inverted by environmental factors, such as the temperature, pressure and solvent [9]. This control has been interpreted in terms of the contributions of both enthalpy (ΔH^\ddagger) and entropy (ΔS^\ddagger), allowing an “entropic multidimensional control of chirality” [9].

This review summarizes recent results on enantiodifferentiating photoreactions of several cycloalkenes (other than **1**) and

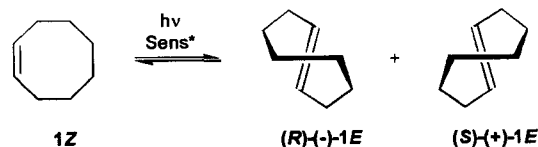


Figure 1. Enantiodifferentiating photoisomerization of **1Z**.

*To whom correspondence should be addressed.

E-mail : inoue@chem.eng.osaka-u.ac.jp

Received & Accepted; October 23, 2002

cycloalkadienes [10]; additionally, selected examples describing *unimolecular photoisomerization* and *bimolecular photocycloaddition* reactions are presented. Although a broad spectrum of chiral sensitizers have been applied under a variety of conditions, we will focus on the most important and successful chromophore/auxiliary pairs (Charts 1 and 2, *vide infra*).

DISCUSSION

Unimolecular Enantiodifferentiating Photoisomerizations. Cycloheptene (2)

Compared to its higher homologues, (*E*)-cycloheptene (**2E**) has found only little attention in synthetic organic chemistry. The main reason for this neglect comes from the thermal instability of **2E** caused by the high strain (20.3 kcal/mol higher in energy than **2Z** [11]). **2E** was first generated by Corey *et al.* *via* the thermal elimination reaction of thionocarbonate **3** followed by an *in situ* trapping with 1,3-diphenylisobenzofuran (**4**) to afford the stable Diels-Alder adduct **5** with *trans*-configuration (Figure 2) [12].

The first photochemical approach to **2E** was made by

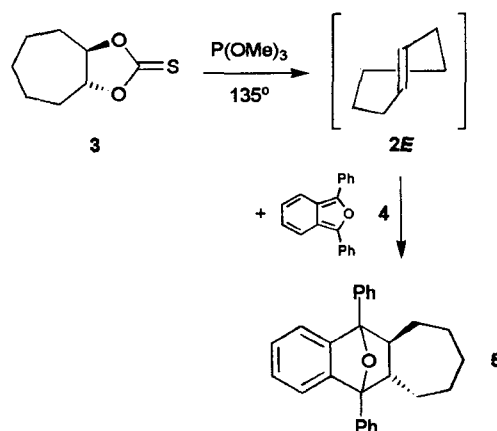


Figure 2. Thermal preparation and subsequent trapping of **2E**.

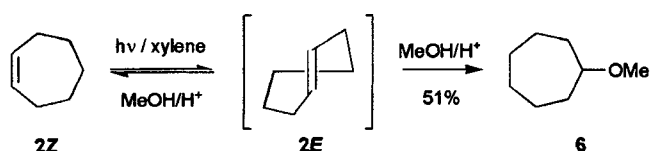


Figure 3. Photochemical generation of **2E** and subsequent trapping in acidic methanol.

Kropp through triplet photosensitization with xylene [13]. Upon irradiation in acidic methanol, addition of the solvent was observed and methoxycycloheptane (**6**) was obtained in 51% yield. From the comparison with the photochemical behavior of other cycloalkenes, it was concluded that the addition (most likely) occurred to *E*-isomer **2E** (Figure 3). Later, Inoue *et al.* studied the photochemical generation and thermal regeneration of **2E** in more detail [14,15]. Upon irradiation with methyl benzoate as a sensitizer at -79°C , **2E** was obtained in a high photostationary *E:Z* ratio of 0.24. **2E** remained entirely stable at this temperature but isomerized quantitatively upon warming up to room temperature. Applying the trapping reaction with methanol it was possible to determine the lifetime (τ) of **2E** at various temperatures. In methanol, the lifetimes were in the range: $\tau=9.7$ min at 1°C to 68 min at -15°C [15].

Recently, Nishiyama and coworkers reported the isolation of **2E** as chiral bis(dihydrooxazolyl)pyridine ruthenium complexes [16]. In contrast to (*E*)-cyclooctene (**1E**), enantiomeric discrimination by enantioface-selective coordination was not achieved. They ascribed the different behavior observed for **2E** to its smaller dihedral angle. Thus, the cavity at the coordination site of the ruthenium complex is too wide for enantioselective binding.

Optically active **2E** was preferentially generated for the first time by enantiodifferentiating *Z-E* photoisomerization using chiral aromatic esters as sensitizers [17]. This photochirogenic approach gave optically active **2E**, which was stereospecifically trapped by either a subsequent Diels-Alder reaction with diphenylisobenzofuran (**4**) or by oxidation with OsO_4 , and high *ee*'s of up to 77% were obtained (Figure 4).

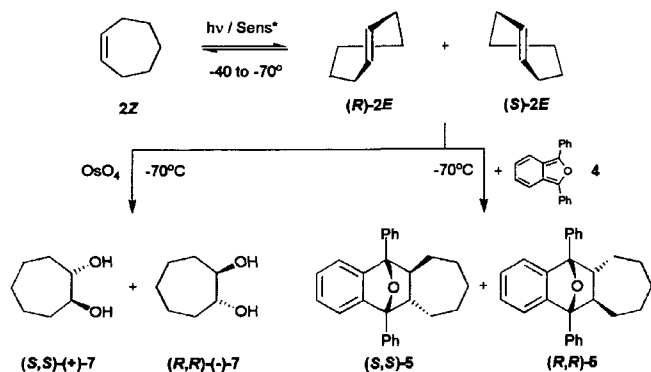


Figure 4. Enantiodifferentiating photoisomerization of **2Z** and subsequent stereospecific trapping of **2E**.

Table 1. Enantiodifferentiating photoisomerization of **2Z** sensitized by chiral tetraalkyl benzenetetracarboxylates (**III**) at low temperatures (irradiation times: 45-90 min) [17]

R* (sensitizer) ^a	Solvent	Temp. [$^{\circ}\text{C}$]	2E		
			<i>ee</i> (%) ^b	Configuration ^c	
(-)-bornyl (a)	pentane	-45	52.1	<i>S</i>	
		-74	67.0	<i>S</i>	
		-80	68.6	<i>S</i>	
		hexane	-43	45.6	<i>S</i>
			-68	63.8	<i>S</i>
			-80	76.8	<i>S</i>
	diethylether	-43	35.7	<i>S</i>	
		-45	35.8	<i>S</i>	
		-55	44.3	<i>S</i>	
		-68	53.6	<i>S</i>	
		-75	56.2	<i>S</i>	
		-80	58.3	<i>S</i>	
(-)-menthyl (b)	hexane	-50	16.9	<i>S</i>	
		-65	21.1	<i>S</i>	
		-77	30.8	<i>S</i>	
		methylcyclohexane	-43	46.2	<i>S</i>
			-55	49.7	<i>S</i>
			-75	66.9	<i>S</i>
	diethylether	-43	-1.6	<i>R</i>	
		-55	6.3	<i>S</i>	
		-70	28.5	<i>S</i>	
		dichloromethane	-45	-16.1	<i>R</i>
			-55	-6.8	<i>R</i>
			-76	13.8	<i>S</i>
(-)-8-phenylmenthyl hexane (c)	-50	-14.3	<i>R</i>		
	-65	-0.7	<i>R</i>		
	-75	4.8	<i>S</i>		
	hexane	-45	66.0	<i>S</i>	
		-55	70.3	<i>S</i>	
		-70	74.1	<i>S</i>	

^aSee Charts 1 and 2.

^bEnantiomeric excess of **2E**. Positive and negative signs for *ee* correspond to the formation of (*S*)-(+)- and (*R*)-(-)-isomer, respectively.

^cAbsolute configuration of **2E**.

When compared to the results of its higher homologue cyclooctene (**1**), the product *ee* of **2E** was generally higher under comparable conditions, but was found to be more sensitive to both temperature and solvent polarity (Table 1).

These unique features of cycloheptene (**2**) were attributed to the faster quenching rate constant [$k_q=(1.1-1.4)\times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for **1Z**; $(1.8-2.7)\times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for **2Z**] and to the reduced conformational relaxation within the exciplex, as estimated from the smaller bathochromic shift for **1Z** [$\lambda_{\text{max}}^{\text{ex}}=410-415 \text{ nm}$ for **1Z**; $408-410 \text{ nm}$ for **2Z**], the latter observed in fluorescence quenching experiments. A reasonable explanation for these findings was based on the smaller ring size of **2Z**, which enables faster quenching of the chiral sensitizer and also the subsequent formation of a more closely interacting exciplex. Thus, the

simple enhancement of the sensitizer-substrate approach through the reduction in steric hindrance leads to high *ee* values of 70–77%. Furthermore, the asymmetric photosensitization of **2Z** revealed a similar temperature-switching behavior of the product chirality, a phenomenon originally reported for cyclooctene (**1**) [4,5]. As for cyclooctene, this finding was interpreted in terms of a significant contribution of the entropy term in the enantiodifferentiating step.

1,3-Cyclooctadiene (**9**)

The thermal synthesis of (*Z,Z*)- and (*E,Z*)-1,3-cyclooctadiene (**9ZZ**, **9EZ**) from cyclooctenylamine **8** was reported by Cope *et al.* [18]. Using the *Hofmann degradation* route, a mixture of *E,Z*- (**9EZ**, 41%) and *Z,Z*-isomer (**9ZZ**, 15%) was obtained (Figure 5).

A photochemical approach to **9EZ** via photosensitized isomerization was first described by Liu in 1967 [19]. The success of the photoisomerization depended on both the sensitizer and the temperature applied. In particular, clean isomerization to **9EZ** was observed below 20°C, whereas at elevated temperatures bicyclo[4.2.0]oct-7-ene (**10**) was formed as the sole product (Figure 6). The (*E,Z*)-isomer **9EZ** was found to be relatively stable up to 60°C but readily cyclized to **10** at higher temperatures, *e.g.* upon refluxing in benzene.

Applying the sensitized photoisomerization route in combination with optical resolution by chiral HPLC, the chiroptical properties of optically active **9EZ** have been examined by Sandström and coworkers [20]. The first successful direct synthetic approach to enantiomeric **9EZ** was achieved by Inoue *et al.* via the enantiodifferentiating photoisomerization of **9ZZ** sensitized by chiral aromatic esters [21] or amides [22] (Figure 7).

Processing a lower singlet energy than its analogue

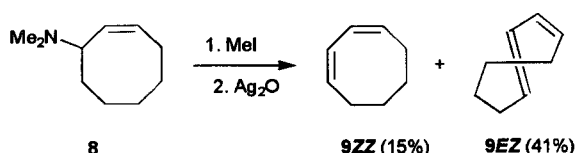


Figure 5. Thermal preparation of **9ZZ** and **9EZ**.

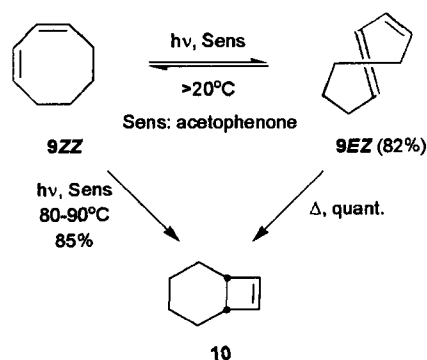


Figure 6. Photochemical transformations of **9ZZ**.

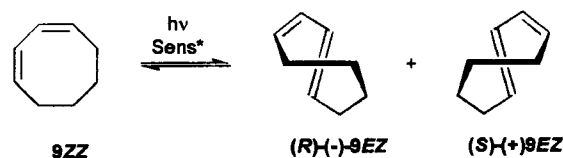


Figure 7. Enantiodifferentiating photoisomerization of **9ZZ**.

Table 2. Enantiodifferentiating photoisomerization of **9ZZ** sensitized by chiral (poly)alkyl arene(poly)carboxylates [21] and amides [22] at various temperatures^a

Sensitizer ^b Type, R*	Solvent	Temp. [°C]	<i>E/Z</i> ratio	9EZ <i>ee</i> (%)
III , (-)-menthyl (b)	pentane	25	0.272	-0.3
		-40	0.223	1.2
IV , (-)-menthyl (b)	pentane ^c	25	0.119	-10.1
		-40	0.162	-17.6
		acetoneitrile	25	0.073
IV , (-)-bornyl (b)	pentane	25	0.017	0.2
		-74	0.139	-5.8
IV , (-)-1-methylheptyl (d)	pentane	25	0.052	-1.5
		-74	0.139	-5.8
IV , (-)-1-methylheptyl (d)	pentane	25	0.115	-2.5
		-74	0.212	-1.2
V , (-)-menthyl (b)	pentane	25	0.118	0.3
		-40	0.131	-0.3
VI , (-)-menthyl (b)	pentane	25	0.119	1.2
		-40	0.138	0.6
VIII , (-)-menthyl (b)	pentane	25	0.124	-0.3
		-40	0.136	-0.5
II , pyrrolidine (j)	pentane	25	0.018	0.8
		-67	0.063	1.2
III , pyrrolidine (j)	pentane	25	0.031	2.4
		-67	0.122	14.3

^aFor more details see references [21] and [22].

^bSee Charts 1 and 2.

^cLarge scale experiment

cyclooctene, **9ZZ** can be sensitized not only with benzene(poly) carboxylates (**I**) but also with naphthalene(di)carboxylates (**II**) and anthracenecarboxylates (not shown in Chart 1) to give moderate *E/Z* ratios (Table 2). The chemical yields of **9EZ** (based on consumed **9ZZ**) were moderate to high (40–70%) even upon prolonged irradiations or at low temperatures. The degree of enantiodifferentiation strongly depended on the polarity of the solvent, as the use of polar solvents, such as acetonitrile and methanol led to dramatic drops in the product's *ee*. Since no exciplex formation was detected upon fluorescence quenching experiments in these solvents, a spontaneous electron transfer from **9ZZ** to the sensitizer was postulated. Support for this assumption came from the low ionization potential of **9ZZ** (IP=8.68 eV [21]). Therefore, the loss of a close and long-lived interaction between chiral sensitizer and substrate most reasonably caused the sudden drop in the product's *ee*.

In pentane at 25°C, the enantiomeric excess of **9EZ** was low for all sensitizers examined except benzenehexacarboxylate (**IV**), which afforded moderately optically active **9EZ** of about 10% under these conditions. Upon lowering the temperature the *ee* value showed relatively small temperature dependence in comparison to the cyclooctene (**1**) case. This finding indicates that the enthalpic as well as entropic differences ($\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$) for the enantiodifferentiating process producing (*R*)- and (*S*)-**9EZ** are less pronounced. Nevertheless, the *ee* values were improved significantly from 10.1% at 25°C to 17.6% at -40°C with the ester **IVb**, and from 2.4% at 25°C to 14.3% at -67°C with the amide **IIIj**. In some cases, the product chirality switched within the temperature range employed, demonstrating that the entropy term still plays an essential but less important role in the enantiodifferentiating sensitization step.

1,5-Cyclooctadiene (**11**)

As for its conjugated homologue **9**, a similar thermal pathway to **11EZ** via two successive *Hofmann degradations* of *N*-methylgranatanine was reported by Cope *et al.* [23]. In slight contrast to the 1,3-diene (**9**) case however, the *E,Z*-isomer (**11EZ**) was obtained in a larger amount as the main isomer (**11EZ**:**11ZZ**=9:1). Later, Cope and coworkers also succeeded in the optical resolution of **11EZ** through a chiral platinum α -methylbenzylamine complex [24]. The photochemical behavior of **11ZZ** has been studied briefly by irradiation in the presence of copper(I) chloride [25]. Under these heterogeneous, photocatalysis conditions, **11ZZ** was converted into a mixture of **11EZ** (4-17%), **11EE** (*ca.* 1%) and tricyclo[3.3.0.0^{2,6}]octane (**12**, 3-49%).

In 1980, Inoue and Takamuku *et al.* described a more detailed study on the alkyl benzoate sensitized isomerization of **11ZZ** and **11EZ** [26]. The photolysis of **11** in the presence of methyl benzoate gave **11EZ** in yields between 11-14% along with *ca.* 3.5-8% of **12**. By comparing the reaction rates for the formation of **12** from either **11ZZ** or **11EZ** it was concluded that **12** was formed predominantly *via* the sensitized photoreaction of the **11EZ** isomer, and a mechanism involving a singlet exciplex was proposed.

When the reaction was performed in acetic methanol only trapping products arising from **11EZ** or **12** were obtained in

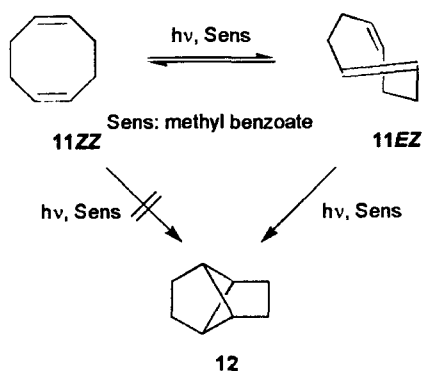


Figure 8. Photochemical transformations of **11ZZ**.

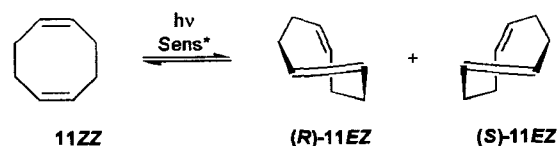


Figure 9. Enantiodifferentiating photoisomerization of **11ZZ**.

significant amounts. Since products indicating the intervention of **11ZZ** were not detected, the photochemical formation of **11ZZ** was ruled out at least under these conditions.

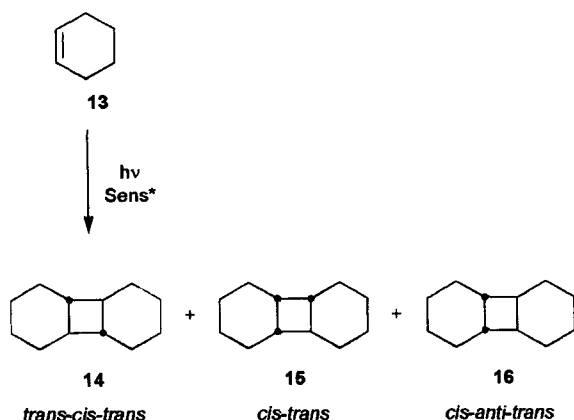
When (-)-menthyl benzoate (**IIb**) was employed as a chiral sensitizer and subjected to the photoisomerization reaction of **11ZZ**, an enantiomeric excess of 1.6% in favor of the (-)-enantiomer of **11EZ** was obtained [26].

Bimolecular Enantiodifferentiating Photocycloadditions. Cyclohexene (**13**)

In contrast to the unimolecular photoisomerizations described above, the photodimerization of cyclohexene (**13**) represents a bimolecular process. This photochemical dimerization has been intensively studied under direct excitation or triplet sensitization conditions [13,27,28]. In all cases, photolysis afforded a mixture of three [2+2] cyclodimers, i.e. *trans-anti-trans* (**14**), *cis-trans* (**15**) and *cis-anti-cis* (**16**), but only dimers **14** and **15** are chiral. The product ratio of **14-16** depended in general on the irradiation conditions and, in the case of *p*-xylene sensitization, also on the solvent and temperature applied. For example, the photosensitization gave **14**, **15** and **16** in a ratio of 1.1:1.8:1.0 in pentane but a ratio of 1.5:2.6:1.0 in diethyl ether. In addition, the ratio of the cyclodimers **15** and **16** slightly decreased on lowering of the temperature.

Recently, the enantiodifferentiating photocyclodimerization of **13** sensitized by a number of optically active benzene(poly) carbonates (**I**) has been described by Inoue and coworkers (Figure 10) [29]. In line with relevant studies on higher cycloalkenes it was presumed that the photoisomerization of **13** proceeded *via* the singlet manifold as indirectly proven by the effect of oxygen added as a triplet quencher. Among the applied sensitizers, only unsubstituted benzoates (**I**) gave good results in terms of chemical and optical yields. This finding was interpreted in terms of steric hindrance of the additional auxiliary groups in all other polycarboxylate sensitizers, which influences the efficiency of the energy transfer. In addition, the extreme instability of **13E** does not allow sufficient dimerization during its short lifetime.

In all experiments, the yields of the cyclodimers increased gradually over the period of irradiation until reaching a plateau, which depended on temperature, solvent, and sensitizer used. Significant *ee*'s were obtained for **14**, whereas no pronounced *ee* was obtained for the *cis-trans* dimer **15**. Since the *ee* for **14** remained constant over the irradiation time at each temperature, an irreversible mechanism without any interconversion between the dimers **14-16** was established. In line with the observations made during xylene sensitization (*vide supra*), the relative

Figure 10. Enantiodifferentiating photodimerization of **13**.

amounts of **14** and **15** increased by lowering the temperature. Since the thermodynamic stability of the cyclodimers decreases in the order **16** > **15** > **14**, the product composition was thus most likely kinetically controlled. Among the chiral alkyl benzoates (**I**), especially saccharide derivatives (**e-i**) served as effective chiral auxiliaries of the sensitizer [30], and gave optically active **14** with enantiomeric excesses up to 68.3% at

Table 3. Enantiodifferentiating photocyclodimerization of **13** sensitized by chiral alkyl benzoates (**I**) [29]^a

R* (sens.) ^b	Solvent	Temp. [°C]	Conv. [%]	Yield [%] (% ee)		
				14	15	16
(-)-menthyl (b)	pentane	25	39	3.4 (-5.1)	6.1 (-0.2)	2.7
		-78	17	0.39 (-18.7)	0.38 (-0.8)	0.08
	diethylether	25	46	4.1 (-4.7)	7.6 (0.1)	3.1
		-78	19	0.52 (-13.1)	0.63 (-0.1)	0.1
		25	36	2.1 (-11.9)	4.0 (-0.4)	1.8
furanose (e)	pentane	25	36	2.1 (-11.9)	4.0 (-0.4)	1.8
		-78	19	0.22 (-51.0)	0.19 (+0.9)	0.05
		25	9	0.4 (-9.1)	0.7 (0.0)	0.3
	diethylether	25	9	0.4 (-9.1)	0.7 (0.0)	0.3
		-78	16	0.36 (-30.5)	0.42 (-1.8)	0.07
		25	36	2.2 (7.0)	4.1 (0.5)	1.5
furanose (f)	pentane	25	36	2.2 (7.0)	4.1 (0.5)	1.5
		-78	16	0.08 (-35.0)	0.08 (-1.7)	0.02
		25	41	2.3 (7.5)	4.1 (0.6)	1.6
	diethylether	25	41	2.3 (7.5)	4.1 (0.6)	1.6
		-78	17	0.36 (-15.4)	0.42 (-0.3)	0.07
		25	38	2.8 (6.7)	5.2 (0.4)	2.4
furanose (g)	pentane	25	38	2.8 (6.7)	5.2 (0.4)	2.4
		-78	18	0.06 (62.8)	0.04 (1.5)	0.01
		25	37	2.0 (6.4)	3.6 (0.7)	1.4
	diethylether	25	37	2.0 (6.4)	3.6 (0.7)	1.4
		-78	19	0.2 (49.4)	0.2 (1.4)	0.05
		25	38	2.1 (-2.1)	4.0 (-0.2)	1.8
pyranose (h)	pentane	25	38	2.1 (-2.1)	4.0 (-0.2)	1.8
		-78	25	0.2 (-68.3)	0.15 (-0.6)	0.04
		25	37	2.3 (-2.5)	4.2 (-0.2)	1.7
	diethylether	25	37	2.3 (-2.5)	4.2 (-0.2)	1.7
		-78	21	0.33 (-55.5)	0.33 (-0.8)	0.06
		25	36	2.5 (0.2)	4.6 (0.1)	2.1
pyranose (i)	pentane	25	36	2.5 (0.2)	4.6 (0.1)	2.1
		-78	18	0.13 (-55.0)	0.11 (-0.4)	0.03
		25	39	3.1 (0.7)	5.7 (0.0)	2.3
	diethylether	25	39	3.1 (0.7)	5.7 (0.0)	2.3
		-40	49	3.3 (-6.5)	4.8 (0.0)	1.2

^aFor more examples and details see reference [29].^bSee Charts 1 and 2.

-78°C in pentane, whereas **15** remained consistently racemic under all conditions (Table 3 gives selected data).

In general, the photodimerization with furanose and pyranose esters (**e-i**) gave low to moderate *ee*'s at 25°C in both pentane and diethyl ether, but the *ee* values increased rapidly by lowering the temperature. The most outstanding fact is that the product *ee* was enhanced to 68% in pentane at -78°C for the **Ih** sensitizer, giving the highest *ee* value ever reported for an enantiodifferentiating photosensitized cyclodimerization. By comparing the effect of saccharide substituents, it was concluded that only a modification close to the chromophore can effect the stereochemical outcome of the asymmetric photosensitization. Interestingly, the product chirality switched in some cases within the experimental temperature range. For example, sensitization with **If** favored (+)-**14** at -40°C or higher temperatures, while the antipodal (-)-**14** was predominately formed below -40°C. This finding unambiguously proved the significant contribution of the entropic factor in the enantiodifferentiating photocyclodimerization of **13** as already reported for cyclooctene (**1**) and cycloheptene (**2**).

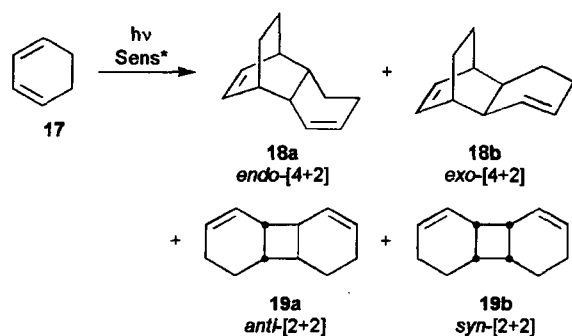
The lack of enantioselectivity in *cis-trans* dimer **15** may be striking, but a reasonable explanation came from the postulation of two parallel cyclodimerization pathways from the common intermediate (*E*)-cyclohexene (**13E**) [29]. Of these pathways, only one (to **14**) can preserve the chiral information induced in **13E** upon enantiodifferentiating photosensitization, the other one (to **15**) cannot.

1,3-Cyclohexadiene (17)

The photodimerization of 1,3-cyclohexadiene (**17**) to the isomeric [4+2] and [2+2] cyclodimers **18** and **19** has been investigated under a wide variety of conditions. In contrast to the thermal version, which solely affords the *endo*- and *exo*-Diels-Alder products (**18a** and **18b**) in poor yields after prolonged reaction time [31], the photochemical pathway leads to mixtures of [4+2] and [2+2] cyclodimers. The product composition hereby depended on the irradiation conditions. Direct excitation of **17** at 254 nm gave the *exo*-[4+2] adduct **18b** and both *anti*- and *syn*-[2+2] adducts **19a** and **19b** in a ratio of 1:4.4:2.3 together with other dimers [32]. Under triplet photosensitization conditions the same products **18b**, **19a**, and **19b** were obtained in *ca.* 1:3:1 ratio but in higher combined yields [33]. In contrast, the photoinduced electron-transfer (PET) reaction of **17** predominantly led to the *endo*-dimer **18a** in improved yields [33,34], and thus the *endo/exo* ratio of **18** can be used as an indication of the involvement of a PET mechanism.

Inoue and coworkers recently studied the enantiodifferentiating photosensitized cyclodimerization of **17** (Figure 11) [35]. Although a number of benzenepolycarboxylates (**A**) and naphthalene(poly)carboxylates (**B**) were employed as sensitizers, overall *ee*'s were generally low.

Among the three chiral products (**18a**, **18b** and **19a**), only **18b** was obtained as an optically active species with a maximum enantiomeric excess of 8.2% (Table 4 gives selected data). In

Figure 11. Enantiodifferentiating photodimerization of **17**.

the cyclohexene (**13**) case the best results were obtained with the photosensitizer possessing protected saccharides (**e**, **g**, **h**). Thus, it was postulated that the “microenvironmental polarity” around the chromophore [30] plays the crucial role in determining the photoreactivity and the *ee* of the products. The photosensitization involving 1,4-naphthalenedicarboxylates (**VII**) with saccharide auxiliaries gave different results in toluene, and the *endo*-product **18a** was obtained in low yields. Additionally, as compared to the estimated average product

ratio of **18b:19a:19b** (1.3:3.0:1.1 at 25°C and 1.3:3.0:0.7 at -41°C), slightly enhanced formation of **18b** was observed. Upon irradiation in diethylether, the yield of **18a** relative to **19a** was slightly increased for the saccharide containing sensitizers, whereas photosensitization with the menthyl ester (**VIIb**) in ether gave no **18a** *endo*-product at all, but instead gave a product ratio similar to that obtained upon irradiation in pentane or toluene. Hence, the formation of **18a** and the different product ratios observed for the saccharide-substituted sensitizers were attributed to the enhanced microenvironmental polarity around the sensitizer chromophore. Consequently, the charge-transfer interaction is stabilized under such conditions, while the dissociation to a free radical ion pair is prevented by the low bulk polarity. The combination of these effects keeps a closer stereochemical interaction between the chiral sensitizer and the substrate **17**. In acetonitrile, the effect of the saccharide auxiliaries vanishes, and photosensitization by both menthyl (**VIIb**) and saccharide (**VIII**) esters gave mainly the PET product **18a**, and all of the chiral byproducts obtained were racemic.

The observation that only the *exo*-[4+2] cyclodimer **18b** was obtained with significant *ee*'s led to the reasonable explanation that an independent cyclodimerization channel to

Table 4. Enantiodifferentiating photocyclodimerization of **17** sensitized by chiral (poly)alkyl arene(poly)carboxylates [35]^a

R* (sens.) ^b	Solvent	Temp. [°C]	Conv. [%]	Yield [%] (% <i>ee</i>) ^c			
				18a	18b	19a	19b
III , (-)-menthyl (b)	pentane	25	44	0	2.3 (2.5)	6.0 (-0.9)	1.9
		-43	49	0	1.3 (2.8)	3.4 (-1.5)	0.8
	toluene	25	56	0	1.7 (-0.6)	4.3 (-1.0)	1.7
		-41	22	0	1.1 (0.3)	2.6 (-0.7)	0.6
VII , (-)-menthyl (b)	pentane	25	92	0	17.9 (0.0)	47.5 (-1.9)	15.9
		-43	36	0	1.6 (0.8)	4.0 (-1.4)	1.0
	toluene	27	76	0	15.6 (0.1)	41.4 (-0.9)	14.0
		-41	59	0	3.8 (0.9)	10.0 (0.1)	2.4
		-41	13	0	2.1 (1.4)	5.4 (-0.3)	1.8
	diethylether	25	16	0	2.1 (1.4)	5.4 (-0.3)	1.8
		-41	13	0	1.5 (0.4)	3.8 (-0.2)	0.9
	acetonitrile	25	78	26.4 (-0.1)	5.0 (0.2)	7.8 (-1.1)	1.9
25		51	0	7.3 (0.4)	18.1 (-1.3)	5.4	
VII , furanose (e)	pentane	25	64	0.5 (^d)	4.5 (-5.3)	10.8 (0)	4.1
		-41	17	0.9 (^d)	3.2 (-2.2)	7.1 (-0.6)	2.1
	diethylether	25	^d	0.3 (^d)	2.8 (-4.6)	6.3 (-0.3)	2.0
		-41	^d	0.5 (^d)	1.3 (-6.4)	2.7 (-0.4)	0.6
VII , pyranose (h)	toluene	25	52	0.5 (^d)	3.8 (-7.6)	8.1 (-0.3)	3.1
		-41	49	0.6 (^d)	1.4 (-0.2)	3.2 (-0.4)	0.5
	diethylether	25	^d	0.4 (^d)	2.3 (-4.1)	4.7 (0.3)	1.4
		-41	^d	0.5 (^d)	1.1 (-2.5)	2.3 (-0.7)	0.6
VII , pyranose (i)	toluene	25	31	0.6 (^d)	5.0 (-5.1)	10.8 (-0.3)	4.2
		-41	24	0.8 (^d)	4.1 (-2.4)	9.7 (-0.8)	1.2
	diethylether	25	^d	0.3 (^d)	2.0 (-6.7)	4.6 (0.3)	1.3
		-41	^d	0.3 (^d)	0.8 (-8.2)	1.8 (-1.3)	0.4
acetonitrile	25	54	21.0 (0.0)	1.9 (0.4)	1.4 (0.7)	0.4	

^aFor more examples and details see reference [35].

^bSee Charts 1 and 2.

^cTentative sign of *ee*.

^dNot determined.

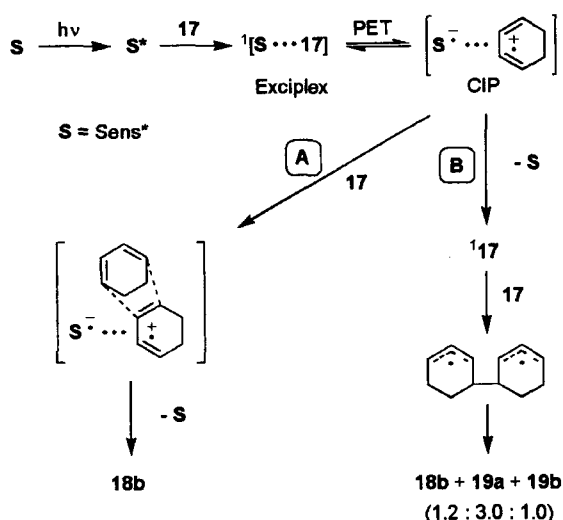


Figure 12. Mechanistic scenario.

18b (path A) operates in addition to the established biradical route (path B) that has been postulated (Figure 12). This pathway involves either an exciplex or contact ion pair (CIP) generated from **17** and the chiral sensitizer. In the case of the saccharide sensitizers, this intermediate is assumed to be stabilized *via* the microenvironmental polarity around the chromophore, allowing the transfer of chiral information from the sensitizers to the cyclodimer.

Based on the differences in the product ratio obtained with the saccharide- vs. non-saccharide-substituted sensitizers, and assuming that products **18b**, **19a**, and **19b** formed *via* the biradical channel (path B) are racemic and obtained in a fixed ratio of 1.15:3.0:1.02, it was possible to estimate the “*net*” *ee* of **19b** produced solely through the independent exciplex route (path A). Thus, in the case of the photosensitization by **VIIIh** in toluene at 25°C, 19% of **19b** was calculated to be formed *via* the exciplex with a net *ee* of 40%. Similarly, 10%

and 12% of **19b** were estimated to be formed *via* the exciplex channel upon photosensitization by **VIIIi** in ether at 25°C and -41°C with net *ee*'s of 65% and 70%, respectively.

CONCLUSION

We have demonstrated that asymmetric photosensitization can serve as a powerful methodology for transferring and inducing chirality through the electronically excited state. By using only a catalytic amount of optically active sensitizer, the highest enantiomeric excess of 77% ever reported was reached for a photosensitized unimolecular isomerization (**2Z**-to-**2E**), and of 68% for a bimolecular photocycloaddition (**13**-to-**14**). Furthermore, the concept of *multidimensional control of chirality* provides us with a useful and convenient tool to control the stereochemistry and stereoselectivity of the desired photoproduct. This concept may be transferable to other thermal or biochemical reactions where weak interactions are involved as key factors.

Acknowledgements – This publication is dedicated to the memory of Professor Sang-Chul Shim. YI expresses his deep appreciation to all of the enthusiastic coworkers mentioned in the references, who established the basis for the results presented in this review. We would additionally like to thank Dr. Guy A. Hembury for assistance in the preparation of this manuscript.

APPENDIX

A variety of chiral sensitizers are used in the literature for pursuing the photoreactions described above. Among them, we have tried to select the most valuable or representative examples. The interested reader should therefore refer to the

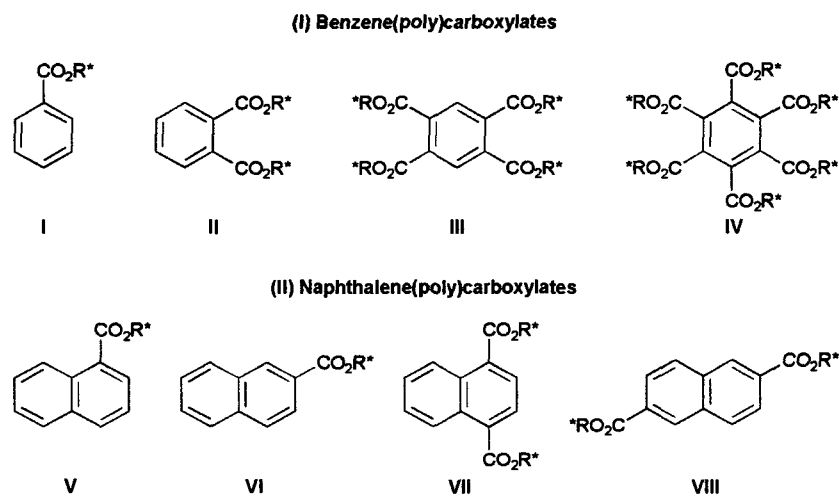


Chart 1. List of arene(poly)carboxylate chromophores.

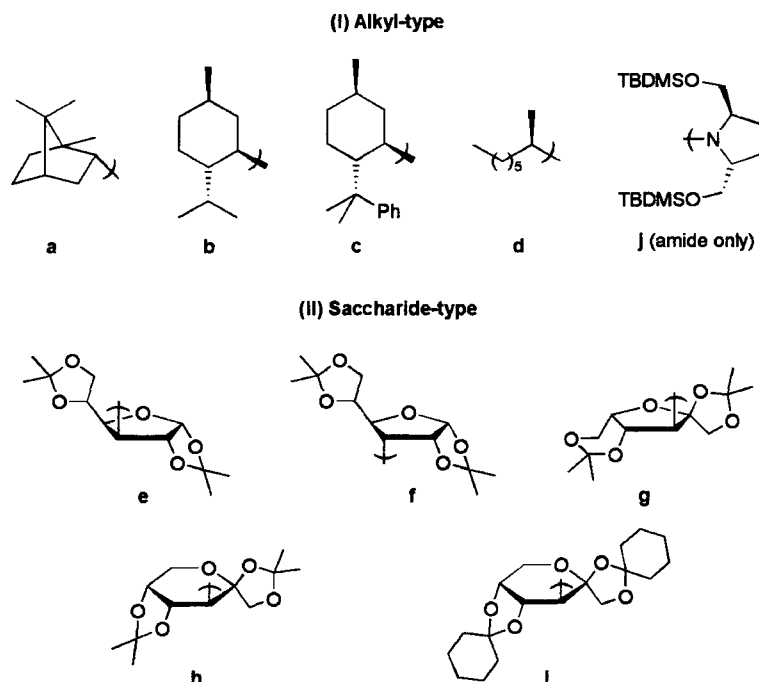


Chart 2. List of chiral auxiliaries.

original article to find a detailed and full list of all sensitizer systems applied. Chart 1 summarizes the selected arene(poly) carboxylate chromophores, whereas Chart 2 gives a list of all chiral auxiliaries attached to the chromophore. The combination of Roman number and small letter describes the corresponding chromophore/auxiliary pair; *e.g.*, **IIIb** represents *tetra*(-)-menthyl 1,2,4,5-benzenetetracarboxylate.

REFERENCES

- Rau, H. (1983) Asymmetric photochemistry in solution. *Chem. Rev.* **83**, 535-547.
- Inoue, Y. (1992) Asymmetric photochemical reactions in solution. *Chem. Rev.* **83**, 535-547.
- Everitt, S. R. L. and Inoue, Y. (1999) Asymmetric photochemical reactions in solution. *In: Organic Molecular Photochemistry*. Ed. by Ramamurthy, V. and Schanze, K., Marcel Dekker, New York, pp. 71-130.
- Inoue, Y., Wada, T., Asaoka, S., Sato, H. and Pete, J.-P. (2000) Photochirogenesis: multidimensional control of asymmetric photochemistry. *Chem. Commun.*, 251-259.
- Inoue, Y. (1995) Asymmetric synthesis through photosensitization: state of the art. *J. Synth. Org. Chem.* **53**, 348-357 (in Japanese).
- Hammond, G. S. and Cole, R. S. (1965) Asymmetric induction during energy transfer. *J. Am. Chem. Soc.* **87**, 3256-3257.
- Inoue, Y., Matsushima, E. and Wada, T. (1998) Pressure and temperature control of product chirality in asymmetric photochemistry. Enantiodifferentiating photoisomerization of cyclooctene sensitized by chiral benzenepolycarboxylates. *J. Am. Chem. Soc.* **120**, 10687-10696.
- Inoue, Y., Ikeda, H., Kaneda, M., Sumimura, T., Everitt, S. R. L. and Wada, T. (2000) Entropy-controlled asymmetric photochemistry: switching of product chirality by solvent. *J. Am. Chem. Soc.* **122**, 406-407.
- Inoue, Y., Sugahara, N. and Wada, T. (2001) Vital role of entropy in photochirogenesis. *Pure Appl. Chem.* **73**, 475-480.
- For a recent review on photoinduced isomerization reactions of cycloalkenes, see: Mori, T. and Inoue, Y. (2003) Photochemical isomerization of cycloalkenes. *In: CRC Handbook of Photochemistry and Photobiology*. 2nd edition. Ed. by Horspool, W. H., CRC Press Inc., Washington DC, in print.
- Burkert, U. and Allinger, N. L. (1982) Molecular mechanics. *In: ACS Monograph 177*. Ed. by Caserio, M. C., ACS, Washington DC.
- Corey, E. J., Carey, F. A. and Winter, A. E. (1965) Stereospecific syntheses of olefins from 1,2-thionocarbonates and 1,2-trithiocarbonates. *trans-Cycloheptene*. *J. Am. Chem. Soc.* **87**, 934-935.
- Kropp, P. J. (1969) Photochemistry of cycloalkenes. V. Effects of ring size and substitution. *J. Am. Chem. Soc.* **91**, 5783-5791.
- Inoue, Y., Ueoka, T., Kuroda, T. and Hakushi, T. (1981) *trans-Cycloheptene*. Photochemical generation and thermal *trans-cis* isomerization. *J. Chem. Soc., Chem. Comm.* 1031-1033.
- Inoue, Y., Ueoka, T., Kuroda, T. and Hakushi, T. (1983) Singlet photosensitization of simple alkenes. Part 4. *cis-trans* Photoisomerization of cycloheptene sensitized by aromatic

- esters. Some aspects of the chemistry of *trans*-cycloheptene. *J. Chem. Soc., Perkin Trans. 2*, 983-988.
16. Nishiyama, H., Naitoh, T., Motoyama, Y. and Aoki, K. (1999) Chiral bis(dihydrooxazolyl)pyridineruthenium complexes of *trans*-cyclooctene and *trans*-cycloheptene. *Chem. Eur. J.* **5**, 3509-3513.
 17. Hoffmann, R. and Inoue, Y. (1999) Trapped optically active (*E*)-cycloheptene generated by enantiodifferentiating *Z-E* photoisomerization of cycloheptene sensitized by chiral aromatic esters. *J. Am. Chem. Soc.* **121**, 10702-10710.
 18. Cope, A. C. and Bumgardner, C. L. (1956) Cyclic polyolefines. XL. *cis-cis*- and *trans-trans*-1,3-Cycloöctadiene from cycloöcten-3-yl-dimethylamine. *J. Am. Chem. Soc.* **78**, 2812-2815.
 19. Liu, R. S. H. (1967) Photosensitized isomerization of 1,3-cyclooctadienes and conversion to bicyclo[4.2.0]oct-7-ene. *J. Am. Chem. Soc.* **89**, 112-114, and references therein.
 20. Isaksson, R., Roschester, J., Sandström, J. and Wistrand, L.-G. (1985) Resolution, chiral dichroism spectrum, molecular structure, and absolute configuration of *cis,trans*-1,3-cyclooctadiene. *J. Am. Chem. Soc.* **107**, 4074-4075.
 21. Inoue, Y., Tsuneishi, H., Hakushi, T. and Tai, A. (1997) Optically active (*E,Z*)-1,3-cyclooctadiene: first enantioselective synthesis through asymmetric photosensitization and chiroptical property. *J. Am. Chem. Soc.* **119**, 472-478.
 22. Shi, M. and Inoue, Y. (1998) Enantiodifferentiating photoisomerization of (*Z*)-cyclooctene and (*Z,Z*)-cycloocta-1,3-diene sensitized by chiral aromatic amides. *J. Chem. Soc. Perkin Trans. 2*, 1725-1729.
 23. Cope, A. C., Howell, C. F., Bowers, J., Lord, R. C. and Whiteside, G. M. (1967) Cyclic polyolefins. XLV. *cis,trans*-1,5-Cyclooctadiene. *J. Am. Chem. Soc.* **89**, 4024-4027, and references therein.
 24. Cope, A. C., Hecht, J. K., Johnson Jr., H. W., Keller, H. and Winkler, H. J. S. (1966) Molecular asymmetry of olefins. V. Resolution of *cis-trans*-1,5-cyclooctadiene. *J. Am. Chem. Soc.* **88**, 761-763.
 25. Whitesides, G. M., Goe, G. L. and Cope, A. C. (1969) Irradiation of *cis,cis*-cyclooctadiene in the presence of copper(I) chloride. *J. Am. Chem. Soc.* **91**, 2608-2616, and references therein.
 26. Goto, S., Takamuku, S., Sakurai, H., Inoue, Y. and Hakushi, T. (1980) Singlet photosensitization of simple alkenes. Part 2. Photochemical transformation of cyclo-octa-1,5-diene sensitized by aromatic ester. *J. Chem. Soc., Perkin Trans. 2*, 1678-1682.
 27. Kropp, P. J., Snyder, J. J., Rawlings, P. C. and Fravel Jr., H. G. (1980) Photochemistry of cycloalkenes. 9. Photodimerization of cyclohexene. *J. Org. Chem.* **45**, 4471-4474, and references therein.
 28. Salomon, R. G., Folting, K., Streib, W. E. and Kochi, J. K. (1974) Copper(I) catalysis in photocycloadditions. II. Cyclopentene, cyclohexene, and cycloheptene. *J. Am. Chem. Soc.* **96**, 1145-1152.
 29. Asaoka, S., Horiguchi, H., Wada T. and Inoue, Y. (2000) Enantiodifferentiating photocyclodimerization of cyclohexene sensitized by chiral benzenecarboxylates. *J. Chem. Soc., Perkin Trans. 2*, 737-747.
 30. The same sensitizers have been effectively applied to the enantiodifferentiating photoaddition of alcohols to 1,1-diphenylalkenes: Asaoka, S., Kitazawa, T., Wada, T. and Inoue, Y. (1999) Enantiodifferentiating anti-Markovnikov photoaddition of alcohols to 1,1-diphenylalkenes sensitized by chiral naphthalenecarboxylates. *J. Am. Chem. Soc.* **121**, 8486-8498.
 31. Valentine, D., Turro, Jr., J. T. and Hammond, G. S. (1964) Thermal and photosensitized dimerization of cyclohexadiene. *J. Am. Chem. Soc.* **86**, 5202-5208.
 32. Schenck, G. O., Mannsfeld, S. P., Schomburg, G. and Krauch, C. H. (1964) Strahlenchemische Cyclodimerisation von 1,3-Cyclohexadien und neuartige Bildungsweisen von Diels-Alder-Addukten. *Z. Naturforschg.* **19b**, 18-22.
 33. Vondenhof, M. and Mattay, J. (1990) 1,1'-Binaphthalene-2,2'-dicarbonitrile in photochemically sensitized enantiodifferentiating isomerizations. *Chem. Ber.* **123**, 2457-2459.
 34. Calhoun, G. C. and Schuster, G. B. (1984) Radical cation and triplex Diels-Alder reactions of 1,3-cyclohexadiene. *J. Am. Chem. Soc.* **106**, 6870-6871.
 35. Asaoka, S., Ooi, M., Jiang, P., Wada, T. and Inoue, Y. (2000) Enantiodifferentiating photocyclodimerization of cyclohexa-1,3-diene sensitized by chiral arenecarboxylates. *J. Chem. Soc., Perkin Trans. 2*, 77-84.