

Enantiodifferentiating photocyclodimerization of cyclohexene sensitized by chiral benzenecarboxylates

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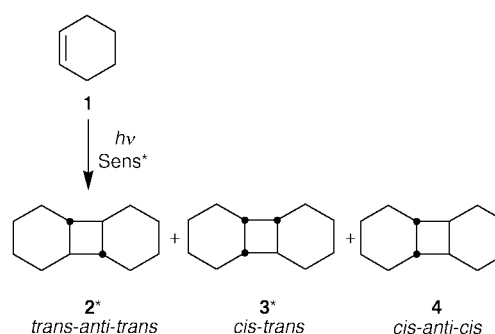
The photosensitized cyclodimerization of (*Z*)-cyclohexene (**1Z**) was performed over a range of temperatures in the presence of chiral benzene(poly)carboxylate sensitizers, giving *trans-anti-trans*-, *cis-trans*- and *cis-anti-cis*-[2 + 2]-cyclodimers **2–4**. Of the two chiral cyclodimers (**2**, **3**), only **2** was obtained optically active with enantiomeric excesses as high as 68.3% at $-78\text{ }^{\circ}\text{C}$, whereas **3** was consistently racemic under various reaction conditions employed. The detailed reaction mechanism and the origin of enantiodifferentiation have been elucidated and involve the initial enantiodifferentiating photoisomerization of **1Z** to the highly reactive (*E*)-isomer (**1E**) and the subsequent stereospecific concerted cyclodimerization with **1Z** giving optically active **2** which is competing with the non-stereospecific stepwise cyclodimerization to racemic **2** and **3**.

Enantiodifferentiating photosensitization, which necessitates only a catalytic amount of optically active compound as chiral sensitizer, provides us with the most chiral source-efficient photochirogenetic methodology for transferring and multiplying chirality through the electronically excited state.¹ For that reason, a considerable amount of effort has been devoted to this mechanistically intriguing and synthetically important interdisciplinary field between photochemistry and asymmetric synthesis.^{1–13} However, this strategy has rarely been successful in giving optical yield higher than 6.7%, which was originally reported for the photosensitized enantiomeric isomerization of *trans*-1,2-diphenylcyclopropane in the pioneering work by Hammond and Cole.² Recently, we have shown that the enantiodifferentiating geometrical photoisomerization of (*Z*)-cyclooctene sensitized by chiral benzenepolycarboxylates gives the optically active (*E*)-isomer in fairly high enantiomeric excesses (ees) of up to 64%, and unprecedentedly the product chirality is inverted by changing the temperature^{5*d–j*} and also by applying hydrostatic pressure.^{5*k*} In the most recent study, it has been demonstrated that the enantiodifferentiating photosensitized isomerization of (*Z*)-cycloheptene at low temperatures gives the highly strained (*E*)-isomer in the highest yet ee of 77% at $-80\text{ }^{\circ}\text{C}$.^{5*l*}

In contrast to such unimolecular enantiodifferentiating photoisomerizations, only a limited number of attempts have been made on bimolecular enantiodifferentiating photoaddition reactions.^{14–16} It is of significant interest and importance to extend the study on asymmetric photochemistry to photosensitized addition reactions which have been most widely explored from the mechanistic and synthetic points of view.¹⁷ The enantiodifferentiating [2 + 2] photocyclodimerizations of aryl vinyl ethers and 4-methoxystyrene were examined in the presence of optically active naphthalenecarboxylates as sensitizers to give the corresponding cyclobutane derivatives in good chemical yields only in acetonitrile but with extremely low ees (<1%).¹⁴ Kim and Schuster reported the first successful asymmetric photochemical study on the [4 + 2] photocycloaddition of (*E*)- β -methylstyrene with cyclohexa-1,3-diene, sensitized by (–)-1,1'-bi(2,4-dicyanonaphthalene), which gave the [4 + 2]-cycloadduct, of 15% ee, at $-65\text{ }^{\circ}\text{C}$.¹⁵ Recently, we have

reported that the enantiodifferentiating polar addition of alcohols to 1,1-diphenylalk-1-enes sensitized by optically active naphthalene(di)carboxylates gives the optically active anti-Markovnikov adduct with optimized ees of up to 33%, and also that unusual switching of the product chirality is induced by changing the irradiation temperature, leading to the formation of antipodal products at different temperatures and also to the 'inverted' temperature dependence which gives higher ees at higher temperatures.^{16*a,b*}

The enantiodifferentiating photocyclodimerization of cyclohexa-1,3-diene has been investigated using optically active arene(poly)carboxylates as sensitizers to give two [4 + 2]- and two [2 + 2]-cyclodimers. Only the *exo*-[4 + 2]-cyclodimer was obtained as optically active product among the three chiral cyclodimers. Although the ee of the cyclodimer was not specifically high (<8%), the contrasting behavior of the ee of each product upon enantiodifferentiating photosensitization has clearly allowed us to sort out the mechanistic ambiguity.^{16*c*} In this context, it is interesting to investigate the photosensitized cyclodimerization of cyclohexene **1** to a mixture of *trans-anti-trans*-, *cis-trans*- and *cis-anti-cis*-[2 + 2]-cyclodimers **2–4** (Scheme 1) using optically active sensitizers, since competing



Scheme 1

concerted and stepwise mechanisms have been proposed to be involved in the photocyclodimerization.^{18–20} It is also in our further interest to examine the effect of smaller ring size,

Chiral Sensitizers

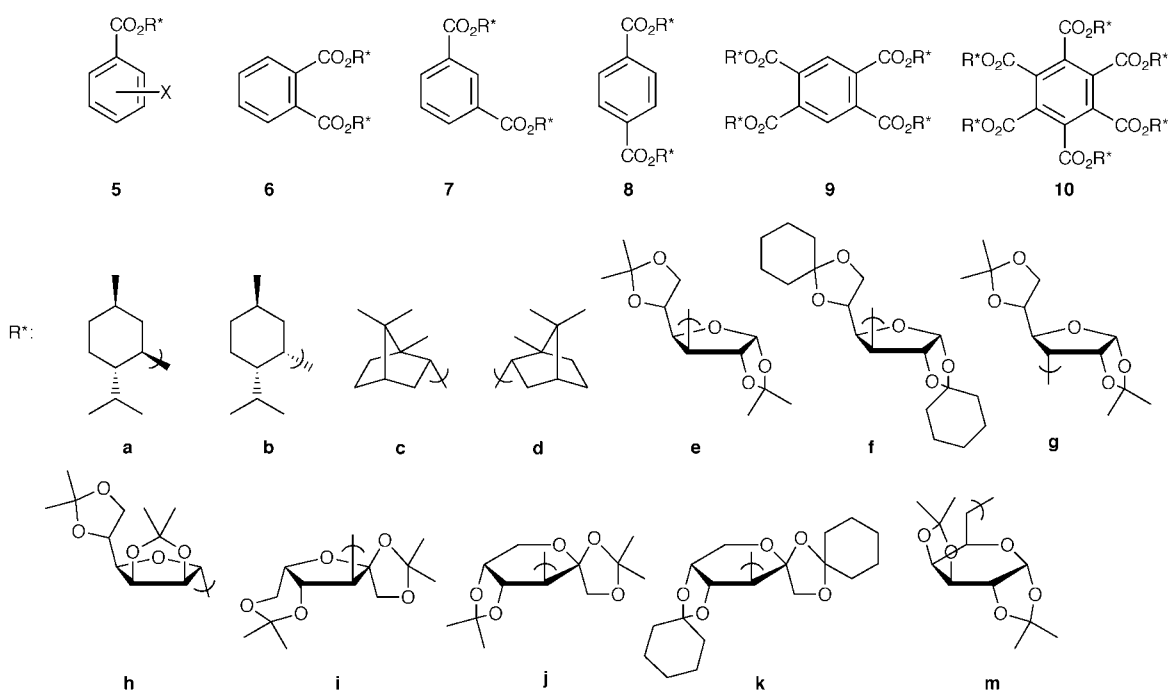


Chart 1

reduced steric hindrance, and less flexible skeleton upon both the photosensitization and the enantiodifferentiation processes, by comparing the asymmetric photochemical behavior of **1** with that of cyclooctene^{5a,b,d,i,k,l} and cycloheptene.^{5l} Here, we report the results of our study on the enantiodifferentiating photocyclodimerization of cyclohexene sensitized by optically active benzene(poly)carboxylates, and we will discuss the detailed mechanism and intermediates involved in the enantiodifferentiation and subsequent cyclodimerization processes.

Results and discussion

The photocyclodimerization of **1** has been investigated under direct excitation and triplet sensitization conditions.^{18–20} The direct irradiation of **1** in pentane produced a mixture of three [2 + 2]-cyclodimers, *i.e.* *trans-anti-trans* (**2**), *cis-trans* (**3**), and *cis-anti-cis* (**4**), in the proportions 2.0:2.6:1.0. The *p*-xylylene-sensitization of **1** in aprotic media also afforded a mixture of cyclodimers **2–4**, product proportions of which were different from those obtained in the direct excitation and which varied appreciably with solvent and temperature used.^{18c} Thus, the xylene-photosensitization gave **2**, **3** and **4** in the proportions 1.1:1.8:1.0 and 1.5:2.6:1.0 in pentane and diethyl ether, respectively. The ratio of **3**:**4** slightly decreased on lowering the temperature.

In the present study, we employed a variety of optically active benzene(poly)carboxylates (**5–10**) (Chart 1) as chiral sensitizers for the enantiodifferentiating photocyclodimerization of **1**. As reported previously,⁵ benzene(poly)carboxylates have widely been employed as effective singlet sensitizers for the enantiodifferentiating photoisomerization of cycloalkenes, and they allow us to examine a wide variety of chiral auxiliaries introduced to the vicinity of the chromophore.

Sensitization mechanism

In view of the relevant studies on cyclooctene and cycloheptene where the singlet mechanism is well evidenced and accepted,⁵ we presumed that the present photoisomerization of cyclohexene also proceeded through the singlet manifold. In our previous studies,^{5b,j,l} we have demonstrated that the fluorescence

of the singlet sensitizers **9** and **10** is efficiently quenched by cyclooctene and cycloheptene at near-diffusion limited rates of 10^9 – 10^{10} dm³ mol⁻¹ s⁻¹. Furthermore, our recent comparative study on the photoisomerizations of cyclooctene sensitized by benzyl (–)-menthyl ether and by (–)-menthyl benzoate has revealed that the benzyl ether, which would be expected to sensitize cyclooctene in the triplet manifold, behaves as a singlet/triplet dual-function sensitizer, depending on the substrate concentration, while the benzoate functions as a pure singlet sensitizer over a wide range of cyclooctene concentration.⁵ⁱ Thus, the chiral *ether* gives an extremely low photostationary *E/Z* quotient, *i.e.* $(E/Z)_{\text{pss}} = 0.015$, with an appreciable ee of $1.29 \pm 0.01\%$ at very high cyclooctene concentrations (>100 mmol dm⁻³), where the singlet dominates the photosensitization, while the same sensitizer affords a much higher $(E/Z)_{\text{pss}}$ of 0.22 and almost negligible ee ($<0.5\%$) at low concentrations, where the singlet sensitizer is not efficiently quenched and suffers intersystem crossing to the triplet. In contrast, the chiral *ester* gave invariant $(E/Z)_{\text{pss}}$ of 0.24 and ee of $2.6 \pm 0.1\%$ over the whole concentration range employed (5 – 500 mmol dm⁻³). Therefore, we concluded that the enantiodifferentiating photosensitization is inefficient in the triplet manifold.⁵ⁱ Unfortunately, the benzoates employed in this study do not fluoresce, but the fluorescence of the other benzenepolycarboxylates such as **9** and **10** are quite efficiently quenched by cycloalkenes, even by cyclopentene, probably through the weak charge-transfer interaction between sensitizer and substrate, leading to the formation of an exciplex intermediate. Hence, the failure of the benzenepolycarboxylates to efficiently sensitize the photoisomerization of cyclohexene may be attributable to their lower singlet energy as well as the structural rigidity of cyclohexene which diminishes the probability of 'non-vertical' energy transfer within the exciplex.

In the present study, we examined the effects of oxygen, added as a triplet quencher, on the photosensitization of **1** with **5j** to find that the presence of oxygen does diminish the product yields but never affects the relative ratio or ee of the products, as described later in more detail. Thus, this observation eliminates the possibility of the triplet sensitization as the major pathway. We will also demonstrate that all of the enthalpy–entropy compensation plots of the activation parameters

Table 1 Enantiodifferentiating photocyclodimerization of cyclohexene **1** sensitized by (–)-menthyl benzene(poly)carboxylates **5a–10a** in pentane at 25 °C^a

Entry	Sensitizer		Irradiation time t/h	Conversion (%)	Yield (%) (% ee ^c)		
	X	E_s^b			2	3	4
1	5a	H	4	39	3.4 (–5.1)	6.1 (–0.2)	2.7
2			24	69	4.9 (–5.3)	9.0 (–0.2)	4.0
3		2-CF ₃	24	38	0.2 (+0.1)	0.3 (+1.2)	0.1
4		3-CF ₃	24	56	2.3 (–3.4)	4.3 (–0.4)	1.9
5		4-CF ₃	24	44	0.7 (–5.7)	1.2 (+0.6)	0.5
6		3,5-(CF ₃) ₂	24	49	1.6 (–1.7)	2.9 (–0.4)	1.3
7		4-CN	24	20	0	0	0
8		2-OH	24	15	0	0	0
9	6a		24	31	0	0	0
10	7a		24	51	1.1 (–4.7)	2.1 (–0.8)	0.9
11	8a		24	40	0.1 (+2.3)	0.2 (–1.1)	0.1
12	9a		24	33	0	0	0
13	10a		24	29	0	0	0

^a [1] = 20 mmol dm^{–3}; [sensitizer] = 5 mmol dm^{–3}. ^b Singlet energy of sensitizer in kcal mol^{–1} (1 cal = 4.184 J), estimated from the absorption 0–0 band in pentane (ref. 5g). ^c Enantiomeric excess determined by chiral GLC.

obtained for C₆–C₈ cycloalkenes fall on the same regression line with an excellent correlation coefficient. This fact indicates the operation of a common, most probably singlet, mechanism in the enantiodifferentiating photosensitization of these cycloalkenes.

Chemical and quantum yields

In search of the most effective sensitizers for the photocyclodimerization of **1**, a series of benzene(poly)carboxylates **5–10** with various chiral auxiliaries (**a–l**) were examined. In a typical run, the photosensitization of **1** (20 mmol dm^{–3}) was performed in the presence of benzene(poly)carboxylate (5 mmol dm^{–3}) in pentane at 25 °C to give cyclodimers **2–4**. Of these three [2 + 2]-cyclodimers, **2** and **3** are chiral, as indicated by an asterisk in Scheme 1. The chemical yields and ees, determined by gas–liquid chromatographic analysis over a chiral stationary phase, are summarized in Tables 1 and 2. No other peaks were found in the 'dimer region' of GLC retention time, and the formation of bicyclohexyl was clearly ruled out by the direct comparison on GLC with an authentic sample. Furthermore, the relative proportions of products **2**:**3**:**4** were not affected by catalytic hydrogenation of the irradiated solution over Pd/C, which clearly indicates the absence of any unsaturated product overlaying the GLC peaks of **2–4**.

In order to determine the sign of optical rotation of the product, a preparative-scale photosensitization of **1** with **5e** was carried out and the product mixture was subjected to preparative gel permeation chromatography (GPC) separation. Although the GPC column used was achiral, the ee of the product was shown to be the same before and after the isolation procedure. The isolated *trans-anti-trans* isomer **2** afforded a negative optical rotation ($\alpha = -0.0038 \pm 0.0006^\circ$) at 589 nm. In Tables 1 and 2, the sign of the ee-value for **2** represents the direction of optical rotation, *i.e.* a positive value indicates the formation of (+)-**2** as the dominant enantiomer. The cyclodimer **3** was also isolated in the same preparative-scale experiment, but its ee was too low (<1%) to allow us to determine the sign of the optical rotation. Then, the sign of ee of **3**, shown in the Tables, is only tentative, representing the order of elution from a Supelco β -DEX 325 column; *i.e.* a positive value means the predominant formation of the first eluting enantiomer.

The photocyclodimerizations sensitized by a series of chiral benzene(poly)carboxylates **5a–10a** with (–)-menthyl auxiliary were performed in pentane at 25 °C (runs 1 and 9–13). As shown in Table 1, benzoate **5a** gave cyclodimers **2–4** in a combined chemical yield of 18% (26% yield based on the conversion), while isophthalate **7a** and terephthalate **8a** gave **2–4**

in much lower yields than benzoate **5a**, and the use of pyromellitate **9a** and mellitate **10a** resulted in decreased conversions and no formation of cyclodimers. The product yield appears to be determined by the singlet energy (E_s) of the sensitizer. Although the E_s of phthalate **6a** is higher than those of **7a** and **8a**, no cyclodimers were produced, for which the steric hindrance caused by the two menthoxy carbonyl groups at adjacent *ortho* positions would be responsible. This seems reasonable since such steric hindrance will not totally prohibit the approach of substrate but decelerates the energy transfer within the exciplex formed owing to the greater distance and less intimate interaction between the substrate and sensitizer. The highest ee of 5.3% was obtained for **2** upon sensitization with (–)-menthyl benzoate **5a** in pentane at 25 °C, while no appreciable ee was obtained for *cis-trans*-dimer **3** in all cases.

Among the menthyl benzene(poly)carboxylates examined, menthyl benzoate appeared to be the best choice in view of both chemical and optical yields. Hence, the effects of substitution on the aromatic ring were systematically investigated (runs 3–8 in Table 1). 4-Cyano- and 2-hydroxybenzoates with lower E_s than that of unsubstituted benzoate (X = H) gave much lower conversions and no cyclodimers. Possessing a higher E_s , trifluoromethyl-substituted benzoates [X = 2-, 3-, 4-CF₃ and 3,5-(CF₃)₂] gave the cyclodimers, only in much decreased chemical yields. Thus, the introduction of both electron-donating and -withdrawing groups equally diminished the product yield dramatically, which is rationalized by the increased steric hindrance and/or lower E_s induced by the substitution. The ees of **2** obtained upon sensitization with the substituted benzoates were much lower than that obtained with unsubstituted benzoate (5.3% ee), except for 4-(trifluoromethyl)benzoate which gave **2** of 5.7% ee.

In sharp contrast to the cyclooctene and cycloheptene cases investigated under comparable conditions,⁵ all of the substituted benzoates and benzenepolycarboxylates failed to give appreciable yields of cyclodimers. The quantum yields were also determined for the formation of products **2**, **3** and **4** upon sensitization with **5e** as 2.9×10^{-3} , 5.3×10^{-3} and 2.4×10^{-3} , respectively. The combined quantum yield was as low as 0.01, which is much smaller than the value (0.32) determined for the *Z-to-E* photoisomerization of cyclooctene sensitized by **5a**.^{5b} Judging from the fact that the sensitization behavior of cyclohexene is extremely sensitive to both steric hindrance and E_s , the inefficient energy-transfer to the substrate is at least in part responsible for the low quantum yields. This low efficiency may be attributed to the conformational rigidity of cyclohexene as compared with the higher homologs, such as the vertical, or Franck–Condon, singlet of a 1,2-dialkylethylene (≈ 130 kcal

Table 2 Enantiodifferentiating photodimerization of cyclohexene **1** sensitized by chiral benzoates **5a–1^a**

Entry	Sensitizer	Solvent	Temperature <i>T</i> /°C	Irradiation time <i>t</i> /h	Conversion (%)	Yield (%) (% ee ^b)				
						2	3	4		
1	5a	pentane	25	4	39	3.4 (−5.1)	6.1 (−0.2)	2.7		
2			0	8	61	6.1 (−5.5)	9.9 (0.0)	3.8		
3			−40	24	37	2.9 (−7.3)	3.9 (−0.1)	1.1		
4			−68	48	50	2.6 (−13.1)	3.1 (0.0)	0.7		
5			−78	48	17	0.39 (−18.7)	0.39 (−0.8)	0.08		
6			25	4	46	4.1 (−4.7)	7.6 (+0.1)	3.1		
7			0	8	63	6.2 (−5.8)	10.2 (−0.3)	3.4		
8			−40	24	39	3.6 (−7.4)	4.9 (−0.2)	1.2		
9			−68	48	50	3.0 (−10.2)	3.8 (0.0)	0.7		
10	−78	48	19	0.52 (−13.1)	0.63 (−0.1)	0.10				
11	5b	pentane	25	4	43	3.6 (+2.4)	6.3 (0.0)	3.0		
12			0	8	59	5.1 (+2.6)	8.3 (+0.2)	3.2		
13			−40	24	37	2.3 (−0.6)	3.0 (+0.3)	0.9		
14			25	4	42	3.6 (+2.2)	6.8 (0.0)	2.8		
15			0	8	60	5.9 (+2.5)	9.8 (+0.2)	3.3		
16			−40	24	37	2.9 (−1.5)	4.0 (0.0)	1.0		
17			25	4	42	3.6 (−6.0)	6.7 (−0.1)	3.0		
18			0	8	59	5.2 (−7.7)	8.2 (−0.5)	3.1		
19			−40	24	31	2.1 (−14.9)	2.7 (−0.1)	0.8		
20	−68	48	46	2.1 (−27.0)	2.2 (−0.4)	0.5				
21	−78	48	24	0.37 (−30.5)	0.37 (−1.4)	0.08				
22	5c	diethyl ether	25	4	42	3.7 (−5.8)	6.8 (−0.2)	2.7		
23			0	8	61	6.0 (−8.2)	9.7 (−0.3)	3.2		
24			−40	24	35	2.4 (−13.0)	3.2 (−0.4)	0.8		
25			−68	48	46	2.8 (−21.5)	3.2 (+0.6)	0.6		
26			−78	48	16	0.36 (−25.6)	0.41 (−1.8)	0.07		
27			25	4	41	4.0 (+6.7)	7.4 (−0.1)	3.4		
28			0	9	66	5.8 (+8.1)	9.4 (−0.3)	3.7		
29			−40	24	54	4.6 (+12.0)	6.3 (+0.2)	2.0		
30			−68	48	49	1.5 (+24.2)	1.7 (+0.3)	0.4		
31	−78	48	22	0.31 (+30.1)	0.32 (+0.6)	0.07				
32	5d	diethyl ether	25	4	47	4.8 (+6.5)	8.8 (−0.5)	3.6		
33			0	9	60	6.5 (+6.8)	11.0 (−0.3)	3.7		
34			−40	24	54	4.6 (+11.2)	6.6 (+0.2)	1.7		
35			25	4	36	2.1 (−11.9)	4.0 (−0.4)	1.8		
36			0	8	54	4.8 (−12.3)	7.9 (−0.4)	3.1		
37			−40	24	43	2.5 (−20.9)	3.3 (−0.3)	1.0		
38			−68	48	40	1.1 (−32.6)	1.2 (−1.6)	0.3		
39			−78	48	19	0.22 (−51.0)	0.19 (+0.9)	0.05		
40			5e	diethyl ether	25 ^c	24	9	0.4 (−9.1)	0.7 (0.0)	0.3
41	25 ^d	24			53	2.8 (−9.8)	4.8 (−0.2)	1.9		
42	25	1			18	1.1 (−11.7)	1.9 (+0.2)	0.8		
		4			43	3.0 (−11.2)	5.5 (−0.5)	2.2		
		8			62	3.3 (−10.1)	6.0 (−0.9)	2.4		
		24			63	3.7 (−10.4)	6.7 (−0.4)	2.7		
43	25 ^e	24			81	4.2 (−9.0)	7.7 (−0.2)	3.0		
44	25 ^f	24			>99	6.0 (−8.7)	10.9 (+0.2)	4.3		
45	−40	1			15	0.6 (−16.7)	0.9 (+0.7)	0.2		
		4	22	0.9 (−14.7)	1.2 (0.0)	0.3				
		8	25	1.5 (−15.3)	2.1 (−0.3)	0.5				
		24	43	2.3 (−15.3)	3.3 (+0.2)	0.8				
46	5f	acetonitrile	−68	48	47	2.1 (−15.7)	2.6 (−0.2)	0.5		
47			−78	48	16	0.36 (−30.5)	0.42 (−1.8)	0.07		
48			25	4	40	2.0 (−9.8)	2.9 (−0.1)	0.8		
49			0	8	54	2.2 (−11.2)	3.1 (+0.1)	0.8		
50			−40	8	36	1.2 (−9.1)	1.5 (−1.2)	0.3		
51			25 ^g	6	67	1.4 (−9.5)	2.3 (+0.6)	0.7		
52			0 ^h	8	55	2.1 (−11.0)	3.1 (+0.1)	0.9		
53			−40 ⁱ	24	46	1.4 (−14.7)	2.0 (−1.0)	0.4		
54			5g	pentane	25	4	34	2.9 (−13.8)	5.5 (−0.5)	2.5
55	0	9			55	4.0 (−14.6)	6.5 (−0.5)	2.5		
56	−40	24			50	3.9 (−19.2)	5.3 (−0.2)	1.7		
57	−68	48			44	1.2 (−37.9)	1.2 (−0.6)	0.3		
58	−78	48			16	0.17 (−54.1)	0.15 (+0.3)	0.04		
59	5h	diethyl ether			25	4	41	4.0 (−13.0)	7.0 (−0.4)	2.8
60					0	9	54	4.7 (−13.8)	7.5 (−0.3)	2.5
61					−40	24	44	2.2 (−19.0)	3.1 (−0.6)	0.8
62					5i	pentane	25	4	36	2.2 (+7.0)
63			0	8			51	3.7 (+8.7)	6.1 (+0.2)	2.3
64			−40	24			29	1.1 (+1.3)	1.5 (+0.3)	0.4
65			−68	48			40	0.87 (−22.2)	0.94 (−0.8)	0.23
66			−78	48			16	0.08 (−35.9)	0.08 (−1.7)	0.02
67			5j	diethyl ether			25	4	41	2.3 (+7.5)
68	0	8					53	4.0 (+9.0)	6.6 (+0.3)	2.2
69	−40	24					29	1.7 (+6.7)	2.4 (−0.5)	0.6

Table 2 (Contd.)

Entry	Sensitizer	Solvent	Temperature T/°C	Irradiation time t/h	Conversion (%)	Yield (%) (% ee ^b)		
						2	3	4
70			-68	48	46	1.4 (-8.7)	1.7 (-1.1)	0.3
71			-78	48	17	0.36 (-15.4)	0.42 (-0.3)	0.07
72	5h	pentane	25	4	38	2.4 (-7.0)	4.6 (-0.3)	2.1
73			0	8	52	4.0 (-7.1)	6.6 (-0.1)	2.6
74			-40	24	23	1.5 (-11.3)	2.0 (-0.5)	0.6
75			-68 ^j	48	16	0.76 (-25.9)	0.82 (-0.7)	0.20
76			-78 ^j	48	10	0.04 (-51.1)	0.04 (+1.4)	0.01
77		diethyl ether	25	4	47	3.6 (-7.5)	6.8 (-0.3)	2.7
78			0	9	54	5.1 (-8.1)	8.4 (-0.8)	2.9
79			-40	24	53	4.4 (-11.0)	6.5 (-0.1)	1.7
80	5i	pentane	25	4	38	2.8 (+6.7)	5.2 (+0.4)	2.4
81			0	8	49	4.0 (+8.8)	6.5 (+0.4)	2.5
82			-40	24	29	1.0 (+24.8)	1.3 (+1.0)	0.4
83			-68	48	36	0.56 (+47.4)	0.53 (+1.7)	0.15
84			-78	48	18	0.06 (+62.8)	0.04 (+1.5)	0.01
85		diethyl ether	25	4	37	2.0 (+6.4)	3.6 (+0.7)	1.4
86			0	8	51	4.0 (+7.4)	6.6 (+0.2)	2.2
87			-40	24	27	1.4 (+14.6)	2.0 (+0.8)	0.5
88			-68	48	40	1.5 (+34.9)	1.7 (+0.9)	0.3
89			-78	48	19	0.20 (+49.4)	0.20 (+1.4)	0.05
90	5j	pentane	25	4	38	2.1 (-2.1)	4.0 (-0.2)	1.8
90a			25 (air) ^k	4	39	0.3 (-2.0)	0.5 (1.7)	0.2
91			0	8	51	3.4 (-2.2)	5.6 (-0.2)	2.2
92			-40	24	33	1.3 (-20.3)	1.7 (-0.3)	0.5
92a			-40 (air) ^k	24	40	0.6 (-20.6)	0.8 (-0.2)	0.2
93			-68	48	42	1.0 (-42.0)	1.0 (-0.1)	0.3
94			-78	48	25	0.20 (-68.3)	0.15 (-0.6)	0.04
94a			-78 (air) ^k	48	22	0.14 (-65.6)	0.10 (1.0)	0.03
95		diethyl ether	25	4	37	2.3 (-2.5)	4.2 (-0.2)	1.7
96			0	8	49	2.5 (-3.1)	4.0 (+0.1)	1.3
97			-40	24	29	1.6 (-12.9)	2.2 (-0.2)	0.5
98			-68	48	47	2.2 (-31.4)	2.5 (0.0)	0.5
99			-78	48	21	0.33 (-55.5)	0.33 (-0.8)	0.06
100	5k	pentane	25	4	36	2.5 (+0.2)	4.6 (+0.1)	2.1
101			0	9	53	3.8 (+0.2)	6.3 (-0.1)	2.4
102			-40	24	44	2.9 (-11.2)	4.0 (-0.1)	1.2
103			-68	48	43	1.0 (-44.0)	1.0 (+0.1)	0.3
104			-78	48	18	0.13 (-55.0)	0.11 (-0.4)	0.03
105		diethyl ether	25	4	39	3.1 (+0.7)	5.7 (0.0)	2.3
106			0	9	55	4.6 (+0.3)	7.8 (+0.1)	2.6
107			-40	24	49	3.3 (-6.5)	4.8 (0.0)	1.2
108	5l	pentane	25	4	40	3.0 (-0.4)	5.5 (-0.1)	2.4
109			0	8	59	5.8 (-0.2)	9.5 (+0.2)	3.7
110			-40	24	31	1.8 (-0.3)	2.4 (+0.4)	0.7
111		diethyl ether	25	4	42	2.3 (-0.5)	4.0 (0.0)	1.6
112			0	8	63	6.9 (-0.4)	11.5 (-0.1)	3.8
113			-40	24	39	2.8 (+1.4)	3.9 (+0.2)	0.9

^a [I] = 20 mmol dm⁻³; [sensitizer] = 5 mmol dm⁻³; irradiation under argon atmosphere, unless noted otherwise. ^b Enantiomeric excess determined by chiral GLC. ^c [I] = 200 mmol dm⁻³. ^d [I] = 25 mmol dm⁻³. ^e [I] = 15 mmol dm⁻³. ^f [I] = 5 mmol dm⁻³. ^g Methoxycyclohexane **11** was also obtained in 12.5% yield. ^h **11** was obtained in 4.5% yield. ⁱ **11** was obtained in 0.4% yield. ^j [Sensitizer] < 5 mmol dm⁻³ due to low solubility. ^k Irradiation performed under air.

mol⁻¹)^{5b} is higher than that of a benzene(poly)carbonate (95–106 kcal mol⁻¹)^{5f} and therefore the energetic tolerance for the rotation around the C=C double bond is essential to facilitate the less favored ‘non-vertical’ energy transfer within the singlet exciplex.^{5b} Furthermore, (*E*)-cyclohexene is much more unstable than (*E*)-cyclooctene and (*E*)-cycloheptene and can exist only as a transient species even at low temperature. Hence, it is likely that (*E*)-cyclohexene produced photochemically is not fully captured by (*Z*)-cyclohexene during its short lifetime, regenerating the *Z*-isomer.

In all cases, the material balance is poor. In typical runs using benzoates (Table 2), the combined yield of cyclodimers can account for only 20–35% of the consumed substrate. Although the formation of 3-cyclohexylcyclohexene and 3,3'-bicyclohexenyl, *via* cyclohexenyl radicals, and other minor radical products was reported previously,^{18–20} we could not detect these radical dimers in significant amounts on GC analysis. Instead, a GPC analysis revealed the presence of a considerable amount

of polymeric products in the irradiated solution. These polymers account for ≈25% of cyclohexene consumed at 25 °C but amount to ≈40% of the conversion at temperatures lower than -40 °C. The average molecular mass, calibrated with polystyrene, was 960 for the polymers obtained at 25 °C, and 1100–1150 for those obtained at <-40 °C. Upon sensitization with methyl benzoate, a small amount of an oxetane derivative from the Paternó-Büchi reaction of sensitizer with cyclohexene or a cycloadduct to the aromatic ring was detected on GLC-MS analysis: *m/z* (relative intensity) 218 (M⁺, 16%), 159 (M⁺ - CO₂-Me, 100), but a further search for such by-products from the chiral benzoates was not successful, since they did not elute within a reasonable retention time from the GC columns employed.

In practice, only unsubstituted benzoate appears to be able to satisfy the steric requirement for efficient energy transfer to cyclohexene and to give appreciable chemical and optical yields, while the sensitizer–substrate distance is the most crucial factor

that determines the efficiencies of both energy transfer and enantiodifferentiation.⁵ Hence, we have concentrated on the photosensitization of cyclohexene **1** by a series of unsubstituted benzoates with various chiral ester auxiliaries.

Product ratio and enantiomeric excess

In order to investigate the effect of chiral auxiliary upon the product ee, the enantiodifferentiating photosensitization of **1** was performed in the presence of a series of optically active benzoates **5a–l** as chiral sensitizers in pentane and diethyl ether at various temperatures ranging from 25 to -78 °C. The results are summarized in Table 2. In all runs, the yields of cyclodimers increased gradually over the period of irradiation, ultimately reaching a plateau after prolonged irradiation, which was dependent on the temperature, solvent and sensitizer used. In contrast, the ee of **2** remained constant within experimental error of $\pm 0.8\%$ ee (standard deviation) over the irradiation period, as exemplified by runs 42 and 45 (Table 2) for cyclodimerization of **1** sensitized by **5e** in pentane at 25 and -40 °C, respectively. These results indicate that the photocyclodimerization of **1** is not reversible and that the product **2** is not subject to any further reactions under the irradiation conditions. The product proportions also remain constant over the irradiation period at both 25 and -40 °C, ruling out the possibility of interconversion between **2–4** by secondary photoepimerization.^{19,20} Thus all three isomers are clearly the primary products of photocyclodimerization of **1**.

In order to unambiguously identify the excited state involved, we tried to rule out, experimentally, possible intervention of the triplet route to products **2–4**. Although representative triplet quenchers, such as penta-1,3-diene, isoprene and ferrocene, cannot be used in the present system as these compounds show significant absorption at the irradiation wavelength (254 nm), we examined the effect of oxygen on the conversion, chemical yield and ee-value by performing the photosensitization with **5j** under air. As can be seen from runs 90, 90a, 92, 92a, 94 and 94a in Table 2, the photosensitizations of **1** with **5j** in aerated pentane at 25, -40 and -78 °C afforded the same products **2–4** in significantly reduced yields, along with small amounts of unidentified, probably oxidation, products which eluted immediately after the substrate on GLC. Despite the much reduced yields of **2–4**, exactly the same product proportions and ees were obtained for **2–4** in both aerated and argon-saturated solutions. We may conclude therefore that the triplet-sensitization mechanism, which should be influenced more or less by the presence of oxygen, is not appreciably involved in this benzoate-sensitized enantiodifferentiating photocyclodimerization.

The singlet sensitization with benzoates **5a–l** gave cyclodimers **2**, **3** and **4** in the same proportions of 1.2:2.2:1.0 in pentane at 25 °C, irrespective of the sensitizer used. However, the product proportions were affected significantly by the irradiation temperature, although the same product proportions were obtained for all sensitizers at each temperature. The relative proportions of **2:3:4** obtained in pentane were 1.2:2.2:1.0 at 25 °C, 1.6:2.6:1.0 at 0 °C, 2.5:3.4:1.0 at -40 °C, 3.8:4.0:1.0 at -68 °C, and 4.6:4.1:1.0 at -78 °C. Obviously, the relative contribution of **3** and, particularly, **2** increases with decreasing temperature. The use of diethyl ether as a solvent also led to slightly different proportions (**2:3:4** = 1.4:2.5:1.0 at 25 °C), which are independent of the sensitizer used at each temperature but are again dependent on the temperature. Similar temperature and solvent dependence was reported in the *p*-xylene-sensitized photodimerization of **1**.^{18c} Thermodynamically, the cyclodimer **2** is least stable and **4** the most stable.^{18c,20} Hence, the product distribution in the photodimerization is most likely to be controlled predominantly kinetically, and the activation energy for the cyclodimerization to **2** is the smallest.

The ee of **2** also depends critically on the irradiation temperature. Thus, the ee obtained upon sensitization with the menthyl ester **5a** was 5.0% at 25 °C but was enhanced, by lowering the temperature, up to 18.7% at -78 °C in pentane (runs 1–5). The ees in diethyl ether were comparable to those obtained in pentane at temperatures higher than -40 °C and slightly lower below that temperature (runs 6–10). The epimeric neomenthyl ester **5b** gave much smaller ees ($<3\%$) even at low temperatures, but the product chirality was switched within the experimental temperature range in both pentane and diethyl ether; *i.e.* (+)-**2** was favored by 2–3% ee above 0 °C, while antipodal (–)-**2** was obtained in 0.5–1.5% ee at -40 °C (runs 11–16). Similar temperature switching of product chirality has been reported rather generally in the photosensitized enantiodifferentiating isomerization of cyclooctene,^{5a–h} cycloocta-1,3-diene⁵ⁱ and cycloheptene^{5k} and the photosensitized enantiodifferentiating polar addition of alcohols to 1,1-diphenylalk-1-enes.^{16b} This apparently unusual phenomenon has been reasonably rationalized in terms of the entropy term.^{16c,5} The antipodal sensitizer pair **5c** and **5d** gave the respective enantiomer pair, (–)- and (+)-**2**, in the same ee at each temperature in both pentane and diethyl ether, although the ee obtained in pentane was higher than that in diethyl ether at each temperature, reaching 30% at -78 °C.

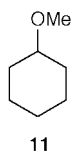
We further examined the saccharide derivatives, which were used as effective chiral auxiliaries of the sensitizers for the enantiodifferentiating photoaddition of alcohol to 1,1-diphenylalk-1-enes^{16b} and photocyclodimerization of cyclohexa-1,3-diene.^{16c} A series of furanose **5e–i** and pyranose derivatives **5j–l** were employed in this study. The photosensitization with benzoate **5e**, which possesses a diacetone glucose auxiliary, was first examined in diethyl ether (runs 42, 45–47). The ee of **2** obtained at 25 °C was 10.9% on average but was enhanced by lowering the temperature (up to 30.5% at -78 °C).

The effect of substrate concentration ($5–200$ mmol dm⁻³) on the chemical and optical yields of cyclodimers was investigated in diethyl ether at 25 °C (runs 40–44). The ee of **2** was almost independent of the concentration of **1**. Although the chemical yields of cyclodimers based on the initial concentration of **1** are better at lower concentrations, the net amount of cyclodimers produced increases with substrate concentration and is saturated above 20 mmol dm⁻³. In contrast, both the product proportions of cyclodimers and the product yield based on the conversion were independent of the concentration of substrate. These results indicate that three cyclodimers **2–4** share a common intermediate which is relatively long lived and can be completely trapped by 20 mmol dm⁻³ of **1**. These features are compatible with the mechanism proposed previously for the triplet sensitization,^{18–20} which involves photochemical production of highly reactive (*E*)-cyclohexene followed by thermal reactions with ground-state **1**.

The effect of solvent on the product ee was studied in some detail in the photosensitization with **5e** (runs 35–53 in Table 2). In spite of the significant change in polarity from pentane ($E_T = 31.0$ kcal mol⁻¹ at 25 °C)²¹ to diethyl ether ($E_T = 34.5$),²¹ then to acetonitrile ($E_T = 46.0$),²¹ and finally to methanol ($E_T = 55.5$),²¹ the product ees obtained in these solvents were comparable to each other at least at 25 and 0 °C. However, moderate solvent dependence was observed at temperatures lower than -40 °C. Thus, the sensitization in pentane afforded cyclodimer **2** of 21% ee at -40 °C and 51% ee at -78 °C, respectively, whereas the use of polar solvents caused appreciable decreases in ee to 9–16% at -40 °C and to 31% at -78 °C.

The photosensitization in methanol is of particular interest, since the methanol adduct, methoxycyclohexane **11**, was obtained at the higher temperatures in moderate yields (12.5, 4.5 and 0.4% at 25, 0 and -40 °C, respectively) at the expense of the cyclodimers without any accompanying significant changes in the conversion. This result clearly indicates that methanol as

a trapping agent does not intercept the electronically excited state but rather competes with **1** for the common reactive intermediate in the ground state. As reported previously,¹⁸ the *p*-xylene-photosensitization of **1** in acidic methanol affords only **11** and no cyclodimers. It has been proposed that the formation of **11** involves the initial *Z*–*E* photoisomerization of **1**, followed by the ground-state protonation of the resulting highly strained (*E*)-cyclohexene (**1E**), rather than the protonation of an excited-state cyclohexene.¹⁸ This proposal has been supported by studies on the photoisomerization of cycloheptene and 1-phenylcyclohexene, which clearly demonstrate the intervention of a ground-state intermediate possessing a lifetime much longer than that expected for an excited state.^{22,23} It is concluded therefore that three cyclodimers **2**–**4** are formed from **1E** as the common intermediate generated upon benzoate-sensitized photoisomerization of **1Z**.



Photosensitization with **5f**, which has more bulky cyclohexylidene protecting groups than **5e**, afforded only slightly enhanced ees in both pentane and ether (runs 54–61). This is not unexpected, since the cyclohexylidene groups are located away from the chromophore and are not well recognized by the substrate. Interestingly, the product chirality was apparently switched in both pentane and diethyl ether within the experimental temperature range upon sensitization with **5g**; (+)-**2** was favored at –40 °C or higher temperatures, while the antipodal (–)-**2** was produced in excess below –40 °C (runs 62–71). This observation clearly indicates the significant contribution of the entropic factor in this enantiodifferentiating photocyclodimerization of **1**, as reported for the enantiodifferentiating photoisomerization of the higher homologs.^{1b,c,5}

We also investigated the photosensitization behavior of other furanose esters **5h** and **5i**, which differ in the steric hindrance around the asymmetric carbon (C-1) connected to the ester oxygen. Photosensitization with **5h**, carrying one oxygen and one secondary carbon adjacent to C-1, gave slightly lower ees in all solvents at each temperature than the corresponding values obtained with **5e**, which has two secondary carbons around C-1 (runs 72–79). In the case of **5i**, which has one secondary and one tertiary carbon around C-1, the obtained ee was considerably enhanced up to 63% in pentane at –78 °C (runs 80–89).

It is also interesting to examine the photosensitization with pyranose ester **5j** (runs 90–99), which possesses one secondary and one tertiary carbon around C-1. Photosensitization with **5j** afforded **2** only in very low ee (2.1%) at 25 °C, but the ee

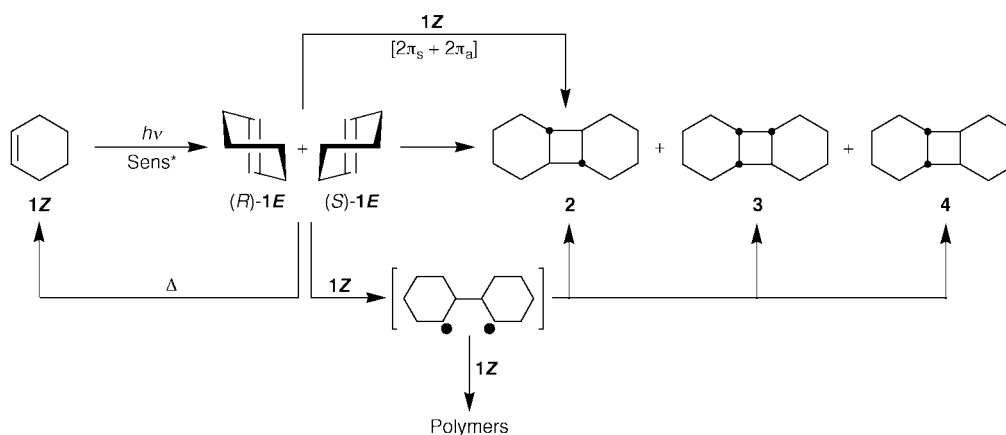
increased rapidly with lowering temperature in both pentane and diethyl ether. Ultimately the product ee was enhanced up to 68% in pentane at –78 °C. This is the highest ee-value ever reported for an enantiodifferentiating photosensitized cyclodimerization. In the case of **5k**, possessing more bulky cyclohexylidene protecting groups at the peripheral positions, the product ee obtained at each temperature was almost comparable or slightly lower than that for **5j** (runs 100–107). This is consistent with the results obtained for the furanose esters **5e** and **5f**, reinforcing the hypothesis that only a modification that is close to the chromophore can affect the stereochemical outcome of the asymmetric photosensitization.²⁴ In this context, it is very intriguing to examine the protected saccharide **1** with a primary hydroxy group (Chart 1). The fact that the photosensitization with **5l** failed to give appreciable enantiodifferentiation at any temperature (runs 108–113) not only supports this theory but also indicates that the stereogenic center should be directly attached to the ester oxygen of the arenecarboxylate sensitizers. In other words, primary alcohols are poor chiral auxiliaries for this type of photosensitizer simply due to the elongated distance between the stereogenic center and the chromophore with which the substrate interacts.

As amply demonstrated above, only *trans*-*anti*-*trans*-cyclodimer **2** is produced in good ee, whereas the *cis*-*trans*-cyclodimer **3** obtained is always racemic. In view of the consistent product proportions observed for various sensitizers at each temperature, it is reasonable to postulate that the common intermediate, most likely (*E*)-cyclohexene **1E**, undergoes two parallel cyclodimerization pathways, one of which can preserve the chiral information induced in the common intermediate upon enantiodifferentiating photosensitization but the other cannot.

Cyclization mechanism

On the basis of the mechanism reported perviously^{18–20} and the facts obtained in this study, we propose a modified reaction mechanism illustrated in Scheme 2. This mechanism involves the initial enantiodifferentiating *Z*–*E* photoisomerization of **1Z**, followed by the ground-state cycloaddition of chiral **1E** produced photochemically to another molecule of **1Z**.

trans-*anti*-*trans*-Cyclodimer **2** has the right stereochemistry as anticipated for the concerted $[2\pi_s + 2\pi_a]$ cycloaddition of **1E** to **1Z** from the Woodward–Hoffmann rules,²⁵ assuming the *E*-isomer reacts suprafacially.²⁶ The copper(I)-sensitized photodimerization of **1** predominantly affords isomer **2**, and a mechanism which involves the concerted cyclodimerization of (*Z*)- and (*E*)-cyclohexene within the coordination sphere of copper(I) has been proposed.²⁰ As found in this study, appreciable enantiodifferentiation was attained only for **2**, yet the relative product proportions did not depend on the sensitizer used. These facts indicate that the sensitizer is not directly



Scheme 2

involved in the cycloaddition process and that cyclodimer **2** is produced through the concerted $[2\pi_s + 2\pi_a]$ cycloaddition of **1E** to **1Z** in the ground state, retaining the chirality of the initially formed **1E**.

In contrast, *cis-trans*-cyclodimer **3** and *cis-anti-cis*-cyclodimer **4** are believed to be formed through non-concerted processes on the basis of their stereochemistry.^{18–20} Since the sensitizers used in this study do not show any hydrogen-abstracting ability and the relative proportions of **2–4** did not change throughout the irradiation period, the interconversion among **2–4** through photoepimerization, which has been reported for triplet ketone-sensitized photodimerization,^{19,20} is clearly ruled out. Alternatively, cyclodimer **3** could arise from the concerted cycloaddition of two molecules of **1E** in the ground state. However, the relative yield of **3** was not enhanced by increasing the light intensity or by lowering the temperature.^{18c} Eventually, this possibility is completely eliminated by our own result that no appreciable enantiodifferentiation was observed for **3**, under the conditions that gave good ees for **2**. It is concluded that cyclodimer **3**, and probably **4**, is produced through the non-stereospecific stepwise cycloaddition of **1E** to **1Z** in the ground state, affording a 1,4-biradical with a loss of the optical activity of **1E** induced photochemically. The formation of polymeric products may also rationalize the radical intermediate.

Activation parameters

In order to quantitatively analyze the temperature effect on the product ee of **2**, the natural logarithm of the relative rate constant affording (+)- and (–)-**2**, *i.e.* $\ln(k_+/k_-)$, is plotted as a function of reciprocal temperature. The relative rate constant (k_+/k_-) is experimentally equivalent to the quotient $(100 + \%ee)/(100 - \%ee)$. In sharp contrast to the cyclooctene and cycloheptene cases,^{1b,c,5} the plot did not give a straight line but instead a curvature for each sensitizer, and the apparent slope increased with decreasing temperature, as shown in Fig. 1 for the photosensitization with **5d**, **5g** and **5i** in pentane. As stated above, the relative ratio of non-concerted products **3** and **4** to concerted product **2** decreases with lowering temperature, *i.e.* the ratio (**3** + **4**):**2** decreases from 2.7:1.0 at 25 °C to 1.1:1.0 at –78 °C in pentane. It is thus inferred that cyclodimer **2** obtained at high temperatures contains a significant contribution from the non-concerted cyclodimerization path to racemic **2**, and the dramatic enhancement of ee at low temperatures is achieved by the predominant contribution of the concerted $[2\pi_s + 2\pi_a]$ process to the formation of **2**.

In the present study, the activation parameters for the enantiodifferentiating photodimerization were calculated from the temperature dependence of the ee of **2** obtained at low temperatures (<–40 °C), according to the differential Arrhenius and Eyring equations (1) where ΔE represents the

$$\begin{aligned} \ln(k_+/k_-) &= -\Delta E/RT + \ln(A_+/A_-) \\ &= -\Delta\Delta H^\ddagger/RT + \Delta\Delta S^\ddagger/R \end{aligned} \quad (1)$$

differential activation energy, A_+/A_- the relative frequency factor, and $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ the differential enthalpy and entropy changes of activation. According to eqn. (1), a plot of $\ln(k_+/k_-)$ -value against reciprocal temperature should give a straight line, as has been reported for the enantiodifferentiating photoisomerization of cyclooctene and cycloheptene.^{1b,c,5} As discussed above, only at low temperatures, where the contribution of the non-concerted path can be neglected, is the ee of initially formed **1E** completely transferred to cyclodimer **2**. Hence the linear fit of the plot was carried out by using the ees obtained at temperatures lower than –40 °C to give a good straight line, as exemplified in Fig. 1 (solid lines). The relative frequency factor (A_+/A_-) and the differential enthalpy and entropy change ($\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$) thus obtained are summar-

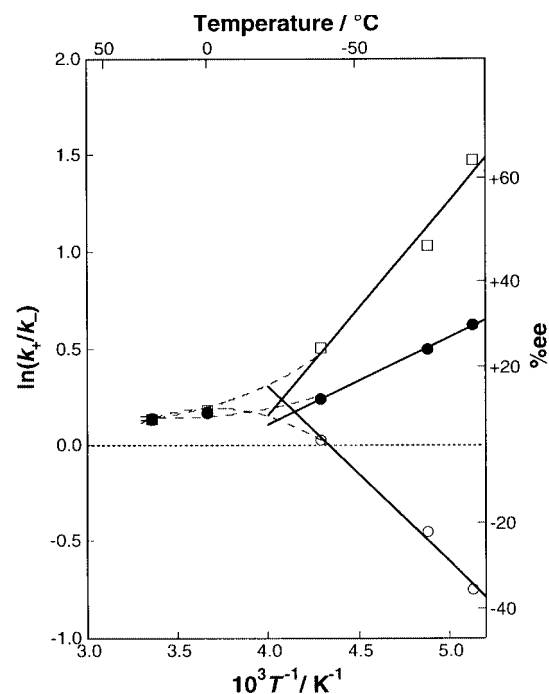


Fig. 1 Temperature dependence of enantiomeric excess (ee) of **2**: the logarithm of relative rate constant (k_+/k_-) plotted as a function of reciprocal temperature in enantiodifferentiating photocyclodimerization of **1** sensitized by **5d** (●), **5g** (○) and **5i** (□) in pentane.

ized in Table 3, along with the equipodal temperature (T_0), at which the product chirality is switched since $\Delta\Delta H^\ddagger = T_0\Delta\Delta S^\ddagger$.

In asymmetric synthesis, the optical yield has been believed to be enhanced in general by lowering the reaction temperature. This widespread hypothesis is found to be true only when the chiral recognition is governed exclusively by the enthalpic factor and where the contribution of entropy is negligible, *i.e.* $\Delta\Delta S^\ddagger = 0$. However, none of the sensitizers employed here give null $\Delta\Delta S^\ddagger$, which is the origin of the unusual temperature-switching phenomenon, as reported previously for the enantiodifferentiating photoisomerization of cyclooctene and cycloheptene.^{1b,c,5} Although the obtained non-zero $\Delta\Delta S^\ddagger$, which possesses the same sign as $\Delta\Delta H^\ddagger$, predicts the chirality switching at the equipodal temperature (T_0) for each sensitizer, the switching phenomenon was actually observed only for **5b** and **5g** in the actual range of irradiation temperature. This is simply because the contribution of the non-concerted dimerization to **2** cannot be neglected at higher temperatures.

It is of great interest to examine the general validity of the compensatory enthalpy–entropy relationship, which has been observed for the enantiodifferentiating photoisomerization of cyclooctene and cycloheptene.^{1b,c,5} In Fig. 2, all of the $\Delta\Delta S^\ddagger$ -values obtained are plotted against the $\Delta\Delta H^\ddagger$ -values to afford an excellent linear relationship: $\Delta\Delta H^\ddagger = 0.249\Delta\Delta S^\ddagger - 0.01$ (correlation coefficient 0.997). The isokinetic temperature is determined as $T_{\text{iso}} = 249$ K, which is in good agreement with those reported for cyclooctene and cycloheptene.^{5g,j} The comparable T_{iso} obtained for all of the cycloalkenes indicates that essentially the same enantiodifferentiation mechanism operates in the asymmetric photosensitization of cycloalkenes. Hence the *Z*-to-*E* photoisomerization of cyclohexene is concluded to be the key step in the enantiodifferentiating photocyclodimerization of **1**. This is the first definitive evidence for the mechanism of the photocyclodimerization of cyclohexene, for which (*E*)-cyclohexene has been proposed as a plausible intermediate, and the enantiodifferentiating photosensitization has revealed that the mechanism involves the concerted and non-concerted paths in the formation of the three cyclodimers.

Table 3 Activation parameters and equipodal temperatures (T_0) for the formation of **2** in enantiodifferentiating photocyclodimerization of cyclohexene **1** sensitized by chiral benzoates **5a–k**^a

Sensitizer	Solvent	$\Delta\Delta H^\ddagger/b/$ kcal mol ⁻¹	$\Delta\Delta S^\ddagger/c/$ mol ⁻¹ K ⁻¹	A_+/A_-^d	$T_0^e/^\circ\text{C}$
5a	pentane	0.52	1.96	2.68	-7
	diethyl ether	0.26	0.82	1.51	41
5c	pentane	0.80	2.81	4.12	10
	diethyl ether	0.62	2.14	2.93	16
5d	pentane	-0.89	-3.36	0.18	-7
5e	pentane	1.53	5.79	18.4	-10
	diethyl ether	0.73	2.66	3.81	1
5f	pentane	1.85	7.24	38.2	-17
5g	pentane	1.81	7.82	51.2	-42
	diethyl ether	1.06	4.80	11.2	-53
5i	pentane	-2.22	-8.56	0.013	-14
	diethyl ether	-1.81	-7.22	0.026	-23
5j	pentane	2.75	11.1	270	-26
	diethyl ether	2.18	8.93	89.6	-30
5k	pentane	2.41	9.90	146	-29

^a All activation parameters were obtained by Arrhenius and Eyring treatment of the optical yields. ^b Differential enthalpy of activation: $\Delta H^\ddagger_+ - \Delta H^\ddagger_-$. ^c Differential entropy of activation: $\Delta S^\ddagger_+ - \Delta S^\ddagger_-$. ^d Relative frequency factor. ^e Equipodal temperature, at which no appreciable enantiodifferentiation occurs.

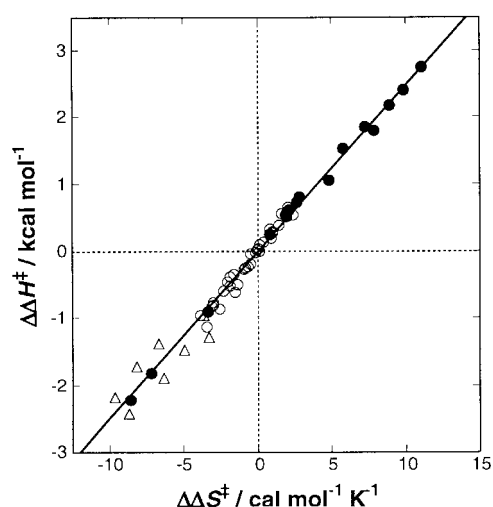


Fig. 2 Enthalpy-entropy compensation plot for the differential activation parameters obtained in the enantiodifferentiating photocyclodimerization of cyclohexene (●) and photoisomerization of cycloheptene (△) and cyclooctene (○) sensitized by chiral benzene-(poly)carboxylates.

Experimental

General

Mps were measured with a Yanaco MP-300 apparatus and are uncorrected. ¹H and ¹³C NMR spectra were obtained on a JEOL GX-400 or GSX-270 spectrometer for solutions in CDCl₃. IR spectra were obtained on a JASCO FT/IR-230 instrument. Electronic spectra were recorded on a JASCO V-550 instrument. Optical rotations were determined at 589 nm in a thermostatted conventional 10 cm cell, using a JASCO DIP-1000 polarimeter. $[\alpha]_D$ -Values are given in units of 10⁻¹ deg cm² g⁻¹.

Enantiomeric excesses of **2** and **3** were determined by gas-liquid chromatography (GLC) over a 30 m chiral capillary column (Supelco β-Dex325) at 110 °C, using a Shimadzu GC-14B instrument connected to a Shimadzu C-R6A integrator.

Quantum yields of products **2–4**, formed upon sensitization with **5e**, were determined by comparison with the quantum yield of the benzoate-sensitized *Z*-to-*E* photoisomerization of cyclooctene reported previously.^{5b} Pentane solutions of **1** and cyclooctene (20 mM) containing **5e** (5 mM) were prepared, purged with argon, and irradiated at 25 °C at 254 nm

using a 30 W low-pressure mercury lamp in a merry-go-round apparatus.

GPC analysis of polymeric products was carried out on a 300 × 7.5 mm PLgel 5 μm Mixed-C column (Polymer Laboratories) using a JASCO GPC-900 instrument.

Materials

Pentane used as solvent was stirred over conc. sulfuric acid until the acid layer no longer turned yellow, washed with water, neutralized with aq. sodium hydrogen carbonate, dried over sodium sulfate, and then distilled fractionally. Diethyl ether was refluxed with potassium hydroxide and then fractionally distilled from sodium. Spectrograde acetonitrile (Dojin) was used without further purification. Methanol was fractionally distilled from magnesium turnings. Cyclohexene **1** (TCI) was purified by fractional distillation, followed by column chromatography on activated aluminium oxide (ICN Biomedicals).

Optically active alcohols and some saccharide derivatives used in the preparation of the sensitizers were commercially available: (-)-menthol and (-)-borneol from TCI; 1,2:5,6-di-*O*-isopropylidene- α -D-glucopyranose from Wako; (+)-neomenthol, (+)-borneol, 1,2:5,6-di-*O*-isopropylidene- α -D-allofuranose, 2,3:5,6-di-*O*-isopropylidene- α -D-mannofuranose and 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose from Aldrich.

The other sugar derivatives were prepared from D-glucose, D-fructose and L-sorbose according to the procedures reported by Kartha,²⁷ Kang *et al.*,²⁸ and Cheng *et al.*,²⁹ respectively.

1,2:5,6-Di-*O*-cyclohexylidene- α -D-glucopyranose, 1,2:4,5-di-*O*-isopropylidene- β -D-fructopyranose and 1,2:4,5-di-*O*-cyclohexylidene- β -D-fructopyranose were prepared in a similar manner, as reported previously.^{16b,c}

1,2:4,6-Di-*O*-isopropylidene- α -L-sorbofuranose: $[\alpha]_D^{25} -23.5$ (*c* 0.99, acetone) {lit.,^{29a} $[\alpha]_D^{25} -24.7$ (*c* 1.03, acetone)}; mp 73 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.23 (s, 3H), 1.28 (s, 3H), 1.35 (s, 3H), 1.38 (s, 3H), 2.07 (s, 1H), 3.74–4.29 (m, 6H); *m/z* 260 (M⁺, 7%), 245 (100), 159 (30), 144 (28), 117 (36), 101 (46).

Optically active benzene(poly)carboxylates employed as chiral sensitizers were prepared from the corresponding alcohols and acid chlorides as reported previously.³⁰

(+)-Bornyl benzoate **5d** (Found: C, 78.80; H, 8.59. Calc. for C₁₇H₂₂O₂: C, 79.03; H, 8.58%); $[\alpha]_D^{30} +45.0$ (*c* 1.02, CHCl₃); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2954, 2879, 1716, 1602, 1452, 1273, 1176, 1117, 1068, 1026, 980, 712; $\lambda_{\text{max}}(\text{Et}_2\text{O})/\text{nm}$ 227.2 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 13 100), 270.2 (898); $\delta_{\text{H}}(\text{CDCl}_3)$ 0.92 (m, 6H), 0.97 (m, 3H), 1.12 (d, *J* 11.7 Hz, 1H), 1.25–1.50 (m, 2H), 1.75–1.95 (m, 2H), 2.10–

2.25 (m, 1H), 2.43–2.57 (m, 1H), 5.11 (d, J 11.7 Hz, 1H), 7.48 (m, 2H), 7.57 (m, 1H), 8.06 (m, 2H); m/z 258 (M^+ , 45%), 136 (39), 121 (20), 109 (24), 105 (100).

(–)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene- α -D-glucopyranos-3-yl benzoate **5e** (Found: C, 63.20; H, 6.84. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[a]_D^{30}$ –50.1 (c 1.01, $CHCl_3$); $\nu_{max}(KBr)/cm^{-1}$ 2970, 2870, 1720, 1610, 1460, 1380, 1270, 1170, 1080, 1040, 960, 890, 860, 730; $\lambda_{max}(Et_2O)/nm$ 228.4 ($\epsilon/dm^3 mol^{-1} cm^{-1}$ 15 100), 272.0 (1180); $\delta_H(CDCl_3)$ 1.26 (s, 3H), 1.31 (s, 3H), 1.41 (s, 3H), 1.55 (s, 3H), 4.09 (m, 1H), 4.34 (m, 3H), 4.62 (d, J 3.9 Hz, 1H), 5.49 (d, J 2.9 Hz, 1H), 5.94 (d, J 3.9 Hz, 1H), 7.45 (m, 2H), 7.58 (m, 1H), 8.02 (m, 2H); m/z 365 (M^+ + 1, 24%), 349 (41), 307 (96), 154 (31), 137 (27), 105 (100).

(–)-3-Deoxy-1,2:5,6-di-*O*-cyclohexylidene- α -D-glucopyranos-3-yl benzoate **5f** mp 116 °C (Found: C, 67.52; H, 7.21. Calc. for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26%); $[a]_D^{30}$ –33.2 (c 1.00, $CHCl_3$); $\nu_{max}(KBr)/cm^{-1}$ 2935, 1716, 1450, 1367, 1273, 1165, 1115, 1074, 1012, 941, 930, 715; $\lambda_{max}(Et_2O)/nm$ 228.4 ($\epsilon/dm^3 mol^{-1} cm^{-1}$ 16 000), 271.6 (1340); $\delta_H(CDCl_3)$ 1.25–1.80 (m, 20H), 4.00–4.20 (m, 2H), 4.33 (m, 2H), 4.62 (d, J 3.9 Hz, 1H), 5.55 (m, 1H), 5.95 (d, J 3.4 Hz, 1H), 7.45 (m, 2H), 7.56 (m, 1H), 8.02 (m, 2H); m/z 444 (M^+ + 1, 20%), 401 (12), 347 (46), 154 (31), 141 (24), 136 (24), 105 (100).

(+)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene- α -D-allofuranos-3-yl benzoate **5g** mp 76 °C (Found: C, 62.56; H, 6.48. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[a]_D^{30}$ +124.3 (c 1.04, $CHCl_3$); $\nu_{max}(KBr)/cm^{-1}$ 2985, 2893, 1724, 1454, 1377, 1277, 1115, 1030, 864, 717; $\lambda_{max}(Et_2O)/nm$ 228.4 ($\epsilon/dm^3 mol^{-1} cm^{-1}$ 15 500), 272.0 (1070); $\delta_H(CDCl_3)$ 1.33 (s, 6H), 1.41 (s, 3H), 1.55 (s, 3H), 3.96–4.01 (m, 1H), 4.09–4.14 (m, 1H), 4.32–4.38 (m, 2H), 4.96–4.99 (m, 1H), 5.06–5.10 (m, 1H), 5.90 (d, J 3.4 Hz, 1H), 7.46 (m, 2H), 7.59 (m, 1H), 8.06 (m, 2H); m/z 365 (M^+ + 1, 2%), 349 (40), 307 (80), 137 (12), 105 (100).

(+)-2,3:5,6-Di-*O*-isopropylidene- α -D-mannofuranosyl benzoate **5h** mp 128 °C (Found: C, 62.55; H, 6.43%); $[a]_D^{30}$ +40.5 (c 1.01, $CHCl_3$); $\nu_{max}(KBr)/cm^{-1}$ 2989, 2940, 1724, 1454, 1377, 1292, 1255, 1209, 1084, 968, 849, 712; $\lambda_{max}(Et_2O)/nm$ 228.6 ($\epsilon/dm^3 mol^{-1} cm^{-1}$ 14 000), 271.4 (1260); $\delta_H(CDCl_3)$ 1.38 (s, 6H), 1.46 (s, 3H), 1.53 (s, 3H), 4.00–4.20 (m, 3H), 4.41–4.44 (m, 1H), 4.87–4.96 (m, 2H), 6.37 (s, 1H), 7.50 (m, 2H), 7.59 (m, 1H), 8.02 (m, 2H); m/z 365 (M^+ + 1, 37%), 349 (26), 307 (27), 291 (13), 289 (17), 243 (24), 185 (100), 154 (84), 137 (68), 127 (21), 105 (98).

(–)-3-Deoxy-1,2:4,6-di-*O*-isopropylidene- α -L-sorbofuranos-3-yl benzoate **5i** (Found: C, 62.81; H, 6.78%); $[a]_D^{30}$ –48.0 (c 1.00, $CHCl_3$); $\nu_{max}(KBr)/cm^{-1}$ 2993, 2935, 1728, 1454, 1377, 1269, 1115, 1072, 937, 852, 714; $\lambda_{max}(Et_2O)/nm$ 228.2 ($\epsilon/dm^3 mol^{-1} cm^{-1}$ 15 200), 271.8 (1080); $\delta_H(CDCl_3)$ 1.26 (s, 3H), 1.40 (s, 3H), 1.44 (s, 3H), 1.46 (s, 3H), 4.01–4.41 (m, 5H), 4.46–4.48 (m, 1H), 5.38 (d, J 1.5 Hz, 1H), 7.45 (m, 2H), 7.58 (m, 1H), 8.06 (m, 2H); m/z 365 (M^+ + 1, 5%), 349 (24), 307 (62), 154 (11), 137 (13), 105 (100).

(–)-3-Deoxy-1,2:4,5-di-*O*-isopropylidene- β -D-fructopyranos-3-yl benzoate **5j** mp 111 °C (Found: C, 62.61; H, 6.54%); $[a]_D^{30}$ –162.1 (c 1.02, $CHCl_3$); $\nu_{max}(KBr)/cm^{-1}$ 2940, 1684, 1585, 1454, 1371, 1300, 1186, 1115, 1028, 910, 854, 773, 709; $\lambda_{max}(Et_2O)/nm$ 228.8 ($\epsilon/dm^3 mol^{-1} cm^{-1}$ 16 800), 271.8 (1240); $\delta_H(CDCl_3)$ 1.37 (s, 3H), 1.41 (s, 3H), 1.52 (s, 3H), 1.62 (s, 3H), 4.10–4.32 (m, 3H), 4.37 (m, 2H), 4.47 (m, 1H), 5.39 (d, J 8.3 Hz, 1H), 7.45 (m, 2H), 7.58 (m, 1H), 8.10 (m, 2H); m/z 365 (M^+ + 1, 10%), 105 (100).

(–)-3-Deoxy-1,2:4,5-di-*O*-cyclohexylidene- β -D-fructopyranos-3-yl benzoate **5k** mp 116 °C (Found: C, 67.49; H, 7.22. Calc. for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26%); $[a]_D^{30}$ –146.1 (c 1.02, $CHCl_3$); $\nu_{max}(KBr)/cm^{-1}$ 2931, 2860, 1724, 1448, 1263, 1101, 916, 708; $\lambda_{max}(Et_2O)/nm$ 228.6 ($\epsilon/dm^3 mol^{-1} cm^{-1}$ 16 500), 271.6 (1260); $\delta_H(CDCl_3)$ 1.25–1.95 (m, 20H), 3.89 (m, 2H), 4.17 (m, 2H), 4.29 (m, 1H), 4.46 (dd, J 5.9, 7.8 Hz, 1H), 5.37 (d, J 7.8 Hz, 1H), 7.45 (m, 2H), 7.58 (m, 1H), 8.09 (m, 2H); m/z 444 (M^+ + 1, 12%), 347 (36), 154 (10), 105 (100).

(–)-6-Deoxy-1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranos-6-yl benzoate **5l** (Found: C, 62.48; H, 6.60. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[a]_D^{30}$ –59.4 (c 1.04, $CHCl_3$); $\nu_{max}(KBr)/cm^{-1}$ 2989, 2931, 1724, 1454, 1380, 1272, 1214, 1173, 1107, 1072, 1007, 895, 714; $\lambda_{max}(Et_2O)/nm$ 227.4 ($\epsilon/dm^3 mol^{-1} cm^{-1}$ 13 200), 271.8 (950); $\delta_H(CDCl_3)$ 1.34 (s, 3H), 1.36 (s, 3H), 1.48 (s, 3H), 1.52 (s, 3H), 4.16–4.21 (m, 1H), 4.32–4.37 (m, 2H), 4.39–4.57 (m, 2H), 4.66 (dd, J 2.4, 7.8 Hz, 1H), 5.57 (d, J 4.9 Hz, 1H), 7.47 (m, 2H), 7.56 (m, 1H), 8.06 (m, 2H); m/z 365 (M^+ + 1, 76%), 347 (36), 349 (29), 307 (29), 154 (20), 137 (23), 105 (100).

Photolysis

All irradiations were performed in a temperature-controlled water- (25 °C), methanol–propan-2-ol- (–40 °C) or methanol–ethanol- (–68 and –78 °C) bath. The light source employed was a conventional 30 W low-pressure mercury lamp fitted with a Vycor sleeve (Eikosha). A solution (3 cm³), containing cyclohexene **1** (5–200 mmol dm^{–3}), optically active sensitizer **5–10** (5 mmol dm^{–3}), and cycloheptane (5 mmol dm^{–3}) added as an internal standard, was irradiated at 254 nm under an argon atmosphere in a quartz tube (1 cm id) placed near the lamp surface, the whole system being immersed in the cooling bath.

Product isolation

In a preparative run using an annular vessel (300 cm³), the photolyzed solution of **1** was first subjected to preparative TLC on silica gel with ethyl acetate–hexane (1:99) as eluent, and then separated on a GPC column (Jaigel 1-H and 2-H, Japan Analytical Industry) to give chemically pure cyclodimers **2–4**. No trace of fragments derived from the decomposition of the chiral sensitizer was detected by GLC or NMR of the isolated products.

trans-anti-trans-Tricyclo[6.4.0.0^{2,7}]dodecane **2** $\delta_C(CDCl_3)$ 26.7, 31.2, 50.5 (lit.,²⁰ δ_C 26.5, 31.0, 50.3); HRMS Calc. for $C_{12}H_{20}$ (M^+): 164.1564. Found: M^+ , 164.1547; m/z 164 (M^+ , 22%), 135 (30), 121 (30), 107 (19), 95 (43), 82 (79), 67 (100).

cis-trans-Tricyclo[6.4.0.0^{2,7}]dodecane **3** $\delta_C(CDCl_3)$ 22.5, 23.1, 23.9, 25.9, 26.7, 27.4, 31.2, 37.6, 39.7, 41.8, 44.4 [lit.,²⁰ δ_C 22.2–30.9 (8 resonances), 37.2, 39.3, 41.6, 44.2]; HRMS Calc. for $C_{12}H_{20}$ (M^+): 164.1564. Found: M^+ , 164.1549; m/z 164 (M^+ , 25%), 135 (18), 121 (18), 107 (11), 95 (25), 82 (100), 67 (87).

cis-anti-cis-Tricyclo[6.4.0.0^{2,7}]dodecane **4** $\delta_C(CDCl_3)$ 23.2, 27.3, 34.4 (lit.,²⁰ δ_C 23.1, 27.1, 34.3); HRMS Calc. for $C_{12}H_{20}$ (M^+): 164.1564. Found: M^+ , 164.1570; m/z 164 (M^+ , 21%), 135 (8), 121 (6), 107 (4), 96 (8), 82 (100), 67 (75).

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