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STUDIES ON PHOTOSENSITIZED ENANTIODIFFERENTIATING BIMOLECULAR REACTIONS

2000

SADAYUKI ASAOKA

STUDIES ON PHOTOSENSITIZED ENANTIODIFFERENTIATING BIMOLECULAR REACTIONS

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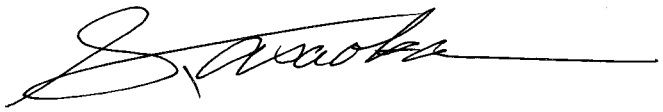
Preface

The work of this thesis has been carried out under the guidance of Professor Yoshihisa Inoue at the Department of Molecular Chemistry, Graduate School of Engineering, Osaka University.

The objective of this thesis is to develop novel and general strategies for photosensitized enantiodifferentiating bimolecular reactions. The author hopes that the results and conclusions presented in this thesis contribute to further development of asymmetric photochemistry.



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List of Publications

1. Enantiodifferentiating Anti-Markovnikov Photoaddition of Alcohols to 1,1-Diphenylalkenes Sensitized by Chiral Naphthalenecarboxylates
   S. Asaoka, T. Kitazawa, T. Wada and Y. Inoue
   J. Am. Chem. Soc., **121**, 8486-8498 (1999).

2. Enantiodifferentiating Photocyclodimerization of Cyclohexa-1,3-diene Sensitized by Chiral Arenecarboxylates
   S. Asaoka, M. Ooi, P. Jiang, T. Wada and Y. Inoue
   J. Chem. Soc., Perkin Trans. 2, 77-84 (2000).

3. Enantiodifferentiating Photocyclodimerization of Cyclohexene Sensitized by Chiral Benzenecarboxylates
   S. Asaoka, H. Horiguchi, T. Wada and Y. Inoue
   J. Chem. Soc., Perkin Trans. 2, in press.

4. Photochirogenesis: Multidimensional Control of Asymmetric Photochemistry
   Y. Inoue, T. Wada, S. Asaoka, H. Sato and J.-P. Pete
   J. Chem. Soc., Chem. Commun., in press.

Contents

General Introduction

Photochemistry provides us with a unique method for activating ground-state molecules to the electronically excited states and possesses several advantages over the thermal counterpart. As the photochemical reactions proceed through the excited-state potential surfaces, highly strained and/or thermally unstable compounds, which are unique to photochemistry, are often obtained as photoproducts in good yields. Another essential advantage of photochemistry is the very wide range of applicable temperature. Since the activation energy is insignificant in general on the excited-state potential surface and the temperature does not affect the reaction mechanism in most cases, one can freely assess the effect of temperature on the photochemical reactions without worrying about the switching of the mechanim.

Recently, there is a rapidly increasing demand for various optically active compounds not only in chemistry but also in medicinal, pharmaceutical and biological science and technology.[1,2] To meet such a demand, a wide variety of enzymatic and catalytic thermal asymmetric reactions have been developed,[1-6] and the asymmetric synthesis is one of the most crucial current interests in organic chemistry. Nevertheless, the use of photochemical reactions in asymmetric synthesis is rather limited so far and does not seem very successful, except for diastereodifferentiating photoreactions. This is simply because we do not completely understand the factors and principles that govern the stereodifferentiating process in the electronically excited states, and also because we have not fully utilized the advantages of photochemistry mentioned above. However, asymmetric photochemistry is not a simple combination or extension of photochemistry and asymmetric synthesis but requires development of a new concept. Thus, understanding the factors and mechanisms operating in asymmetric photochemical processes is a keen interest of contemporary chemistry.

The history of asymmetric photochemistry well dates back to the late 19th century, when le Bel (1974)[7] and van't Hoff (1994)[8] proposed the "absolute asymmetric synthesis (AAS)" using circularly polarized light (CPL). The AAS using CPL is of much interest and curiosity in view of the origin of homochirality in the biosphere, although its synthetic applications are obviously limited. From the synthetic point of view, the diastereodifferentiating photoreaction is

more promising, but this strategy has a drawback that such an intramolecular chiral discrimination process inevitably necessitates a stoichiometric amount of built-in chiral auxiliary. In 1975, the first diastereodifferentiating photoreaction was reported by Martin for the photocyclization of 1,2-diarylethylene with a chiral ester group to "pre-helicene",[9] and a wide variety of diastereodifferentiating photoreactions have been investigated and employed in asymmetric syntheses, affording high diastereomeric excesses which often exceed 90% in the optimized cases.[10b,c]

In contrast to the diastereodifferentiating photoreaction, the enantiodifferentiating photosensitization is a much more difficult but quite attractive approach to the photochemical production of optically active compounds from prochiral substrates, where the photochemical chirality transfer and multiplication can be achieved using a catalytic amount of optically active sensitizer.[10] The first enantiodifferentiating photosensitization was reported by Hammond and Cole in 1965 for the photoisomerization of 1,2-diphenylcyclopropane sensitized by an optically active naphthalene derivative.[11] Since then, a considerable amount of effort was devoted to the study of enantiodifferentiating photosensitized reactions, but the enantiomeric excess (ee) of the obtained product never exceeded 7% for more than two decades.[10] This is simply due to the lack of effective methodologies to control the weak short-lived interactions between chiral sensitizer and substrate in the electronically excited state.[10]

A decade ago, Inoue and coworkers reported that the enantiodifferentiating geometrical photoisomerization of cyclooctene sensitized by chiral polyalkyl benzenepolycarboxylates affords moderate to good optical yields up to 40% at low temperatures,[12d] demonstrating for the first time that sufficient enantiodifferentiation can be attained even in the excited state. Quite interestingly, they further revealed that the product chirality is inverted simply by changing temperature[12] and pressure[13] without using the antipodal sensitizer. This switching of product chirality was shown to be exclusively entropic in origin through the temperature-dependence study of the product ee. Very recently, Hoffmann and Inoue have shown that the enantiodifferentiating photoisomerization of (*Z*)-cycloheptene sensitized by chiral benzenecarboxylates affords labile (*E*)-cycloheptene, which was subsequently trapped as a Diels-Alder adduct, in high ee's of up to 77%.[12l]

Unfortunately, most efforts on the enantiodifferentiating photosensitization have hitherto been concentrated on the investigations of unimolecular photoreactions as exemplified above.[10-12] The corresponding studies on bimolecular photoreactions have rarely been reported and do not appear to be very successful so far, although such studies undoubtedly expand the scope of asymmetric photochemistry greatly.[10] Inoue *et al.* investigated the enantiodifferentiating [2+2] photocyclodimerizations of aryl vinyl ether and 4-methoxystyrene in acetonitrile in the presence of optically active naphthalenecarboxylate sensitizers to give the corresponding cyclodimers in extremely low ee's (<1%).[14] Kim and Schuster reported that the [4+2] photocycloaddition of *trans*-β-methylstyrene to 1,3-cyclohexadiene, sensitized by (–)-1,1'-bis(2,4-dicyanonaphthalene) in toluene at -65 °C, gave the cycloadduct in 15% ee,[15] but in extremely poor chemical yield. It should be emphasized that, in these photoaddition reactions, the excited-state termolecular interactions, involving the short-lived excited sensitizer, substrate and reagent, are to be precisely controlled in order to attain efficient enantiodifferentiation, in which no one has succeeded yet.

There is another challenging subject in the asymmetric photosensitization. In the foregoing studies, the researchers have carefully avoided the photoinduced electron-transfer (PET) reactions, since the use of polar solvent, which is essential for the efficient PET, inevitably accelerates the dissociation of the radical cation/anion pair generated in the PET process, which however can easily ruin the possible enantiodifferentiating interactions in the initial photosensitization step.[10b,c] Hence, it has been believed that the optical and chemical yields are conflicting and often incompatible with each other in PET reactions and therefore the intervention of energy-transfer process is the essential condition for efficient photochemical asymmetric induction.[10b]

In the present study, the author wish to expand the scope and limitations of the conventional asymmetric photochemistry by materializing the highly efficient photosensitized enantiodifferentiating bimolecular reactions which are comparable to the unimolecular counterparts and also by elucidating a novel strategy to use the PET reactions in asymmetric photochemistry.

In Chapter 1, the enantiodifferentiating anti-Markovnikov photoaddition of alcohols to 1,1-diphenyl-1-alkenes sensitized by chiral naphthalenecarboxylates is described. The detailed reaction mechanism and excited states involved and the origin of enantiodifferentiation, as well as the reaction kinetics and energetics, have been fully elucidated. A new strategy to overcome the trade-off between chemical and optical yields has also been developed in this typical radical ion-mediated photoaddition reaction.

In Chapter 2, the enantiodifferentiating competitive [4+2] and [2+2] photocyclodimerizations of 1,3-cyclohexadiene sensitized by chiral arenecarboxylate is described. The mechanistic details and the origin of the enantiodifferentiation have been elucidated. The novel strategy established in the enantiodifferentiating anti-Markovnikov photoaddition described in Chapter 1 has been successfully applied to this enantiodifferentiating photocyclodimerization induced by photochemical electron-transfer.

In Chapter 3, the detailed reaction and enantiodifferentiation mechanisms are described for the enantiodifferentiating [2+2] photocyclodimerization of cyclohexene sensitized by chiral benzenecarboxylates. It has been shown that the photocyclodimerization involves the initial enantiodifferentiating *E*-to-*Z* photoisomerization of cyclohexene, followed by the concerted and stepwise thermal cyclodimerizations of optically active (*E*)-cyclohexene produced upon photosensitization with chiral benzoates.

In Chapter 4, the electronic and steric factors controlling uni- and bimolecular photochirogenetic processes in the excited state are discussed from a global point of view, which is compatible with the whole results obtained in the previous and present studies. The combined use of temperature and pressure is proposed as an effective, powerful tool for controlling the product chirality and optical yield in asymmetric photochemistry. Extension of such a methodology leads to a new concept of "synergetic control of photochirogensis" by multiple independent variants, which makes possible to afford high optical yields under readily accessible conditions using conventional chiral sensitizers.

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CHAPTER 1

Enantiodifferentiating Anti-Markovnikov Photoaddition of Alcohols to 1,1-Diphenylalkenes Sensitized by Chiral Naphthalenecarboxylates

Introduction

Recently, much interest has been focused on asymmetric photochemistry.[1] In particular, photosensitized enantiodifferentiating reactions have fascinated (photo)chemists as promising candidates for photochemical *catalytic* asymmetric synthesis. Since the first report on the asymmetric photosensitization of *trans*-1,2-diphenylcyclopropane by Hammond and Cole,[2] a considerable amount of effort has been devoted to the study of enantiodifferentiating photosensitized isomerizations, but in most cases the optical yields obtained in asymmetric photosensitized reactions rarely exceed 10%.[2-13] However, the author have demonstrated that the enantiodifferentiating geometrical photoisomerization of (*Z*)-cyclooctene, sensitized by chiral benzenepolycarboxylates, gives the optically active (*E*)-isomer in exceptionally high ee's (64% at -89 °C) and interestingly the product chirality can be inverted by temperature and pressure changes.[5b,h,k]

In contrast to such relatively widely explored unimolecular enantiodifferentiating photoisomerizations, only a few attempts have been hitherto reported concerning bimolecular enantiodifferentiating reactions. The enantiodifferentiating [2+2] photocyclodimerizations of aryl vinyl ether and 4-methoxystyrene have been attempted in acetonitrile in the presence of optically active naphthalenecarboxylate sensitizers, giving the corresponding cyclodimers in good chemical yields, but extremely low optical yields (<1%).[14] More impressively, Kim and Schuster reported that the [4+2] photocycloaddition of *trans*-β-methylstyrene to 1,3-cyclohexadiene, sensitized by (–)-1,1'-bis(2,4-dicyanonaphthalene) in toluene at -65°C, gave the cycloadduct in 15% ee.[15]

The author has shown that the enantiodifferentiating polar addition of methanol to 1,1-diphenylpropene **1** (R^1 = Me) sensitized by various chiral alkyl naphthalene(di)carboxylates

gave the adduct 1,1-diphenyl-2-methoxypropane (**4a**, R^1 = Me) in low to moderate optical yields. In that study, the product's optical purity (op) appeared to be a function of position and bulk of the sensitizer's chiral ester moiety.[16] Thus, the product's op was enhanced to 27% by increasing the bulk of the ester group of the sterically congested 1,8-naphthalenedicarboxylate (**10b**), while the increased steric hindrance inevitably led to a drastically diminished chemical yield of <2% and necessitated much longer irradiation periods of up to 200 h. No efficient enantiodifferentiating bimolecular reactions that employ chiral photosensitizers have been reported to date, and the elucidation of the enantiodifferentiation mechanism and the attainment of a good optical yield are still challenging themes in asymmetric photochemistry.

The author wishes now to report the results of my study that have enabled me to elucidate the detailed mechanism and intermediates involved in this enantiodifferentiating polar photoaddition, and also to enhance chemical and optical yields. In this study, the author employs series of 1,1-diphenyl-1-alkenes (**1-3**; R^1 = Me, Et, *i*-Pr) as substrates and alcohols (R^2OH; R^2 = Me, Et, *n*-Pr, *i*-Pr, *t*-Bu) as nucleophilic reagents as well as a variety of novel chiral sensitizers in order to overcome the normally encountered trade-off between chemical and optical yields. Based on the unusual effect of temperature upon the optical yields observed in this study, the author has demonstrated that the entropy term plays a definitive role in the crucial step that determines the product chirality and optical yield, not only in the unimolecular photoisomerizations,[5d,e,g] but also in the bimolecular photoaddition reactions. Both of these reactions are governed by weak bi- and termolecular interactions in the exciplex intermediate involving sensitizer, substrate, and/or reagent.

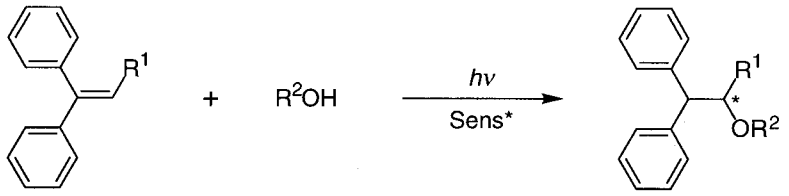
Results and Discussion

Photosensitized Polar Addition of Alcohols to 1,1-Diphenyl-1-alkenes. In the original study by Mizuno *et al.*,[17] the photochemical polar addition of methanol to 1,1-diphenylpropene (**1**) was effected by 9,10-dicyanoanthracene, which acted as an achiral sensitizer in polar solvents. In the present study, the author has employed a variety of optically active (di)alkyl naphthalene(di)carboxylates (**7-12**) as chiral sensitizers for the enantiodifferentiating addition of various alcohols (**a-d**) to a series of 1,1-diphenyl-1-alkenes

(**1-3**), as illustrated in Scheme 1.

Although arene(poly)carboxylates have not frequently been used as sensitizers in photoinduced electron transfer reactions of aromatic alkenes,[17,18] they are attractive, and probably the only, chiral sensitizers for the enantiodifferentiating photoaddition that permit me to examine a wide variety of chiral auxiliaries introduced in the vicinity of chromophore. Fortunately, most of the chiral naphthalene(di)carboxylates employed afforded the alcohol adducts (**4-6**) in good chemical yields of up to 75%, depending on the sensitizer and solvent used, as described below.

Scheme 1



1: R^1 = Me
2: R^1 = Et
3: R^1 = *i*-Pr

a: R^2 = Me
b: R^2 = Et
c: R^2 = *n*-Pr
d: R^2 = *i*-Pr

4a-d
5a,b
6a

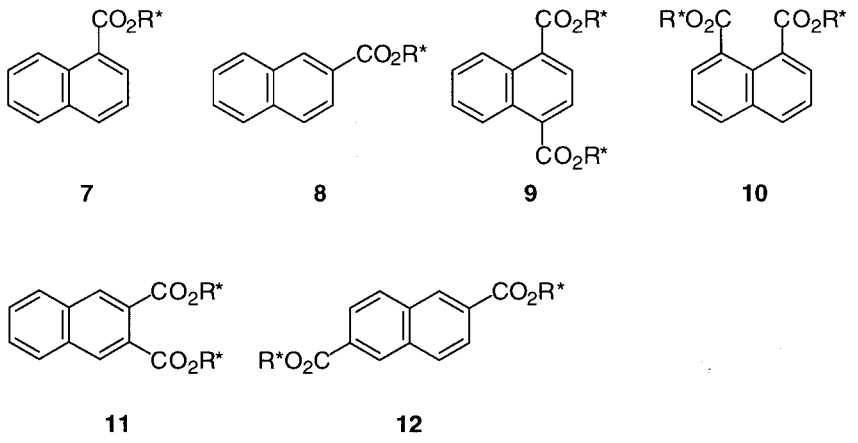
One of the most important factors to consider when performing optically and chemically efficient photoenantiodifferentiation in a reaction that involves electron transfer process and radical ionic species is the choice of solvent. In general, the use of a polar solvent is thought to be essential condition for high chemical yields, but this often ruins the optical yield of the photoproduct as a result of the intervention of free or solvent-separated radical ion pair between the chiral sensitizer and substrate. Thus, in most cases there is a severe trade-off relationship between the chemical and optical yield.[5i,14,15] The author therefore began working on the photoaddition of methanol to 1,1-diphenylpropene (**1**) sensitized by electron-accepting aromatics, a process which is known to proceed even in nonpolar solvents such as benzene[17] and pentane.[16] Furthermore, the author has developed a new strategy to overcome this

apparently inevitable problem concerning the balance between the chemical and optical yield.

Naphthalenecarboxylate Sensitizers. In search of the most effective arenecarboxylate sensitizers for the anti-Markovnikov addition of methanol to **1**, the author examined 1-, 2-, 1,4-, 1,8-, 2,3-, and 2,6-naphthalene(di)carboxylates **7**-**12** with several chiral ester moieties, as illustrated in Chart 1. Using optically active naphthalenecarboxylates (3 mM), the photosensitized addition of methanol to **1** (20 mM) was performed in pentane, methylcyclohexane, or toluene at temperatures ranging from -68 to +60 °C in the presence of 0.5 M methanol, giving the methanol adduct **4a**. The chemical yield and the optical purity (op, calculated from the optical rotation of isolated product) and/or enantiomeric excess (ee, determined by chiral stationary phase gas chromatography) are summarized in Tables 1 and 2,

Chart 1

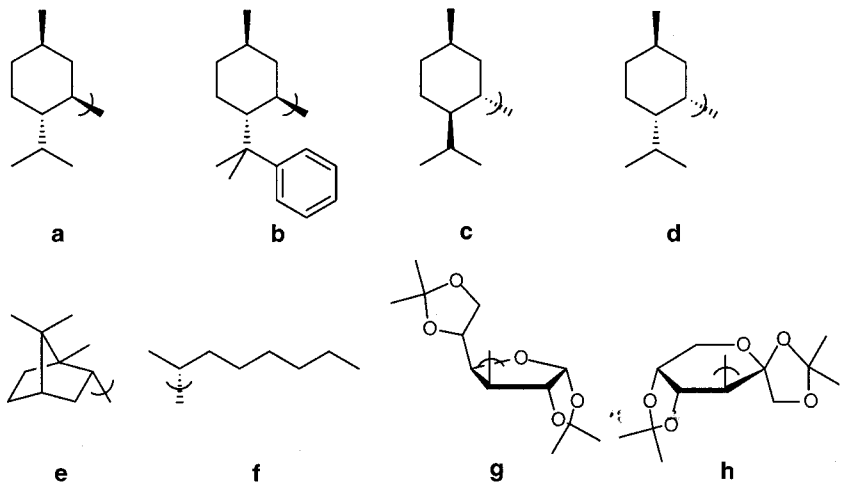
Sens*:



7 **8** **9** **10**

11 **12**

R*:



a **b** **c** **d**

e **f** **g** **h**

Table 1. Enantiodifferentiating Photoaddition of Methanol to 1,1-Diphenylpropene **1** Sensitized by Chiral Naphthalene(di)carboxylates **7**, **8**, **10-12**[a]

entry	sensitizer	solvent	temperature /°C	irradiation time / h	conversion[b] /%	yield[c] /%	ee[d] /%
1	**7a**	methylcyclo-	60	24	11	2	-3.7
2		hexane	25	24	10	1	-2.6
3			-40	48	< 3	< 1	-2.3
4			-68	48	7	2	-1.5
5		toluene	60	24	16	2	-4.2
6			25	24	9	2	-4.0
7			-40	48	17	5	-4.6
8			-68	48	12	< 1	-4.1
9	**7b**	methylcyclo-	60	24	16	4	-8.6
10		hexane	25	24	22	4	-6.3
11			-40	48	18	3	-7.2
12			-68	48	10	2	-6.9
13		toluene	60	24	15	1	-2.2
14			25	24	30	6	-4.8
15			-40	48	29	6	-5.9
16			-68	48	14	3	-5.4
17	**8a**	methylcyclo-	60	24	8	2	-3.4
18		hexane	25	24	< 3	1	-5.2
19			-40	48	13	3	-4.5
20			-68	48	< 3	< 1	-4.3
21		toluene	60	24	5	< 1	-0.1
22			25	24	< 3	< 1	-5.3
23			-40	48	9	1	-2.2
24			-68	48	5	< 1	-2.0
25	**8b**	methylcyclo-	60	24	4	2	-8.2
26		hexane	25	24	4	2	-6.7
27			-40	48	5	3	-6.0
28			-68	48	4	2	-9.5
29		toluene	60	24	< 3	2	-5.6
30			25	24	8	2	-7.0
31			-40	48	12	2	-6.4
32			-68	48	4	1	-7.0
33	**10a**	methylcyclo-	60	24	10	3	-12.1
34		hexane	40	24	9	3	-12.5

35			25	24	< 3	2	-9.4
36			0	48	16	5	-17.2
37			-40	48	11	2	-14.2
38		toluene	60	24	< 3	1	-6.3
39			25	24	< 3	< 1	-7.3
40			-40	48	5	< 1	-8.4
41			-68	48	4	< 1	-5.1
42	**10b**	methylcyclo-	60	24	6	3	-13.2
43		hexane	25	24	< 3	3	-13.6
44			-40	48	< 3	1	-10.3
45			-68	48	< 3	2	-12.1
46		toluene	60	24	< 3	2	-7.2
47			25	24	5	2	-8.2
48			-40	48	< 3	1	-7.0
49			-68	48	< 3	1	-6.9
50	**11a**	methylcyclo-	60	24	33	3	-4.6
51		hexane	40	24	29	3	-6.3
52			25	24	6	2	-5.5
53			0	48	26	5	-5.8
54			-40	48	30	5	-3.9
55		toluene	60	24	18	3	-2.9
56			25	24	7	1	-4.2
57			-40	48	19	2	-4.1
58			-68	48	12	< 1	-3.7
59	**11b**	methylcyclo-	60	24	11	4	-8.6
60		hexane	25	24	15	5	-5.5
61			-40	48	11	4	+5.8
62			-68	48	9	3	-3.3
63		toluene	60	24	9	3	-3.3
64			25	24	15	4	-1.8
65			-40	48	15	3	-0.3
66			-68	48	6	1	-3.8
67	**12a**	methylcyclo-	60	24	42	13	-4.7
68		hexane	25	24	39	12	-9.4
69			0	48	66	23	-7.1
70			-40	48	49	9	-8.6
71		toluene	60	24	36	9	0.0
72			25	24	31	11	-3.7

73			-40	48	44	19	-3.4
74			-68	48	37	9	-0.6
75	**12b**	methylcyclo-	60	24	23	5	+1.8
76		hexane	25	24	42	15	-2.8
77			-40	48	46	16	-8.1
78			-68	48	25	7	-12.0
79		toluene	60	24	22	8	-0.9
80			25	24	46	16	-1.6
81			-40	48	62	31	-3.7
82			-68	48	32	15	-5.5

[a] [**1**] = 20 mM; [Sens*] = 3 mM; [MeOH] = 0.5 M; reaction scale: 4 mL. [b] Loss of starting material determined by GC. [c] Chemical yield determined by GC on the basis of initial concentration of **1**. [d] Enantiomeric excess determined by chiral GC.

where the sign of the op/ee value represents the direction of product's optical rotation, *i.e.* a negative value indicates the formation of (*S*)-(–)-**4a** as the major product.

In all experiments, the product yield increased gradually over the period of irradiation, ultimately reaching a plateau after prolonged irradiation, which was dependent on the sensitizer and solvent used. In contrast, the product's op/ee was remained constant within the experimental error (±0.5% ee) throughout the irradiation period, as exemplified by runs 49-54 in Table 2 for the methanol addition of **1** sensitized by **9h** in toluene at 25 °C. These results clearly indicate that the photosensitized addition of methanol to **1** is not reversible and that the product, **4a**, is not subjected to any further reactions under the photochemical conditions employed. Since appreciable yields of no other products could be detected by GC analysis, the low chemical yields of the methanol adduct **4a**, formed upon sensitization with **7**, **8**, **10**, and **11**, may be attributed to the formation of cross-adducts with the sensitizers,[19] or unidentified oligomeric or polymeric products.

The chemical and optical yields are critical functions of both position and stereochemistry of the alkoxycarbonyl substituent(s) that are introduced to the naphthalene. The trade-off relationship between them appears to be unavoidable in this photosensitized enantiodifferentiating polar addition,[16] in which the development of positive charge on the substrate enhances the product yield[17] on one hand, but simultaneously accelerates the spatial

Table 2. Enantiodifferentiating Photoaddition of Methanol, Ethanol, 1-Propanol, 2-Propanol, and/or *t*-Butanol to 1,1-Diphenylalkenes **1-3** Sensitized by Chiral 1,4-Naphthalenedicarboxylates **9a-h**[a]

entry	alkene	alcohol	sensitizer	solvent	temperature / °C	irradiation time / h	conversion[c] / %	yield[d] / %	op[e] / %	ee[f] / %
1	**1**	MeOH	**9a**	pentane	25	24	98	26	-0.2[b]	-2.3
2					-40	48	64	14	-6.5[b]	-5.4
3					-68	48	54	13	-11.5[b]	-11.7
4				methyl-	60	24	93	61		-2.5
5				cyclo-	25	24	82	53		-4.0
6				hexane	0	48	87	56		-6.2
7					-40	48	60	25		-12.2
8				toluene	60	24	77	41		-1.7
9					25	24	80	52		-2.2
10					-40	48	54	26		-3.4
11					-68	48	44	16		-5.5
12			**9b**	pentane	25	24	91	31	+5.0[b]	+5.1
13					-40	48	61	13	+1.3[b]	+2.6
14					-68	48	61	13	-2.2[b]	-5.6
15				methyl-	60	24	83	46		-1.4
16				cyclo-	25	24	74	44		-1.0
17				hexane	-40	48	55	22		-12.5
18					-68	48	46	15		-17.9
19				toluene	60	24	71	36		-3.8
20					25	24	68	34		-3.7
21					-40	48	65	31		-5.2
22					-68	48	52	21		-3.8
23			**9c**	pentane	25	24	> 99	54	-0.7[b]	
24					-40	48	43	11	+2.2[b]	
25					-68	48	39	13	+4.7[b]	
26			**9d**	pentane	25	24	83	30	-1.8[b]	
27					-40	48	46	22	+1.9[b]	
28					-68	48	38	4	+3.8[b]	
29			**9e**	pentane	25	24	> 99	26		-1.5
30					-40	48	69	13		-0.5
31					-68	48	58	14		-1.6
32			**9f**	pentane	25	24	95	13		-0.6

33					-40	48	62	16		-1.1
34					-68	48	65	11		-2.9
35			**9g**	methyl-	60	24	89	60		-7.7
36				cyclo-	40	24	82	52		-8.0
37				hexane	25	24	85	59		-8.7
38					0	48	76	46		-6.8
39				toluene	60	24	89	55	-11.2 [b]	-11.3
40					25	24	81	57	-9.6 [b]	-10.6
41					-40	48	61	28		-6.3
42					-68	48	48	19		-6.5
43			**9h**	methyl-	60	24	95	66		-10.2
44				cyclo-	40	24	88	59		-8.2
45				hexane	25	24	82	54		-4.7
46					0 [g]	48	78	53		+1.1
47					-40 [g]	48	17	3		+11.2
48				toluene	60	24	86	54		-16.0
49					25	0.5	33	18		-15.6
50						1	48	28		-14.6
51						2	62	40		-16.1
52						4	72	45		-16.3
53						8	73	47		-16.0
54						24	75	47		-15.7
55					-40	48	56	24		-8.8
56					-68	48	44	17		-7.2
57				aceto-	60	24	> 99	75		-0.3
58				nitrile	25	24	> 99	73		-0.4
59					-40	48	> 99	73		-0.2
60	**1**	EtOH	**9h**	methyl-	95	9	62	36		-21.0
61				cyclo-	60	7	84	70		-17.4
62				hexane	25	14	96	68		-8.6
63				toluene	95	9	72	35		-21.7
64					60	10	90	35		-22.3
65					25	31	72	47		-18.9
66	**1**	1-PrOH		methyl-	95	9	82	38		-20.0
67				cyclo-	60	7	96	52		-17.4
68				hexane	25	14	> 99	59		-7.8
69				toluene	95	9	66	22		-20.4
70					60	12	68	32		-23.7

71					25	16	78	40	-21.4
72	**1**	2-PrOH		toluene	60	10	63	3	+32.0 [h]
73					25	31	36	4	+33.4 [h]
74	**1**	*t*-BuOH		toluene	60	10	38	0	–
75					25	31	51	0	–
76	**2**	MeOH	**9h**	methyl-	60	12	97	43	-19.7
77				cyclo-	25	20	98	24	-12.6
				hexane					
78				toluene	60	10	66	18	-23.4
79					25	18	60	29	-24.5
80	**2**	EtOH	**9h**	methyl-	95	6	25	11	+30.6
81				cyclo-	60	6	51	27	+27.8
82				hexane	25	17	83	39	+24.4
83				toluene	95	9	30	7	+26.1
84					60	7	80	12	+28.6
85					25	22	64	34	+25.7
86	**3**	MeOH		toluene	60	10	32	8	+3.8
87					25	18	43	16	+5.8

[a] [**1**] = 20 mM; [Sens*] = 3 mM; [MeOH] = 0.5 M; reaction scale: 4 mL, unless noted otherwise. [b] Reaction scale: 300 mL. [c] Loss of starting material determined by GC. [d] Chemical yield determined by GC on the basis of the initial concentration of **1**. [e] Optical purity of isolated **4a**, calculated from the specific rotation of optical pure (–)-(*S*)-**4a** ($[\alpha]_D^{20}$ = -52.5° ($CHCl_3$)). [f] Enantiomeric excess determined by chiral GC. [g] [Sens*] < 3 mM due to low solubility. [h] Incomplete separation on chiral GC.

separation of the chiral radical ion pair, thus reducing the product's ee. Nevertheless, the author prioritized on the chemical, rather than the optical yield, since a high ee value obtained at the expense of good chemical yield is not attractive, even in such an asymmetric photoreaction. Thus, photosensitizations with naphthalene(di)carboxylates possessing (–)-menthyl and highly bulky (–)-8-phenylmenthyl chiral auxiliaries were conducted at temperatures between -68 and +60 °C for a fixed irradiation period in methylcyclohexane and toluene solutions containing 0.5 M methanol. As shown in Table 1, 1- and 2-naphthalenecarboxylates **7a**,**b** and **8a**,**b** (runs 1-16 and 17-32, respectively) gave only low conversions (4 - 30%) and very low yields (1 - 6%), but the ee's obtained (3 - 9%) were not so poor for this type of bimolecular enantiodifferentiating photosensitization. The use of an aromatic solvent or carrying out the

irradiation at low temperature did not improve either the chemical or optical yield. Although 1,8- and 2,3-naphthalenedicarboxylates **10a,b** and **11a,b** (runs 33-49 and 50-66) gave similarly low conversions (3 - 30%) and yields (1 - 5%) in both solvents at all reaction temperatures studied, the product's ee was considerably improved to 13 - 17% upon sensitization by **10a,b** in methylcyclohexane. Again adjusting the temperature did not appear to affect the product's ee. However, 2,6-naphthalenedicarboxylate sensitizers **12a,b** gave higher conversions (22 - 66%) and yields (5 - 31%) as shown in Table 1 (runs 67-82). The obtained ee's were not very high (9 - 12% at the best), but were found to suffer a dramatic temperature effect, particularly upon sensitization with **12b** in methylcyclohexane. In this case, the absolute configuration of **4a** was inverted from *R* (+1.8% ee) at +60 °C to *S* (-12.0% ee) at -68 °C (runs 75-78). As can be seen from runs 1-22 (Table 2), photosensitizations with 1,4-naphthalenedicarboxylates **9a,b** afforded much higher conversions (50 - 98%) and yields (15 - 60%) under comparable conditions. In order to establish the origin of this difference in reactivity, the author calculated the Rehm-Weller free energy change (ΔG_{et})[20] from the oxidation potential of the substrate **1** (E_{ox} = 1.306 V) and the reduction potentials (E_{red}) and absorption 0-0 bands ($\lambda_{0\text{-}0}$) of sensitizers **7a**-**12a**, all of which are listed in Table 3, along with the quantum yield. Although the photosensitizations were carried out in nonpolar solvents and therefor the quantum yields were generally low in the present cases, the observed differences in photoreactivity are well accounted for in terms of the calculated ΔG_{et} values. Apart from 1,8-naphthalenedicarboxylate **10a**,[21] 1,4-naphthalenedicarboxylate **9a** gave the most negative ΔG_{et} value among the sensitizers examined as well as affording the best chemical and quantum yields. The author therefore focused on a series of sensitizers based on 1,4-naphthalenedicarboxylates with various chiral ester auxiliaries and their ability to effect the photosensitized enantiodifferentiating polar addition to **1**.

Effect of the Chiral Auxiliary. In order to systematically investigate the stereochemical effects of the chiral ester auxiliary upon optical yield, the author examined a series of optically active dialkyl 1,4-naphthalenedicarboxylates **9a-f** with cyclic menthyl and its derivatives/isomers (**a-d**), bicyclic bornyl (**e**), and acyclic 1-methylheptyl (**f**) groups. As can be seen from Table 2, the epimeric menthyl esters **9a,c,d** behave entirely differently to one another

Table 3. Reduction Potentials and Calculated Free Energy Change (ΔG_{et}) for Electron Transfer Process to Singlet Excited State of Chiral Naphthalene(di)carboxylates **7-12a** and Quantum Yields for Photoaddition of Methanol to 1,1-Diphenylpropene **1**

sensitizer	E_{red} [a] / V	$\lambda_{0\text{-}0}$ [b] / nm	ΔG_{et} [c] / kcal mol^{-1}	Φ_{4a} [d]
7a	-2.30	334	-1.15	1.2×10^{-4}
8a	-2.39	339	2.19	2.5×10^{-5}
9a	-1.84	371	-3.22	1.4×10^{-2}
10a	-2.22	334	-2.99	2.5×10^{-4}
11a	-2.30	341	0.61	1.1×10^{-4}
12a	-2.02	357	-2.09	1.8×10^{-3}

[a] Reduction potentials estimated as half-wave potential measured at a platinum electrode, relative to the Ag/AgCl electrode using 0.1 M tetrabutylammonium perchlorate as the electrolyte in acetonitrile. [b] Fluorescence maxima of highest energy emission in frozen EPA (diethyl ether : isopentane : ethanol = 5 : 5 : 2) Glass at 77 K. [c] Based on Weller equation: $\Delta G_{et} = 23.06\ (E_{ox}(D^+/D) - E_{red}(A/A^-)) - \Delta G_{0\text{-}0} - w_p$; oxidation potential of **1** (E_{ox} = 1.306 V) estimated as 0.028V before the peak potential; Coulombic attraction term (w_p) taken to be -1.3 kcal mol^{-1}. [d] Quantum yield of **4a** upon photosensitization of **1** with **7a-12a** in pentane containing 0.5 M methanol.

as chiral sensitizers. The (–)-menthyl ester **9a** afforded (*S*)-(–)-**4a** in 2.3% ee in pentane and 2.5% ee in methylcyclohexane at 25 °C, but the ee was increased to 11.7% at -68°C in pentane and 12.2% at -40°C in methylcyclohexane. In contrast, the neo- and isomenthyl esters **9c** and **9d** gave much smaller ee's (<5%) even at low temperatures, but interestingly the product chirality was switched within the experimental temperature range. Thus, (*R*)-(+)-**4a** was produced preferentially in 1-2% ee in pentane at 25 °C, while antipodal (*S*)-(–)-**4a** was favored in 4-5% ee at -68 °C in the same solvent. Similar temperature switching of product chirality has been reported previously for the enantiodifferentiating photoisomerization of cyclooctene sensitized by chiral benzenepolycarboxylates.[5e,g] Such behavior is also observed to occur upon photosensitization with the sensitizers employed in this study, and this phenomenon is reasonably rationalized as a function of the entropy term, as described below.

The above observations indicate that the absolute configuration of the asymmetric carbon

(C-1) adjacent to the ester oxygen plays the decisive role in determining the product's stereochemistry and optical yield, although the 8-phenyl group introduced in **9b** does not appreciably affect the asymmetric photochemical behavior. It is likely that the favored enantiomer at the low temperature limit, where the effect of entropy is minimized, can be related to the absolute configuration at C-1; *i.e.* (*S*)-(–)-**4a** from (1*R*)-(–)-menthyl esters **9a**,**b** and (*R*)-(+)-**4a** from (1*S*)-(–)-isomenthyl and neomenthyl esters **9c**,**d**. This empirical rule can be extended to photosensitizations with the other chiral alkyl esters **9e**,**f** and saccharide derivatives **9g**,**h**, in which all (1*S*)-sensitizers give the (*R*)-(+)-product.

In sharp contrast to the *normal* temperature dependence of ee observed for alkyl esters **9a**-**9f** (runs 1-34 in Table 2), the saccharide ester **9h** (runs 43-56) displays an *unusual* temperature dependence as well as a dramatic switching of product chirality within the experimental temperature range, although **9g** (runs 35-42) shows more moderate temperature dependence. In the case of **9h**, the product's ee is increased to 16% not by lowering, but by raising the temperature to 60 °C (runs 48-54), and either of the enantiomers of **4a** can be produced predominantly simply by changing the irradiation temperature. These apparently *extraordinary* observations are rationalized in terms of the non-zero differential entropy factor for the enantiodifferentiation process(es), as described below.

Activation Parameters. Recently, the author has found analogous temperature-switching behavior in the enantiodifferentiating *Z*-to-*E* photoisomerization of cyclooctene sensitized by a wide variety of chiral benzenepolycarboxylates.[5d,e,g] The Eyring-type analysis of the ee values of (*E*)-cyclooctene produced at various temperatures has revealed that the product's ee, which is determined exclusively by the differential free energy of activation ($\Delta\Delta G^{\ddagger}$) for the enantiodifferentiating photoisomerization, is governed not only by the differential enthalpy change of activation ($\Delta\Delta H^{\ddagger}$), according to conventional reasoning, but also by the differential entropy change of activation ($\Delta\Delta S^{\ddagger}$). The most important finding arising from this study was that the $\Delta\Delta S^{\ddagger}$ is not always negligible and often plays the key role in determining the product chirality particularly at ambient and higher temperatures.[1b,c]

In the present study, the activation parameters for the enantiodifferentiating photoaddition from the temperature dependence of the ee values obtained at various temperatures were also

determined, according to modified Arrhenius and Eyring equations:

$$\ln (k_R/k_S) = -\Delta E_{R\text{-}S}/RT + \ln (A_R/A_S)$$
$$= -\Delta\Delta H^{\ddagger}_{R\text{-}S}/RT + \Delta\Delta S^{\ddagger}_{R\text{-}S}/R \qquad (1)$$

where k_R and k_S are the apparent rates of formation of (*R*)-(+)- and (*S*)-(−)-**4a**, A_R/A_S represents the relative frequency factor and $\Delta\Delta H^{\ddagger}_{R\text{-}S}$ and $\Delta\Delta S^{\ddagger}_{R\text{-}S}$ are the differential enthalpy and entropy changes of activation, respectively. The relative rate constant (k_R/k_S) is experimentally

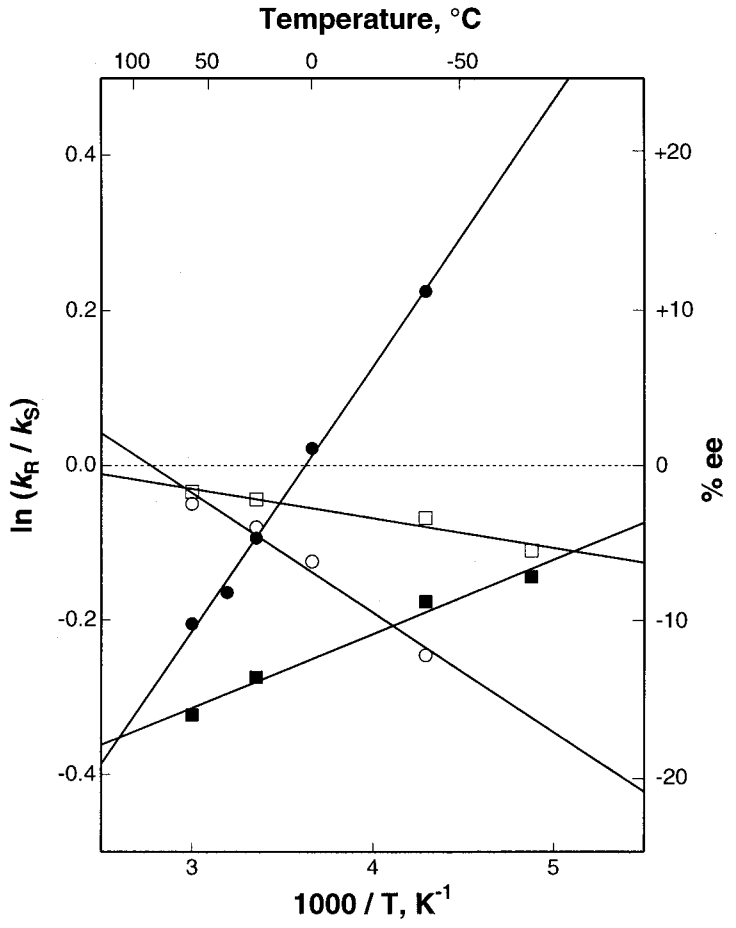


Figure 1. Temperature dependence of the enantiomeric excess (ee): the logarithm of relative rate constant (k_R/k_S) as a function of reciprocal temperature in enantiodifferentiating photosensitized methanol addition to **1** sensitized by **9a** in methylcyclohexane (○) and toluene (□) and by **9h** in methylcyclohexane (●) and toluene (■).

Table 4. Activation Parameters (at 25°C) and Equipodal Temperatures (T_0) for Enantiodifferentiating Photoaddition of Methanol to 1,1-Diphenylpropene **1** Sensitized by Some Chiral 1,4-Naphthalenedicarboxylates[a]

sensitizer	solvent	data point	$\Delta\Delta H^{\ddagger}_{R\text{-}S}$[b] / kcal mol^{-1}	$\Delta\Delta S^{\ddagger}_{R\text{-}S}$[c] / cal mol^{-1} K^{-1}	A_R / A_S[d]	T_0[e] / °C
9a	pentane	3	+0.24	+0.73	1.44	51
	methyl-cyclohexane	4	+0.31	+0.85	1.53	89
	toluene	4	+0.08	+0.17	1.09	178
9b	pentane	3	+0.26	+1.12	1.76	-39
	methyl-cyclohexane	3	+0.45	+1.46	2.08	35
9c	pentane	3	-0.14	-0.50	0.78	6
9d	pentane	3	-0.15	-0.56	0.75	-12
9g	methyl-cyclohexane	3	-0.22	-1.09	0.58	-70
	toluene	4	-0.12	-0.80	0.67	-127
9h	methyl-cyclohexane	5	-0.68	-2.47	0.29	3
	toluene	4	-0.19	-1.19	0.55	-114

[a] All activation parameters obtained by Arrhenius treatment of the optical yields. [b] Differential enthalpy of activation: $\Delta H^{\ddagger}_R - \Delta H^{\ddagger}_S$. [c] Differential entropy of activation: $\Delta S^{\ddagger}_R - \Delta S^{\ddagger}_S$. [d] Relative frequency factor. [e] Equipodal temperature, at which no appreciable enantiodifferentiation occurs.

equivalent to the (100 + %ee)/(100 – %ee) ratio, and the entity of the rate constants will be discussed in more detail later.

According to eq 1, the author plotted the ln (k_R/k_S) values obtained for each sensitizer as a function of reciprocal temperature. This gave good to excellent straight lines, as exemplified in Figure 1 for the photosensitization with **9a** and **9h** in methylcyclohexane and toluene. The relative frequency factor (A_R/A_S) and the differential activation enthalpy and entropy ($\Delta\Delta H^{\ddagger}_{R\text{-}S}$ and $\Delta\Delta S^{\ddagger}_{R\text{-}S}$) are listed in Table 4, along with the equipodal temperature (T_0), at which the product chirality is (expected to be) switched. It should be emphasized that none of the sensitizers employed give null $\Delta\Delta S^{\ddagger}_{R\text{-}S}$ values, or unit A_R/A_S, which is the origin of the unusual

temperature switching phenomena observed. Again, the widespread hypothesis that "lowering temperature leads to higher optical yield" is demonstrated not to be true in the photosensitized photoaddition reaction as well as in photoisomerization reactions.[5] These phenomena are attributable solely to the contribution of the entropic factor in the photochemical, and probably thermal, enantiodifferentiation processes.

Effect of Methanol Concentration. As expected from the radical ionic nature of the intermediate involved, a change in the solvent polarity significantly affected the product's ee. An extreme case is observed for highly polar solvents, such as acetonitrile. As shown in Table 2 (runs 57-59), the photosensitization of **1** by **9h** in acetonitrile containing 0.5 M methanol leads to the formation of racemic product **4a** in high yield at all temperatures examined, while the same photoreaction in toluene containing 0.5 M methanol affords (*S*)-(–)-**4a** in 7-16% ee under

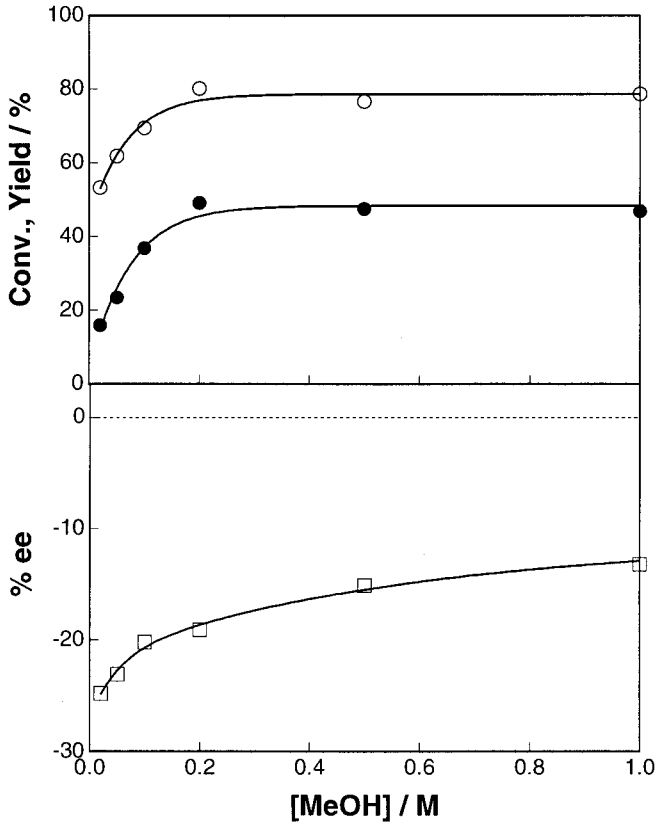


Figure 2. Conversion (○), chemical yield (●), and enantiomeric excess (ee, □) as a function of methanol content in enantiodifferentiating photosensitized methanol addition to **1** (20 mM) photosensitized by **9h** (3 mM) at 25°C.

comparable irradiation conditions (runs 48-56).

In this context, it is crucial to investigate the effect of methanol content on the product's chemical and optical yields. The photosensitization of **1** by **9h** was conducted at 25 °C for a fixed irradiation period (24 h) in toluene with methanol concentrations ranging from 0.02 to 1.0 M, giving the results shown in Figure 2. The conversion and chemical yield rapidly increased with increasing methanol concentration up to 0.2 M, reaching a plateau of 80% conversion and 50%yield. These results seem quite encouraging in the sense that the photoaddition occurs in lower, but appreciable conversions and yields even in a less polar solvent that contains extremely low methanol content (0.02 M). The constant levels of conversion and yield obtained with higher methanol concentrations indicate that a methanol concentration of 0.2 M is sufficient to generate and trap the radical cationic substrate ($\mathbf{1}^{\bullet+}$ or $\mathbf{1}^{\delta+}$).

In contrast, the ee of (*S*)-(–)-**4a** produced was almost halved from 25 to 13% by increasing the methanol from 0.02 to 1.0 M, as shown in Figure 2 (bottom). Taking into account the extremely low ee in acetonitrile, this result clearly indicates that the use of a more polar solvent, or high methanol content, accelerates the separation of the excited sensitizer-substrate complex which has radical ionic character. This generates a solvent-separated or free radical ion pair, in which the enantiodifferentiating interaction between substrate and chiral sensitizer should be much reduced. Fortunately, the high ee's obtained at low methanol concentrations are applicable to practical photochemical asymmetric synthesis, since the low product yield is expected to improve by extending the irradiation time.

Effect of the Alcohol's Bulk. Since the present photochemical polar addition involves the enantiofacially selective nucleophilic attack of an alcohol, the bulk of the alcohol should affect the product yield and ee. Thus, the photoaddition of more bulky alcohols to **1**, sensitized by **9h**, was performed in methylcyclohexane or toluene. The results for the photoaddition of ethanol, 1-propanol, 2-propanol, and *t*-butanol are summarized in Table 2 (entries 60-75). The adducts **4a-d** were all isolated from the photolyzed solutions on a preparative scale and their structures were confirmed spectroscopically.

As shown in Table 2, the primary alcohols, *i.e.* ethanol and 1-propanol (runs 60-65 and 66-71, respectively), afforded the corresponding adducts **4b** and **4c** in good chemical yields

(up to 70%). These yields are comparable or slightly higher than those obtained for methanol, probably as a result of the lower polarity of ethanol (E_T 51.9)[22] or 1-propanol (E_T 50.7)[22] as compared to that of methanol (E_T 55.5).[22] In contrast, the use of 2-propanol (runs 72 and 73) dramatically lowered the yield of adduct **4d** to 3-4%, and *t*-butanol (runs 74 and 75) afforded none of the desired product. These much lower yields is largely attributed to the increased steric hindrance during the nucleophilic attack of the alcohol on the radical cationic substrate $\mathbf{1}^{\delta+\bullet}$ in the exciplex or contact ion pair intermediate, although the lower polarity of 2-propanol (E_T 48.6)[22] and *t*-butanol (E_T 43.9)[22] may also be responsible to some extent.

Interestingly, the product's ee behaved quite differently to the chemical yield. By using the higher primary alcohols, the author obtained much improved ee's for adducts **4b** and **4c** in both methylcyclohexane and toluene at all temperatures investigated. For example, the ee of adduct **4** obtained in methylcyclohexane at 60 °C was increased from -10% for **4a** (run 43) to -17% for both **4b** and **4c** (runs 61 and 67), ultimately affording -20% ee at 95 °C (runs 60 and 66), while the photoreactions in toluene give almost constant ee's of ca. -22% for both **4b** and **4c** at 25-95 °C (runs 63-65 and 69-71). Using the more bulky 2-propanol nucleophile, the ee of product **4d** was further increased to 33% (runs 72 and 73), although the chemical yields are substantially lower. The author may conclude that the bulk and probably polarity of the alcohol can be used as a convenient and effective tool for enhancing the product ee in this enantiodifferentiating photoaddition that involves a charge-transfer exciplex or a contact ion pair.

Effects of Substrate Structure. Since the bulk of the alcohol was demonstrated to dramatically affect the product yield and ee, the author decided to explore the photosensitization of higher homologues of **1**, *i.e.* 1,1-diphenyl-1-butene (**2**) and 1,1-diphenyl-3-methyl-1-butene (**3**), which possess more bulky ethyl and isopropyl substituents on the carbon at which the nucleophilic attack occurs. Photoadditions of methanol to **2** and **3** sensitized by **9h** were performed in methylcyclohexane or toluene over a range of temperature, and the adducts **5a** and **6a**, produced from **2** and **3** respectively, were isolated and characterized spectroscopically. The results are summarized in Table 2 (runs 76-79 and 86-87).

The product's ee obtained in methylcyclohexane at 60 °C was significantly increased from

-10% for **4a** (run 43 in Table 2) to -20% for **5a** (run 76), accompanied by an appreciable decrease of the chemical yield from 66 to 43%. In toluene solution at 60°C, the ee was also improved from -16% for **4a** (run 48) to -23% for **5a** (run 78), but the yield decreased. Similar tendencies were also observed at 25 °C.

The introduction of a more bulky isopropyl group at the olefinic carbon, C-2, led to a considerable decrease in chemical and optical yields of product **6a** in toluene at 25 and 60 °C (runs 86 and 87). These results may be rationalized if it is assumed that the bulky substituent in substrate **3** prevents the formation of a close exciplex with the chiral sensitizer. This must inevitably reduce both steric and electronic interactions within the exciplex leading to low chemical and optical yields.

Optimization of Ee. Using the knowledge obtained from the examinations of a variety of chiral sensitizers, substrates, and alcohols, the author attempted to optimize the conditions for the photosensitized enantiodifferentiating polar addition reaction in order to maximize the product's ee. Although the use of bulky 2-propanol instead of methanol or ethanol in the photoaddition to **1** gave **4a** in up to 33% ee (runs 72 and 73 in Table 2), the chemical yield is unsatisfactory (3-4%), and the author therefore decided to employ a combination of moderately bulky substrate and nucleophile, *i.e.* **2** and ethanol. The photoaddition of ethanol to **2** sensitized by **9h** was performed in methylcyclohexane or toluene at 25-95 °C, and the results are summarized in Table 2 (runs 80-85). The chemical yield was good in both solvents with the highest ee of 30.6% in methylcyclohexane at 95°C. As well as having a chemical yield of 44% based on consumed substrate, this reaction represents the highest ee value for a bimolecular enantiodifferentiating photoreaction ever reported.[14-16]

Quenching of Sensitizer Fluorescence. In order to elucidate the excited state involved and also to evaluate the rate constants for the relevant processes in the photosensitized polar addition, fluorescence quenching experiments with two representative sensitizers **9a** and **9h** were performed in non-degassed pentane, methylcyclohexane, and toluene. The fluorescence spectra of **9a** and **9h** in these solvents were first examined in the presence or absence of methanol (0.5 M). As can be seen from Table 5, the fluorescence maxima of **9a** and **9h** show significant bathochromic shifts of 20-26 nm in toluene as compared with those in

Table 5. Fluorescence Quenching of Chiral Sensitizers by 1,1-Diphenylpropene **1** [a]

sensitizer	solvent	[MeOH] / M	$k_Q\tau^0$ / M^{-1}	τ^0 [b] / ns	k_Q / 10^9 $M^{-1}s^{-1}$	sensitizer λ_{max} / nm	exciplex [c] λ_{max}^{ex} / nm
9a	pentane	0	28.3	3.6	7.9	388 (73.7)	434 (65.9)
		0.5	37.1	3.0	12.0	391 (73.1)	458 (62.4)
	methyl-cyclo-hexane	0	16.3	4.4	3.7	389 (73.5)	438 (65.3)
		0.5	13.6	2.9	4.8	393 (72.7)	459 (62.3)
	toluene	0	6.2	8.5	0.73	408 (70.1)	*d*
		0.5	7.9	7.8	1.0	411 (69.6)	*d*
9h	pentane	0	57.2	6.3	9.1	394 (72.6)	457 (62.6)
		0.5	35.7	3.9	9.2	397 (72.0)	465 (61.5)
	methyl-cyclo-hexane	0	30.5	5.6	5.4	396 (72.2)	459 (62.3)
		0.5	22.1	3.9	5.6	400 (71.5)	467 (61.2)
	toluene	0	10.8	11.6	0.94	420 (68.1)	462 (61.9)
		0.5	12.6	11.5	1.1	423 (67.6)	472 (60.6)

[a] Measured with 0.01 mM aerated solution of sensitizer **9** at 25 °C. [b] Fluorescence lifetime of sensitizers in aerated solution at 25 °C. [c] Exciplex fluorescence obtained by the spectrum subtraction. [d] Exciplex emission not observed.

pentane, whereas the added methanol or the use of methylcyclohexane induce only trivial red-shifts of 1-3 nm. Since the excitation spectra in all three solvents coincide each other, this specific shift in toluene clearly indicates a charge transfer interaction between the sensitizer and solvent.

The sensitizer fluorescence was quenched efficiently by adding up to 70 mM of substrate

1 in the presence or absence of 0.5 M methanol. Representative quenching behavior of **9a** and **9h** in methylcyclohexane is illustrated in Figures 3 and 4. As the fluorescence intensity gradually decreased with increasing concentration of **1**, a new weak emission attributable to an exciplex intermediate emerged at longer wavelengths except for **9a** in toluene, accompanying the isoemissive point at 464 and 467 nm for **9a** and **9h**, respectively. As shown in the insets of

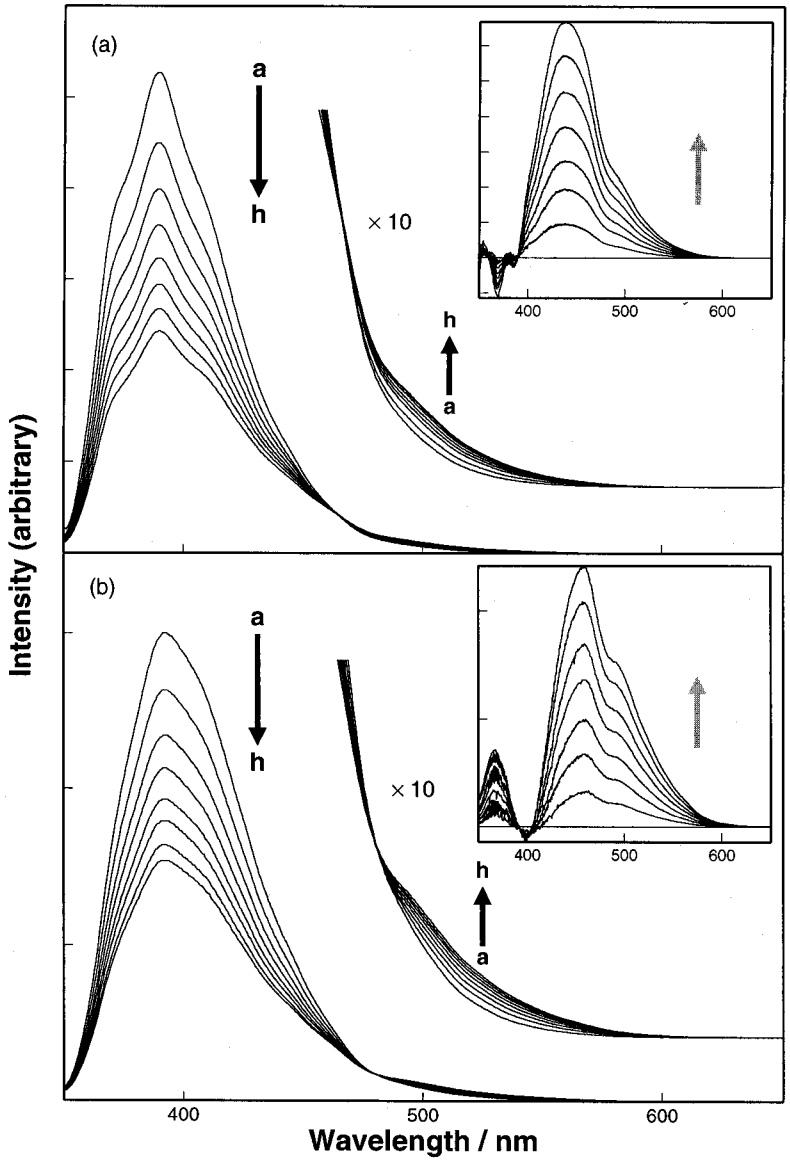


Figure 3. Fluorescence spectra of **9a** excited at 340 nm in methylcyclohexane in the presence (lower traces) and absence (upper traces) of methanol (0.5 M) with varying concentrations of **1**: (a) 0, (b) 10, (c) 20, (d) 30, (e) 40, (f) 50, (g) 60, (h) 70 mM.

Figures 3 and 4 and summarized in Table 5, the exciplex fluorescence peaks, obtained by the spectrum subtraction, occur at 438 and 459 nm for **9a** and **9h**, respectively. The finding that exciplex fluorescence of **9h** appears at longer wavelengths (by 21-23 nm) as compared to that of **9a** may be attributed to an extra stabilization of the exciplex by a higher microenvironmental polarity induced by the polar saccharide moiety. In this context, a similar but less extensive bathochromic shift (6-12 nm, depending on the solvent used) of sensitizer fluorescence of **9h** as

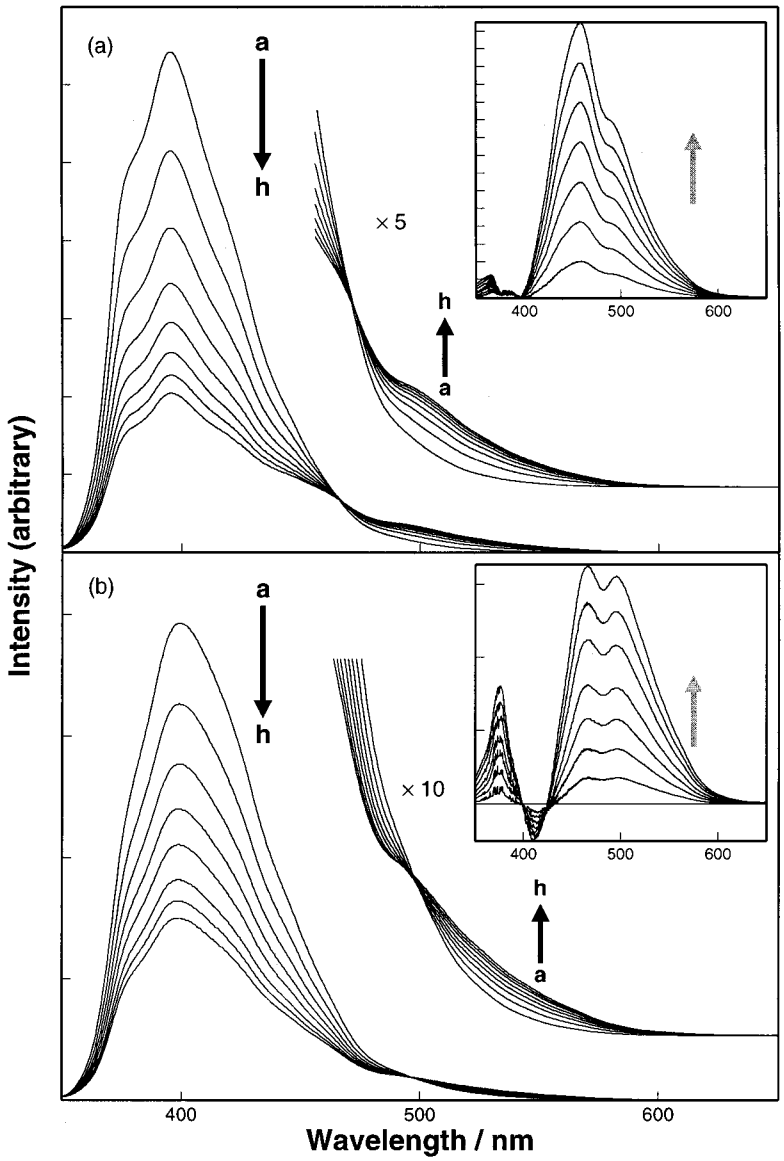


Figure 4. Fluorescence spectra of **9h** excited at 340nm in methylcyclohexane in the presence (lower traces) and absence (upper traces) of methanol (0.5 M) with varying concentrations of **1**: (a) 0, (b) 10, (c) 20, (d) 30, (e) 40, (f) 50, (g) 60, (h) 70 mM.

compared to that of **9a** may also be rationalized by the increased microenvironmental polarity, as the sensitizer fluorescence of **9a** and **9h** shows a bathochromic shift of 3-4 nm by adding 0.5 M methanol to each solvent.

Upon addition of 0.5 M methanol to each solution, the sensitizer fluorescence shifted only slightly to longer wavelengths (3 nm), irrespective of the solvent used. In contrast, the exciplex fluorescence showed much larger bathochromic shifts of 21-24 nm for **9a** and 8-10 nm for **9h** in both pentane and methylcyclohexane, indicating that the exciplex formed between excited **1** and **9** has a strong charge-transfer character. It is also interesting to note that the peak of exciplex fluorescence observed for **9h** in pentane or methylcyclohexane coincides with that observed for **9a** in the same solvent containing 0.5 M methanol. This may indicate that the microenvironmental polarity around the exciplex of **9h** is comparable to the bulk polarity of pentane or methylcyclohexane containing 0.5 M methanol. In the presence of methanol, similar fluorescence quenching behavior was observed for both **9a** and **9h** in all three solvents employed, as exemplified in Figures 3b and 4b.

Using a conventional Stern-Volmer treatment of these quenching data (eq 2), the relative fluorescence intensity (I_F/I_F^0) in the presence and absence of substrate was plotted as a function of the concentration of added **1**, affording an excellent straight line for all combinations of the sensitizers and solvents examined, as shown in Figure 5. From the Stern-Volmer constant ($k_Q\tau^0$) obtained as the slope of the plot and the fluorescence lifetime (τ^0) determined independently by a single photon counting technique, the author can calculate the apparent quenching rate constant (k_Q) for each sensitizer. The results are summarized in Table 5.

$$I_F/I_F^0 = 1 + k_Q\tau^0[Q] \qquad (2)$$

Quenching of Exciplex Fluorescence. In order to reveal the kinetic details of the nucleophilic addition step, the quenching of exciplex fluorescence by methanol was also performed with **9a** and **9h** in pentane, methylcyclohexane, and toluene. Since the exciplex fluorescence was fairly weak and overlapped with the sensitizer fluorescence, the fluorescence lifetime, instead of intensity, was measured in the presence of methanol at concentrations of up

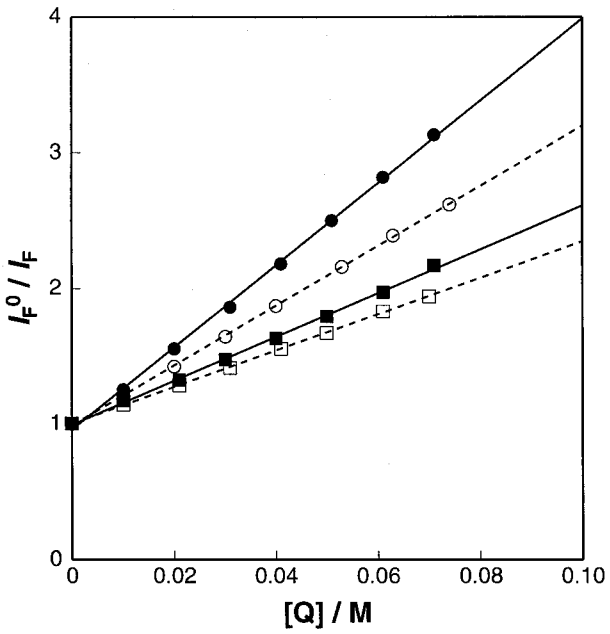


Figure 5. Stern-Volmer plots for fluorescence quenching of **9a** by **1** in the presence (□)/absence (■) of 0.5 M methanol and of **9h** by **1** in the presence (○)/absence (●) of 0.5 M methanol in methylcyclohexane.

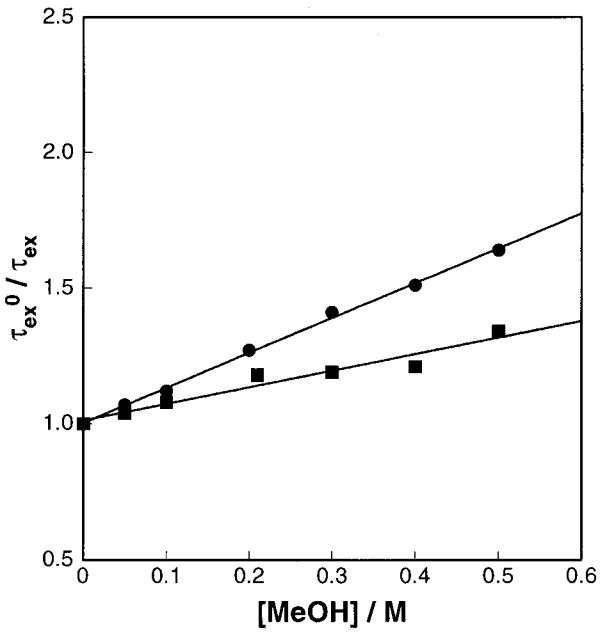


Figure 6. Stern-Volmer plots for fluorescence lifetime of the exciplex between **1** and **9a** (■) or **9h** (●) in the presence of varying amounts of methanol in methylcyclohexane.

Table 6. Fluorescence Lifetime in ns of Chiral Sensitizer (τ) and Exciplex (τ_{ex}) and the Apparent Rate Constant (k_A) for the Quenching of Exciplex Determined by Stern-Volmer Analysis of τ_{ex} at Varying Methanol Content in Some Solvents[a]

[MeOH]	pentane				methylcyclohexane				toluene	
/ M	**9a**		**9h**		**9a**		**9h**		**9h**	
	τ	τ_{ex}	τ	τ_{ex}	τ	τ_{ex}	τ	τ_{ex}	τ	τ_{ex}
0	1.1	4.9	2.0	10.9	2.0	4.9	2.3	11.4	4.7	12.7
0.05	1.3	4.8	1.9	10.7	1.9	4.8	2.2	10.7	4.7	12.0
0.1	1.2	4.7	1.7	9.6	1.8	4.6	2.3	10.2	4.5	11.1
0.2	1.2	4.5	1.5	8.0	1.7	4.2	2.3	9.0	4.4	10.2
0.3	1.3	4.4	1.3	6.9	1.8	4.2	2.3	8.1	4.2	8.9
0.4	1.2	4.3	1.4	6.2	1.8	4.1	2.3	7.5	4.2	8.5
0.5	1.2	4.1	1.4	5.9	1.8	3.7	2.2	7.0	3.8	7.5
1.0	1.2	3.4	1.3	3.9	1.7	3.1	2.3	4.3	3.7	6.3
k_A / M^{-1}		0.43		1.8		0.60		1.6		1.1

[a] Measured with non-degassed pentane solutions containing **1** (20 mM), **9** (0.01 mM), and varying amounts of methanol using a time-correlated single-photon-counting method at 25 °C. The decay profile was fitted to a double exponential curve (χ^2 = 0.5-1.5), and the shorter lifetime obtained was assigned to the sensitizer fluorescence in each case.

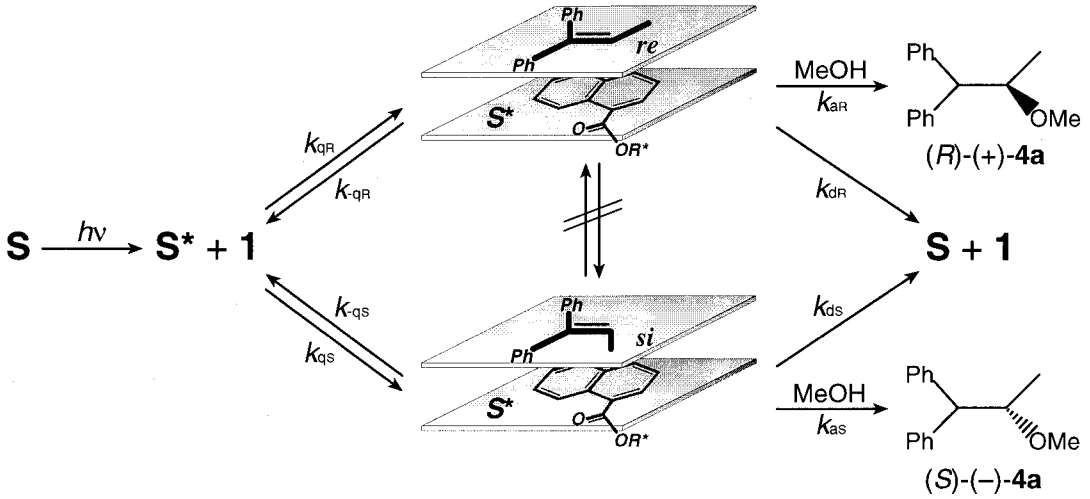
to 1.0 M. The time profile of the whole fluorescence was successfully analyzed in each case as a double-exponential decay with fast and slow components, which correspond to the sensitizer and exciplex fluorescence, respectively. As can be seen from Table 6, the sensitizer lifetime (τ) suffered little or no effects upon the addition of methanol up to 1.0 M, while the exciplex lifetime (τ_{ex}) was significantly shortened. According to the modified Stern-Volmer equation (eq 3), the relative fluorescence lifetime was plotted as a function of the methanol concentration, giving a good to excellent straight line for each sensitizer-solvent combination, as demonstrated in Figure 6. The Stern-Volmer constant (k_A) for each sensitizer is obtained as the slope of the plot.

$$\tau_{ex}^{0}/\tau_{ex} = 1 + k_A[\mathrm{MeOH}] \qquad (3)$$

Mechanism. All of the results obtained above are compatible with the mechanism

proposed previously by Mizuno *et al.* for the achiral photoaddition of methanol to **1** sensitized by 9,10-dicyanoanthracene.[17] In the present study, the use of a chiral sensitizer leads to the formation of a pair of diastereomeric exciplexes upon quenching of the excited singlet state of the enantiomerically pure sensitizer **9** by the prochiral substrate **1**. The author therefore proposes a chirally modified mechanism that involves a diastereomeric exciplex pair, which is equilibrated with the excited sensitizer and is simultaneously subjected to an enantiofacially selective nucleophilic attack by the alcohol. Scheme 2 illustrates the detailed mechanism of the enantiodifferentiating photoaddition of methanol sensitized by chiral sensitizer (**S**) and the rate constants for the relevant processes; *i.e.* k_q and k_{-q} for the formation and dissociation of exciplex, k_d for the radiative and nonradiative decay from the exciplex, and k_a for the addition of alcohol to the exciplex (the subscripts R and S refer to the absolute configurations of the product **4a**).

Scheme 2



In principle, if these two diastereomeric exciplexes possess distinctly different fluorescence maxima and lifetimes, the author can discriminate them spectroscopically as independent species. However, the decay profile of the exciplex fluorescence at longer wavelength does not appear to contain two components in addition to the sensitizer fluorescence, and the two peaks with ca. 30 nm (1200-1300 cm^{-1}) separation, observed in the exciplex fluorescence (insets in Figures 3 and 4), are more likely to be assigned to vibronic fine

structure than to two independent species. This seems quite reasonable, because an energy difference of even 0.4 kcal/mol in the stability or activation energy, which corresponds to a wavelength difference of 2-3 nm in this region, is capable of affording the highest ee's (30-33%) obtained in this study.

Kinetics and Energetics. The specific rate constants, which are assigned to the processes indicated in Scheme 2, are related to the apparent quenching constants k_Q and k_A that have been determined in the Stern-Volmer analyses described above. The calculated rate constants are listed in Table 7.

$$k_Q = k_q\,(1 - k_{-q}/(k_{-q} + k_d + k_a[\mathrm{MeOH}])) \qquad (4)$$

$$k_A = k_a/(k_{-q} + k_d) \qquad (5)$$

As expected from the highly negative ΔG_{et} obtained for **9** (Table 3), the quenching of the sensitizer singlet by substrate **1** proceeds at a rate of 0.6-3.3 x 10^{10} M^{-1} s^{-1}, which is almost comparable to diffusion controlled rates in pentane (k_{diff} 4.4 x 10^{10} M^{-1} s^{-1})[23] and

Table 7. Rate Constants for the Photoaddition of Methanol to **1** Sensitized by Chiral Sensitizers **9a** and **9h** [a]

sensitizer	solvent	k_q /10^9 $M^{-1}s^{-1}$	k_{-q} /10^7 s^{-1}	k_a /10^7 $M^{-1}s^{-1}$	k_d /10^7 s^{-1}	K_{ex} [b] /M^{-1}	ΔG_{ex} [c] /kcal mol^{-1}
9a	pentane	33.0	16.0	8.8	4.9	210	-3.2
	methyl-cyclo-hexane	8.2	11.4	12.3	8.8	72	-2.3
9h	pentane	9.2	0.17	17.0	9.0	5400	-5.1
	methyl-cyclo-hexane	5.9	0.92	11.3	7.9	640	-3.5
	toluene	1.4	2.7	8.5	5.2	52	-2.4

[a] The kinetic parameters calculated from the quenching rate constants k_Q and k_A using the equations (4) and (5). [b] Equilibrium constant for the exciplex formation: $K_{ex} = k_q / k_{-q}$. [c] Free energy change for the exciplex formation calculated from K_{ex}.

methylcyclohexane (k_{diff} 1.4 x 10^{10} M^{-1} s^{-1}).[23] In toluene (k_{diff} 1.8 x 10^{10} M^{-1} s^{-1}),[23] the k_q value falls considerably to 1.4 x 10^9 M^{-1} s^{-1}, probably due to the electron-donating solvation of the excited sensitizer, as demonstrated by the bathochromic shift of sensitizer fluorescence in the aromatic solvent (Table 4).

In sharp contrast to the comparable k_q's for **9a** and **9h** in pentane and methylcyclohexane, the rate of the reverse reaction (k_{-q}) differs by almost 2 orders of magnitude between these two sensitizers, with much greater equilibrium constants (K_{ex}) and stabilization energies (ΔG_{ex}) obtained for **9h** than for **9a**. The large K_{ex} (640 to 5400 M^{-1}) and highly negative ΔG_{ex} (-3.5 to -5.1 kcal/mol) render the exciplex formation of **9h** with **1** practically irreversible in nonpolar solvents. From the fluorescence maxima of the sensitizer and exciplex (λ_{max} and λ_{max}^{ex} in Table 5) and the free energy change upon exciplex formation (ΔG_{ex} in Table 7), the author can draw detailed energy diagrams for the sensitizers **9a** and **9h** and their exciplexes with substrate **1** in pentane at 25 °C, as illustrated in Figure 7a (this has been energy normalized to the ground-state sensitizers). In pentane solution, the exciplex [**9h***•••**1**] (67.5 kcal/mol) is more stabilized than [**9a***•••**1**] (70.5 kcal/mol), although the excited singlets of **9a** and **9h** do not differ appreciably in energy (73.7 and 72.6 kcal/mol). As shown in Figure 7b, the excited singlet of **9h** is more stabilized in toluene (68.1 kcal/mol) than in pentane (72.6 kcal/mol) through the electron-

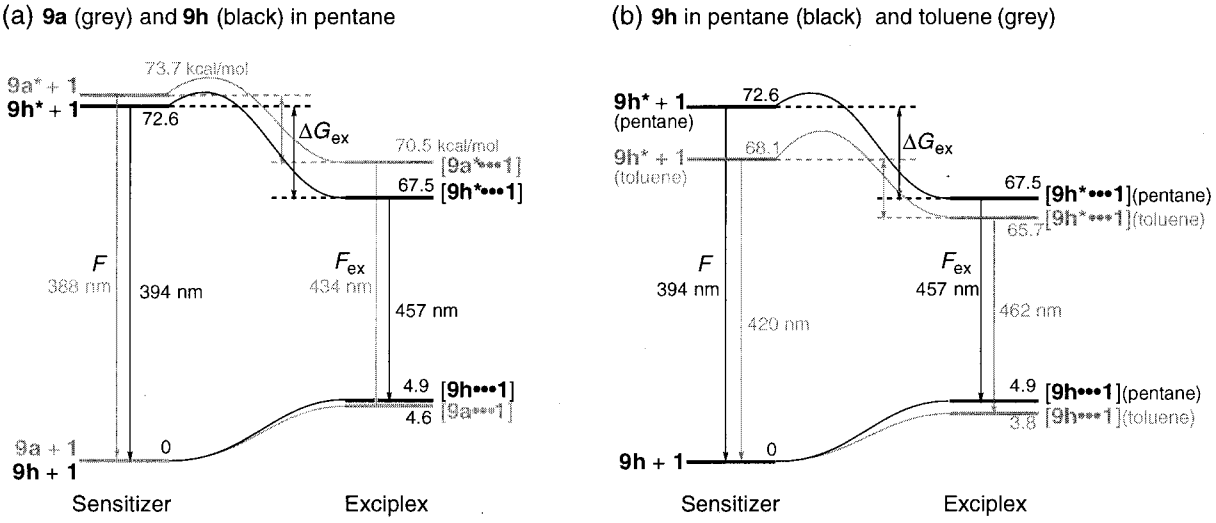


Figure 7. Energy diagram for sensitizers **9a** and **9h** and their exciplexes with **1** in pentane and toluene at 25 °C.

donating interaction with the aromatic solvent, although this extra stabilization is less effective upon exciplex formation with **1**, affording a smaller energy difference (67.5 and 65.7 kcal/mol in pentane and toluene, respectively)

From a kinetic point of view, the formation of the exciplex proceeds at a rate comparable to diffusion, while the subsequent nucleophilic attack of methanol on the electron-deficient substrate **1** contained in the exciplex is much slower (k_a[MeOH] = 4.3-8.5 x 10^7 s^{-1}). This attack is in comparison with exciplex decay (k_d = 4.9-9.1 x 10^7 s^{-1}) and also with exciplex dissociation (k_{-q} = 0.17-16 x 10^7 s^{-1}). the author may conclude, therefore, that the addition of methanol is the rate-determining step in the overall reaction sequence to the adduct **4**.

Judging from the greater bathochromic shifts, longer lifetimes, and larger equilibrium constants observed, the exciplex of **9h** with **1** is obviously more polarized, stabilized, and tightly bound than that of **9a** with **1**. This is probably a result of the increased microenvironmental polarity around the saccharide substituents, and the formation of the more polarized exciplex enhances the enantiofacial selectivity upon formation of the diastereomeric exciplex pair and accelerates the subsequent attack of methanol.

Origin of Enantioselectivity. In the mechanism shown in Scheme 2, the product's ee can be determined either *thermodynamically* by the stability difference between the diastereomeric exciplex pair, or *kinetically* by the difference in the rate of subsequent methanol addition, and this depends critically on the relative rates of the excited-state equilibrium and the subsequent processes. According to the proposed mechanism and the experimental data obtained above, the apparent enantioselectivity (k_R/k_S) used in eq 1 is expressed in further detail as a combination of relevant rate constants (eq 6).

$$k_R/k_S = [(k_{qR}/k_{-qR})k_{aR}]/[(k_{qS}/k_{-qS})k_{aS}]$$
$$= (K_{exR}k_{aR})/(K_{exS}k_{aS}) = (K_{exR}/K_{exS})(k_{aR}/k_{aS}) \qquad (6)$$

It is now apparent that the product's ee is not a simple function of a single pair of rate constants for an enantiodifferentiating process that gives the (*R*)- and (*S*)-adducts, but instead is controlled, in principle at least, by both the relative stability of the diastereomeric exciplexes

(K_{exR}/K_{exS}) and the relative rate of the subsequent addition of methanol (k_{aR}/k_{aS}). The final form of eq 6 clearly indicates that the apparent enantioselectivity (k_R/k_S), *i.e.* the R/S ratio of adduct, is a product of the relative stability (K_{exR}/K_{exS}) and reactivity (k_{aR}/k_{aS}) of the diastereomeric exciplex intermediates.

At this point of my discussion, it should be emphasized that the ln (k_R/k_S)-vs-T^{-1} plot gives a single straight line in most cases, as exemplified in Figure 1. This clearly indicates that the product's ee is determined in a single enantiodifferentiating step, since it is unlikely that the two enantiodifferentiating processes (equilibrium or rate) incidentally possess very close thermodynamic or activation parameters over the entire temperature range in all cases examined. Consequently, either the relative stability (K_{exR}/K_{exS}) or reactivity (k_{aR}/k_{aS}) must be responsible for the good enantiodifferentiation observed in the polar photoaddition of alcohol to **1**. A comparison of the rate constants for methanol addition (k_a), obtained from reactions photosensitized with **9a** and **9h**, leads to the conclusion that the observed enantioselectivity originates from the different thermodynamic stabilities between the diastereomeric exciplexes. As can be seen from the data shown in Tables 5 and 7 or illustrated in Figure 7, the exciplex [$\mathbf{9h}^{\delta-}\cdots\mathbf{1}^{\delta+}$] is 3.0-3.1 kcal/mol more stabilized in energy in nonpolar solvents than [$\mathbf{9a}^{\delta-}\cdots\mathbf{1}^{\delta+}$], which clearly indicates a more polarized, charge-transferred structure for [$\mathbf{9h}^{\delta-}\cdots\mathbf{1}^{\delta+}$]. In spite of the higher positive charge developed on the substrate moiety, the rate of methanol addition (k_a) to [$\mathbf{9h}^{\delta-}\cdots\mathbf{1}^{\delta+}$] is accelerated only by a factor of 1.2-1.9 as compared to [$\mathbf{9a}^{\delta-}\cdots\mathbf{1}^{\delta+}$]. In this context, the minimal differences in stability and polarity between the diastereomeric exciplex pair are not expected to be able to differentiate the rate of methanol attack on each of the diastereomers. The author may therefore conclude that the relative stability (K_{exR}/K_{exS}) is the major source of the observed enantioselectivity in the present asymmetric photoaddition.

Conclusions

In this comprehensive study on the enantiodifferentiating photochemical polar addition of alcohols to 1,1-diphenyl-1-alkenes sensitized by chiral naphthalene(di)carboxylates, the author has revealed several novel mechanistic and synthetic findings of general significance and applicability in discussing and designing uni- and bimolecular asymmetric photochemical

reactions, as outlined below.

1) The "unusual" temperature dependence, giving higher op/ee's at elevated temperatures, and the "unprecedented" switching of product chirality by temperature in a bimolecular process, both of which were reported originally for the enantiodifferentiating geometrical photoisomerizations of cyclooctenes, are neither strange, uncommon behavior, nor specific to the unimolecular photoreactions, but are natural consequences of the entropic contribution to the enantiodifferentiating processes in uni- and bimolecular asymmetric photochemical reactions. This enables me to use the entropic term as a convenient, versatile tool for controlling a wide variety of asymmetric photochemical reactions which are governed by the weak interactions in the exciplex intermediates.

2) The trade-off relationship between chemical and optical yields, which was frequently observed in previous work and thought to be unavoidable, can be overcome by optimizing the internal and external factors such as sensitizer's chromophore and chiral auxiliary, substrate and reagent structures, solvent polarity, and reaction temperature. In particular, the use of saccharides as chiral auxiliaries enhances the chemical and optical yields through the increased microenvironmental polarity, as proven by the increased exciplex fluorescence shift.

3) The detailed reaction and enantiodifferentiation mechanism and the intermediates involved in the enantiodifferentiating polar photoaddition have been elucidated by extensive fluorescence quenching experiments. The kinetics and energetics, as well as the origin of enantiodifferentiation, that have been revealed for the first time for such a bimolecular asymmetric photochemical reaction are a good basis for the future development of this relatively unexplored area of photochemistry.

Experimental Section

General. Melting points were measured with a YANACO MP-300 apparatus and are uncorrected. ^{1}H NMR spectra were obtained on a JEOL GX-400 spectrometer in chloroform-*d*. Infrared spectra were obtained on a JASCO Report-100 instrument. Electronic absorption and fluorescence spectra were recorded on JASCO V-550 and FP-777 instrument, respectively. Optical rotations were determined at 589nm in a thermostated conventional 10 cm cell, using a

JASCO DIP-1000 polarimeter.

Fluorescence lifetimes were measured with 0.01 mM solution of sensitizers in non-degassed pentane, methylcyclohexane, or toluene by means of the time-correlated single-photon-counting method on a Horiba NAES-1100 instrument equipped with a pulsed H_2 light source. The radiation from the lamp was made monochromatic by a 10-cm monochromator, and the emission from sample solution was detected through a Toshiba UV-37 or L-42 filter.

Quantum yields for the product **4a**, formed upon sensitization with **7a-12a**, were determined at 313 nm using a 2-hexanone actinometer.[23,24] A pentane solution of 2-hexanone, the concentration of which was varied from 0.4 to 4.0 M in order to match the absorbance of the relevant sensitizer at 313 nm, and a pentane solution of **1a** (20 mM) containing **7a-12a** (3 mM) and methanol (0.5 M) were prepared, divided into several portions, degassed with argon, and irradiated at 313 nm at 25 °C for several different periods in a merry-go-round apparatus. The quantum yield of **4a** was determined by assuming the quantum yield for the formation of acetone from 2-hexanone to be 0.22, as reported in the literature.[23,24]

Optical purities of **4a** were determined by the comparison of specific rotation with that of the authentic sample prepared independently.[25] Enantiomeric excesses of **4a-d**, **5a-b** and **6a** were determined by gas chromatography over a 15m chiral capillary column (TCI Chiraldex B-DA) at 145°C, using a Shimadzu GC-14B instrument. All GC peaks were integrated with a Shimadzu C-R6A integrator connected to the GC instrument.

Materials. Pentane and methylcyclohexane used as solvents were stirred over concentrated sulfuric acid until the acid layer no longer turned yellow, washed with water, neutralized with aqueous sodium hydrogen carbonate, dried over sodium sulfate, and then distilled fractionally. Toluene and alcohols were fractionally distilled from melting sodium and magnesium turnings, respectively.

1,1-Diphenyl-1-alkenes **1-3** were synthesized by dehydration of the corresponding 1,1-diphenyl-1-alkanols which were prepared by the Grignard reactions of the corresponding ketones with the appropriate alkyl bromides. 1,1-Diphenylpropene (**1**): mp 48.0-48.5°C (lit.[26] 48.5-49.0°C); ^{1}H NMR ($CDCl_3$) δ 1.76 (d, J = 6.8 Hz, 3H), 6.17 (q, J = 7.3 Hz, 1H), 7.17-7.39 (m, 10H). 1,1-Diphenyl-1-butene (**2**): ^{1}H NMR ($CDCl_3$) δ 1.02 (t, J = 7.4 Hz, 3H),

1.99-2.17 (m, 2H), 6.06 (t, J = 7.3 Hz, 1H), 7.00-7.52 (m, 10H). 1,1-Diphenyl-3-methyl-1-butene (**3**): ^{1}H NMR ($CDCl_3$) δ 1.02 (d, J = 6.6 Hz, 6H), 2.44-2.49 (m, 1H), 5.90 (d, J = 9.9 Hz, 1H), 7.11-7.50 (m, 10H).

Most optically active alcohols employed were commercially available: (–)-menthol, (+)-isomenthol and (–)-borneol from TCI; (+)-neomenthol from Aldrich; (–)-2-octanol from Nakarai. Optically pure (–)-8-phenylmenthol was synthesized from (+)-(5*R*)-pulegone according to the procedures reported by Corey *et al.*:[27] $[\alpha]_D^{25}$ -22.5° (*c* 1.92, EtOH) (lit.[27b] $[\alpha]_D^{22}$ -26.3° (*c* 2.30, EtOH)).

Sugar derivatives were prepared from D-glucose and D-fructose according to the procedures reported by Glen *et al.*[28] and Kang *et al.*,[29] respectively. 1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose: $[\alpha]_D^{25}$ -17.2° (*c* 0.80, H_2O); ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.37 (s, 3H), 1.45 (s, 3H), 1.50 (s, 3H), 2.50 (d, J = 3.9 Hz, 1H), 3.98 (dd, J = 3.4, 5.4 Hz, 1H), 4.07 (dd, J = 2.4, 4.8 Hz, 1H), 4.18 (dd, J = 2.4, 6.4 Hz, 1H), 4.26-4.37 (m, 2H), 4.54 (d, J = 3.4 Hz, 1H), 5.94 (d, J = 3.9 Hz, 1H). 1,2:4,5-Di-*O*-isopropylidene-β-D-fructopyranose: $[\alpha]_D^{25}$ -154.6° (*c* 1.10, acetone) (lit.[29] $[\alpha]_D^{28}$ -156.6° (*c* 1.00, acetone)); mp 112-113°C (lit.[29] 117.5-118°C); ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.42 (s, 3H), 1.49 (s, 3H), 1.51 (s, 3H), 3.64 (d, J = 6.8 Hz, 1H), 3.97 (t, J = 8.8 Hz, 1H), 4.06-4.21 (m, 4H).

Optically active naphthalenedicarboxylates employed as chiral sensitizers were prepared from the corresponding alcohols and acid chloride in pyridine.

(–)-Menthyl 1-naphthalenecarboxylate (7a). $[\alpha]_D^{25}$ -80.3 ° (*c* 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.85 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 7.3 Hz, 3H), 0.96 (d, J = 7.3 Hz, 3H), 0.88-1.02 (m, 1H), 1.13-1.25 (m, 2H), 1.59 (m, 2H), 1.75 (m, 2H), 2.03 (m, 1H), 2.23 (m, 1H), 5.07 (dt, J = 4.4, 10.7 Hz, 1H), 7.47-7.64 (m, 3H), 7.88 (d, J = 8.3 Hz, 1H), 8.01 (d, J = 8.3 Hz, 1H), 8.14 (d, J = 7.3 Hz, 1H), 8.91 (d, J = 8.3 Hz, 1H); UV (pentane) λ_{max} (ε) 220.6 (44400), 292.8 nm (7620 $M^{-1}cm^{-1}$); IR (KBr) ν 2950, 2930, 2870, 1710, 1600, 1510, 1460, 1370, 1280, 1240, 1200, 1140, 1010, 960, 780, 660 cm^{-1}; MS (EI) *m/z* (relative intensity) 310 (M^+, 20), 172 (100), 155 (57), 138 (59), 127 (35), 123 (16), 95 (33), 81 (19). Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.07; H, 8.58.

(–)-8-Phenylmenthyl 1-naphthalenecarboxylate (7b). m.p. 105.5-106.5°C;

$[\alpha]_D^{25}$ -95.7° (*c* 1.12, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.92 (d, *J* = 6.8 Hz, 3H), 0.96-1.23 (m, 2H), 1.26 (s, 3H), 1.35 (s, 3H), 1.72 (m, 4H), 2.02-2.25 (m, 2H), 5.16 (dt, *J* = 4.4, 10.7 Hz, 1H), 6.91 (t, *J* = 7.3 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 2H), 7.29 (m, 3H), 7.42-7.62 (m, 3H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 9.00 (d, *J* = 8.8 Hz, 1H); UV (pentane) λ_{max} (ε) 210.8 (49100), 300.6 nm (8400 $M^{-1}cm^{-1}$); IR (KBr) ν 3050, 1850, 1700, 1500, 1270, 1240, 1200, 1130, 1010, 770, 700 cm^{-1}; MS (EI) *m/z* (relative intensity) 386 (M^+, 20), 268 (25), 214 (23), 172 (70), 155 (44), 127 (24), 119 (100), 91 (17). Anal. Calcd for $C_{27}H_{30}O_2$: C, 83.90; H, 7.82. Found: C, 83.41; H, 7.61.

(–)-Menthyl 2-naphthalenecarboxylate (8a). m.p. 73.0-74.0°C; $[\alpha]_D^{25}$ -71.2° (*c* 0.46, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.82 (d, *J* = 6.8 Hz, 3H), 0.94 (m, 6H), 0.93-1.02 (m, 1H), 1.10-1.23 (m, 2H), 1.61 (m, 2H), 1.75 (m, 2H), 2.01 (m, 1H), 2.18 (m, 1H), 5.01 (dt, *J* = 4.4, 10.7 Hz, 1H), 7.51-7.61 (m, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.97 (d, *J* = 8.8 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 8.60 (s, 1H); UV (pentane) λ_{max} (ε) 236.4 (75700), 270.0 (6940), 278.8 (8200), 289.6 (5580), 317.0 (1210), 324.0 (987), 332.0 nm (1780 $M^{-1}cm^{-1}$); IR (KBr) ν 2950, 1710, 1460, 1350, 1290, 1230, 1200, 1130, 1090, 1040, 960, 830, 780 cm^{-1}; MS (EI) *m/z* (relative intensity) 310 (M^+, 21), 172 (100), 155 (90), 138 (90), 127 (52), 123 (25), 95 (52), 81 (28). Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.10; H, 8.52.

(–)-8-Phenylmenthyl 2-naphthalenecarboxylate (8b). m.p. 110.0-111.0°C; $[\alpha]_D^{30}$ -57.1° (*c* 0.98, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.90 (d, *J* = 6.4 Hz, 3H), 0.94-1.60 (m, 4H), 1.25 (s, 3H), 1.37 (s, 3H), 1.68-1.83 (m, 2H), 2.04 (m, 1H), 2.27 (m, 1H), 5.15 (dt, *J* = 4.4, 10.7 Hz, 1H), 6.94 (t, *J* = 7.8 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 2H), 7.29 (m, 2H), 7.54 (m, 2H), 7.71 (m, 2H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.94 (s, 1H); UV (pentane) λ_{max} (ε) 237.2 (68200), 270.0 (6590), 279.4 (7720), 290.0 (5240), 317.8 (1160), 324.6 (936), 333.0 nm (1720 $M^{-1}cm^{-1}$); IR (KBr) ν 2954, 2867, 1701, 1462, 1355, 1284, 1232, 1195, 1132, 1093, 981, 780, 763, 696 cm^{-1}; MS (EI) *m/z* (relative intensity) 386 (M^+, 14), 268 (27), 214 (27), 172 (49), 155 (41), 127 (23), 119 (100), 91 (17). Anal. Calcd for $C_{27}H_{30}O_2$: C, 83.90; H, 7.82. Found: C, 83.80; H, 7.91.

(–)-Dimenthyl 1,4-naphthalenedicarboxylate (9a). m.p. 93.5-94.5°C; $[\alpha]_D^{25}$ -

89.8° (*c* 0.98, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (d, *J* = 6.8 Hz, 6H), 0.93 (d, *J* = 6.8 Hz, 6H), 0.97 (d, *J* = 6.3 Hz, 6H), 0.92-1.01 (m, 2H), 1.13-1.26 (m, 4H), 1.52-1.63 (m, 4H), 1.75 (m, 4H), 2.01 (m, 2H), 2.24 (m, 2H), 5.07 (dt, *J* = 4.4, 10.7 Hz, 2H), 7.64 (dd, *J* = 3.4, 6.8 Hz, 2H), 8.04 (s, 2H), 8.80 (dd, *J* = 3.4, 6.8 Hz, 2H); UV (pentane) λ_{max} (ε) 201.6 (74100), 241.8 (26600), 315.8 nm (8120 $M^{-1}cm^{-1}$); IR (KBr) ν 2950, 2930, 2870, 1720, 1520, 1460, 1390, 1370, 1290, 1250, 1200, 1190, 1140, 1100, 1030, 990, 980, 960, 920, 870, 830, 780 cm^{-1}; MS (EI) *m/z* (relative intensity) 492 (M^+, 10), 337 (12), 216 (26), 199 (41), 138 (100), 123 (16), 95 (33), 81 (23). Anal. Calcd for $C_{32}H_{44}O_4$: C, 78.01; H, 9.00. Found: C, 77.94; H, 8.95.

(–)-Bis(8-phenylmenthyl) 1,4-naphthalenedicarboxylate (9b). m.p. 69.0-70.0°C; $[\alpha]_D^{25}$ -84.8° (*c* 1.11, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.85-1.39 (m, 8H), 0.94 (d, *J* = 6.4 Hz, 6H), 1.27 (s, 6H), 1.34 (s, 6H), 1.68-1.77 (m, 4H), 2.11-2.23 (m, 4H), 5.15 (dt, *J* = 3.9, 10.7 Hz, 2H), 6.86 (t, *J* = 7.3 Hz, 2H), 7.01 (t, *J* = 7.8 Hz, 4H), 7.21-7.26 (m, 6H), 7.61 (dd, *J* = 3.4, 6.3 Hz, 2H), 8.85 (dd, *J* = 3.4, 6.3 Hz, 2H); UV (pentane) λ_{max} (ε) 202.4 (75800), 243.8 (24500), 320.8 nm (8220 $M^{-1}cm^{-1}$); IR (KBr) ν 3080, 3050, 3030, 2950, 2920, 2850, 1710, 1600, 1580, 1520, 1500, 1460, 1440, 1390, 1370, 1290, 1240, 1180, 1140, 1130, 1100, 1020, 980, 780, 760, 700 cm^{-1}; MS (EI) *m/z* (relative intensity) 644 (M^+, 11), 312 (21), 214 (33), 199 (27), 119 (100), 105 (13), 91 (15). Anal. Calcd for $C_{44}H_{54}O_4$: C, 81.95; H, 8.13. Found: C, 81.83; H, 8.20.

(–)-Dimenthyl 1,8-naphthalenedicarboxylate (10a). m.p. 161.5-162.5°C; $[\alpha]_D^{25}$ -89.8° (*c* 0.98, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (d, *J* = 6.8 Hz, 6H), 0.99 (d, *J* = 6.8 Hz, 12H), 0.93-1.08 (m, 2H), 1.12-1.30 (m, 4H), 1.55-1.70 (m, 4H), 1.76 (m, 4H), 2.23-2.36 (m, 4H), 4.90 (dt, *J* = 4.4, 10.8 Hz, 2H), 7.51 (m, 2H), 7.94 (m, 4H); UV (pentane) λ_{max} (ε) 219.2 (40200), 292.4 nm (8990 $M^{-1}cm^{-1}$); IR (KBr) ν 2950, 2930, 2870, 1720, 1520, 1460, 1390, 1370, 1290, 1250, 1200, 1190, 1140, 1100, 1030, 990, 980, 960, 920, 870, 830, 780 cm^{-1}; MS (EI) *m/z* (relative intensity) 492 (M^+, 1), 217 (34), 199 (100), 138 (25), 95 (11), 83 (11). Anal. Calcd for $C_{32}H_{44}O_4$: C, 78.01; H, 9.00. Found: C, 77.99; H, 9.15.

(–)-Bis(8-phenylmenthyl) 1,8-naphthalenedicarboxylate (10b). m.p. 171.5-172.5°C; $[\alpha]_D^{25}$ -41.6° (*c* 1.71, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88-1.47 (m, 8H), 0.95 (d, *J* =

6.3 Hz, 6H), 1.33 (s, 6H), 1.47 (s, 6H), 1.64 (m, 4H), 2.22-2.37 (m, 4H), 5.12 (dt, *J* = 3.9, 10.3 Hz, 2H), 7.07-7.19 (m, 4H), 7.24-7.31 (m, 6H), 7.38 (d, *J* = 7.8 Hz, 4H), 7.83 (d, *J* = 7.8 Hz, 2H); UV (pentane) λ_{max} (ε) 215.0 (46900), 295.8 nm (8660 $M^{-1}cm^{-1}$); IR (KBr) ν 3050, 2950, 1710, 1600, 1500, 1450, 1380, 1280, 1200, 1150, 910, 840, 770, 700 cm^{-1}; MS (EI) *m/z* (relative intensity) 644 (M^+, 2), 311 (43), 214 (42), 199 (100), 119 (94), 105 (53), 91 (22). Anal. Calcd for $C_{44}H_{54}O_4$: C, 81.95; H, 8.13. Found: C, 81.93; H, 8.22.

(–)-Dimenthyl 2,3-naphthalenedicarboxylate (11a). m.p. 94.0-94.5°C; $[\alpha]_D^{25}$ -84.1° (*c* 0.88, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (d, *J* = 6.8 Hz, 6H), 0.92 (d, *J* = 7.3 Hz, 6H), 0.96 (d, *J* = 6.4 Hz, 6H), 0.87-0.97 (m, 2H), 1.09-1.22 (m, 4H), 1.48-1.57 (m, 4H), 1.73 (m, 4H), 2.02 (m, 2H), 2.26 (m, 2H), 5.00 (dt, *J* = 4.4, 10.7 Hz, 2H), 7.61 (dd, *J* = 3.4, 6.4 Hz, 2H), 7.93 (dd, *J* = 3.4, 6.4 Hz, 2H) , 8.19 (s, 2H); UV (pentane) λ_{max} (ε) 235.2 (72900), 269.6 (6770), 279.2 (6330), 320.2 (1090), 333.8 nm (1410 $M^{-1}cm^{-1}$); IR (KBr) ν 2950, 1720, 1460, 1370, 1290, 1210, 1120, 1030, 960, 900, 760 cm^{-1}; MS (EI) *m/z* (relative intensity) 492 (M^+, 3), 355 (24), 217 (100), 199 (98), 167 (10), 138 (29), 95 (23), 83 (25). Anal. Calcd for $C_{32}H_{44}O_4$: C, 78.01; H, 9.00. Found: C, 77.73; H, 9.08.

(–)-Bis(8-phenylmenthyl) 2,3-naphthalenedicarboxylate (11b). m.p. 87.0-88.0°C; $[\alpha]_D^{25}$ -67.3 ° (*c* 1.35, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86-1.25 (m, 8H), 0.93 (d, *J* = 6.4 Hz, 6H), 1.31 (s, 6H), 1.38 (s, 6H), 1.61 (m, 4H), 2.11 (m, 2H), 2.23 (m, 2H), 5.14 (dt, *J* = 3.9, 10.3 Hz, 2H), 6.86 (t, *J* = 7.3 Hz, 2H), 7.09 (t, *J* = 7.8 Hz, 4H), 7.27 (d, 4H), 7.59 (dd, J = 3.4, 6.4 Hz, 2H), 7.68 (s, 2H), 7.82 (dd, *J* = 2.9, 5.9 Hz, 2H); UV (pentane) λ_{max} (ε) 209.6 (34700), 237.0 (60800), 269.6 (6610), 280.0 (5940), 321.4 (1120), 335.0 nm (1450 $M^{-1}cm^{-1}$); IR (KBr) ν 2950, 1720, 1600, 1500, 1450, 1290, 1220, 1120, 1040, 980, 900, 780, 700 cm^{-1}; MS (EI) *m/z* (relative intensity) 644 (M^+, 2), 431 (22), 311 (24), 217 (100), 199 (56), 119 (93), 105 (46), 91 (23). Anal. Calcd for $C_{44}H_{54}O_4$: C, 81.95; H, 8.13. Found: C, 81.68; H, 8.22.

(–)-Dimenthyl 2,6-naphthalenedicarboxylate (12a). m.p. 131.0-133.0°C; $[\alpha]_D^{25}$ -85.8° (*c* 0.43, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.83 (d, *J* = 6.8 Hz, 6H), 0.95 (d, *J* = 6.8 Hz, 12H), 0.94-1.02 (m, 2H), 1.10-1.23 (m, 4H), 1.58-1.67 (m, 4H), 1.76 (m, 4H), 2.01 (m, 2H), 2.18 (m, 2H), 5.02 (dt, *J* = 4.4, 10.7 Hz, 2H), 8.00 (d, *J* = 8.8 Hz, 2H), 8.12 (d, *J* =

8.8 Hz, 2H) , 8.61 (s, 2H); UV (pentane) λ_{max} (ε) 242.8 (99800), 273.0 (10500), 283.2 (16000), 293.8 (14900), 331.4 (2420), 347.6 nm (3210 $M^{-1}cm^{-1}$); IR (KBr) ν 2930, 2850, 1710, 1450, 1370, 1330, 1270, 1170, 1120, 1080, 960, 910, 760 cm^{-1}; MS (EI) *m/z* (relative intensity) 492 (M^+, 7), 337 (23), 199 (41), 171 (14), 138 (100), 123 (18), 95 (38), 81 (23). Anal. Calcd for $C_{32}H_{44}O_4$: C, 78.01; H, 9.00. Found: C, 78.14; H, 9.18.

(–)-Bis(8-phenylmenthyl) 2,6-naphthalenedicarboxylate (12b). m.p. 186.5-187.5°C; $[\alpha]_D^{25}$ -36.8° (*c* 0.46, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.91 (d, *J* = 6.4 Hz, 6H), 0.95-1.55 (m, 8H), 1.24 (s, 6H), 1.37 (s, 6H), 1.73 (m, 2H), 1.89 (m, 2H), 2.24 (m, 2H), 2.31 (m, 2H), 5.15 (dt, *J* = 3.9, 10.3 Hz, 2H), 6.90 (t, *J* = 7.3 Hz, 2H), 7.09 (t, *J* = 7.8 Hz, 4H), 7.28 (d, 4H), 7.68 (m, 4H), 7.85 (s, 2H); UV (pentane) λ_{max} (ε) 211.0 (32200), 244.6 (88300), 274.4 (9870), 284.6 (14900), 295.2 (14600), 334.0 (2350), 350.0 nm (3020 $M^{-1}cm^{-1}$); IR (KBr) ν 3050, 2950, 1700, 1600, 1500, 1270, 1180, 1130, 1100, 980, 760, 700 cm^{-1}; MS (EI) *m/z* (relative intensity) 644 (M^+, 7), 525 (13), 312 (10), 214 (32), 199 (22), 119 (100), 105 (13), 91 (12). Anal. Calcd for $C_{44}H_{54}O_4$: C, 81.95; H, 8.13. Found: C, 82.60; H, 8.34.

(+)-Diisomenthyl 1,4-naphthalenedicarboxylate (9c). m.p. 82.5-83.5°C; $[\alpha]_D^{25}$ +22.2° (*c* 0.92, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.94 (d, *J* = 6.4 Hz, 6H), 1.00 (d, *J* = 6.8 Hz, 6H), 1.03 (d, *J* = 6.8 Hz, 6H), 1.27-1.35 (m, 2H), 1.50-1.98 (m, 16H), 5.44 (m, 2H), 7.64 (dd, *J* = 3.4, 6.8 Hz, 2H), 8.09 (s, 2H), 8.87 (dd, *J* = 3.4, 6.8 Hz, 2H); UV (pentane) λ_{max} (ε) 201.8 (76200), 242.2 (27000), 316.0 nm (8060 $M^{-1}cm^{-1}$); IR (KBr) ν 2950, 2930, 2870, 1710, 1580, 1520, 1460, 1390, 1370, 1340, 1280, 1250, 1190, 1130, 1030, 840, 770 cm^{-1}; MS (EI) *m/z* (relative intensity) 492 (M^+, 10), 337 (10), 216 (25), 199 (40), 138 (100), 123 (13), 95 (34), 81 (17). Anal. Calcd for $C_{32}H_{44}O_4$: C, 78.01; H, 9.00. Found: C, 77.79; H, 8.97.

(+)-Dineomenthyl 1,4-naphthalenedicarboxylate (9d). m.p. 156.0-158.0°C; $[\alpha]_D^{25}$ +32.6° (*c* 0.97, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.91 (d, *J* = 6.8 Hz, 6H), 0.93 (d, *J* = 7.3 Hz, 6H), 0.96 (d, *J* = 8.3 Hz, 6H), 1.02-1.60 (m, 10H), 1.69-1.84 (m, 6H), 2.19 (m, 2H), 5.59 (m, 2H), 7.66 (dd, *J* = 3.4, 6.8 Hz, 2H), 8.10 (s, 2H), 8.92 (dd, *J* = 3.4, 6.8 Hz, 2H); UV (pentane) λ_{max} (ε) 201.8 (73800), 242.8 (29200), 318.0 nm (8460 $M^{-1}cm^{-1}$); IR (KBr) ν

2950, 2920, 2870, 1710, 1580, 1520, 1460, 1450, 1370, 1280, 1250, 1210, 1190, 1150, 1140, 1030, 980, 920, 900, 870, 840, 780 cm^{-1}; MS (EI) *m/z* (relative intensity) 492 (M^+, 14), 337 (10), 216 (21), 199 (35), 138 (100), 123 (10), 95 (28), 81 (13). Anal. Calcd for $C_{32}H_{44}O_4$: C, 78.01; H, 9.00. Found: C, 77.82; H, 8.98.

(–)-Dibornyl 1,4-naphthalenedicarboxylate (9e). m.p. 171.0-172.0°C; $[\alpha]_D^{25}$ -41.9° (*c* 1.09, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.94 (s, 6H), 0.98 (s, 6H), 1.01 (s, 6H), 1.21 (dd, *J* = 3.4, 13.7 Hz, 2H), 1.29-1.46 (m, 4H), 1.78-1.83 (m, 4H), 2.05-2.11 (m, 2H), 2.53-2.58 (m, 2H), 5.24 (m, 2H), 7.65 (dd, *J* = 3.4, 6.3 Hz, 2H), 8.12 (s, 2H), 8.85 (dd, *J* = 3.4, 6.3 Hz, 2H); UV (pentane) λ_{max} (ε) 201.8 (72300), 242.0 (29300), 316.0 nm (8870 $M^{-1}cm^{-1}$); IR (KBr) ν 2900, 1695, 1290, 1270, 1235, 1175, 1120, 1040, 1015, 865 cm^{-1}; MS (EI) *m/z* (relative intensity) 488 (M^+, 39), 335 (100), 199 (73), 153 (17), 137 (22), 109 (11). Anal. Calcd for $C_{32}H_{40}O_4$: C, 78.65; H, 8.25. Found: C, 78.40; H, 8.28.

(–)-Bis((1R)-1-methylheptyl) 1,4-naphthalenedicarboxylate (9f). $[\alpha]_D^{25}$ -29.5° (*c* 0.91, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 6H), 1.29-1.47 (m, 16H), 1.42 (d, *J* = 6.4 Hz, 6H), 1.59-1.82 (m, 4H), 5.29 (m, 2H), 7.63 (dd, *J* = 3.4, 6.3 Hz, 2H), 8.04 (s, 2H), 8.81 (dd, *J* = 3.4, 6.8 Hz, 2H); UV (pentane) λ_{max} (ε) 201.8 (71300), 241.8 (27100), 316.0 nm (8080 $M^{-1}cm^{-1}$); IR (KBr) ν 2950, 2930, 2860, 1720, 1580, 1520, 1460, 1380, 1350, 1320, 1280, 1250, 1190, 1140, 1120, 1020, 980, 920, 870, 850, 780, 740 cm^{-1}; MS (EI) *m/z* (relative intensity) 440 (M^+, 40), 328 (32), 311 (24), 216 (100), 199 (37). Anal. Calcd for $C_{28}H_{40}O_4$: C, 76.32; H, 9.15. Found: C, 76.38; H, 9.24.

(–)-Bis(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl) 1,4-naphthalenedicarboxylate (9g). m.p. 89.5-90.5°C; $[\alpha]_D^{27}$ -41.4° (*c* 1.00,' $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.32 (s, 6H), 1.36 (s, 6H), 1.46 (s, 6H), 1.59 (s, 6H), 4.05-4.17 (m, 4H), 4.35 (m, 4H), 4.74 (d, *J* = 3.9 Hz, 2H), 5.61 (m, 2H), 5.96 (d, *J* = 3.4 Hz, 2H), 7.68 (dd, *J* = 3.4, 6.8 Hz, 2H), 8.06 (s, 2H), 8.84 (dd, *J* = 3.4, 6.3 Hz, 2H); UV (methylcyclohexane) λ_{max} (ε) 212.0 (38600), 244.0 (26200), 320.4 nm (7350 $M^{-1}cm^{-1}$); IR (KBr) ν 2988, 1730, 1514, 1459, 1378, 1248, 1136, 1076, 1024, 847, 780, 514 cm^{-1}; MS (EI) *m/z* (relative intensity) 700 (M^+, 3), 685 (69), 541 (10), 441 (100), 199 (53), 154 (18), 101 (93). Anal. Calcd for $C_{36}H_{44}O_{14}$: C, 61.71; H, 6.33. Found: C, 61.61; H, 6.15.

(−)-Bis(1,2:4,5-Di-*O*-isopropylidene-β-D-fructopyranosyl) 1,4-naphthalenedicarboxylate (9h). m.p. 183.5-184.5°C; $[\alpha]_D^{27}$ -192.9° (*c* 1.01, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.36 (s, 6H), 1.38 (s, 6H), 1.49 (s, 6H), 1.64 (s, 6H), 4.04 (m, 4H), 4.17 (m, 4H), 4.29 (m, 2H), 4.48 (dd, *J* = 4.9, 7.8 Hz, 2H), 5.49 (d, *J* = 7.8 Hz, 2H), 7.65 (dd, *J* = 3.4, 6.8 Hz, 2H), 8.18 (s, 2H), 8.86 (dd, *J* = 3.4, 6.8 Hz, 2H); UV (methylcyclohexane) λ_{max} (ε) 211.6 (37400), 244.2 (26200), 320.4 nm (7510 $M^{-1}cm^{-1}$); IR (KBr) ν 2989, 2937, 1725, 1514, 1378, 1459, 1381, 1246, 1134, 1085, 976, 886, 849, 779, 515 cm^{-1}; MS (EI) *m/z* (relative intensity) 700 (M^+, 7), 685 (20), 441 (100), 199 (66), 182 (10), 171 (25), 154 (18), 143 (44), 126 (10). Anal. Calcd for $C_{36}H_{44}O_{14}$: C, 61.71; H, 6.33. Found: C, 62.34; H, 6.43.

Photolysis. All irradiations were carried out in a temperature-controlled water (25°C), methanol/2-propanol (-40°C) and methanol/ethanol (-68°C) bath. The light sources employed were a conventional 300W high-pressure mercury lamp for irradiations at 25°C and an equivalent lamp fitted with a transparent Pyrex vacuum sleeve designed for low-temperature irradiation (Eikosha). A solution (4 or 300 mL), containing 1,1-diphenylalkene **1-3** (20mM), alcohol (0.5mM), optically active sensitizer **7-12** (3mM), and cyclododecane (3mM) added as an internal standard, was irradiated at >300nm under an argon atmosphere in a Pyrex tube (1 cm i.d.) placed near the lamp surface or in an annular Pyrex vessel surrounding the lamp, the whole system being immersed in the cooling bath.

Product Isolation. In preparative runs using an annular vessel (300 mL), the photolyzed solutions of **1-3** were first subjected to column chromatography over silica gel with an ethyl acetate/hexane (3/97) eluent and then to the preparative GC over SE-30 to give chemically pure adducts **4a-d**, **5a-b** and **6a**. No traces of fragments derived from the decomposition of the chiral sensitizer were detected on GC or NMR in the isolated products.

1,1-Diphenyl-2-methoxypropane (**4a**): ^1H NMR ($CDCl_3$) δ 1.11 (d, *J* = 5.9Hz, 3H), 3.27 (s, 3H), 3.88 (d, *J* = 8.3Hz, 1H), 3.92-4.19 (m, 1H), 7.11-7.36 (m, 10H) (lit.[17] δ 1.08 (d, *J* = 6.0Hz, 3H), 3.23 (s, 3H), 3.87 (d, *J* = 8.5Hz, 1H), 4.01 (dq, 1H), 7.1-7.4 (m, 10H)).

1,1-Diphenyl-2-ethoxypropane (**4b**): ^1H NMR ($CDCl_3$) δ 0.86 (t, *J* = 7.3Hz, 3H), 0.91 (t, *J* = 7.0Hz, 3H), 3.04 (m, 1H), 3.35 (m, 1H), 3.75-3.86 (m, 1H), 3.92 (d, *J* = 8.1Hz, 1H), 7.03-7.39 (m, 10H); IR (neat) ν 3060, 3030, 2970, 2930, 2860, 1600, 1580, 1490, 1450,

1370, 1130, 1080, 1030, 960, 760, 740, 700 cm^{-1}; HRMS Calcd for $C_{17}H_{20}O$ (M^+): 240.1513. Found: 240.1514.

1,1-Diphenyl-2-propoxypropane (**4c**): ^1H NMR ($CDCl_3$) δ 0.67 (t, *J* = 7.7Hz, 3H), 1.06 (d, *J* = 5.9Hz, 3H), 1.37 (m, 2H), 3.07 (m, 1H), 3.43 (m, 1H), 3.83 (d, *J* = 8.8Hz, 1H), 4.04 (m, 1H), 7.06-7.36 (m, 10H); IR (neat) ν 3070, 3030, 2970, 2930, 2870, 1660, 1600, 1580, 1490, 1450, 1370, 1330, 1280, 1250, 1130, 1100, 1030, 1000, 940, 910, 760, 740, 700 cm^{-1}; HRMS Calcd for $C_{18}H_{22}O$ (M^+): 254.1670. Found: 254.1675.

1,1-Diphenyl-2-isopropoxypropane (**4d**): ^1H NMR ($CDCl_3$) δ 0.73 (d, *J* = 6.2Hz, 3H), 1.02 (d, *J* = 6.2Hz, 3H), 1.08 (d, *J* = 6.2Hz, 3H), 3.31 (m, 1H), 3.79 (d, *J* = 8.8Hz, 1H), 4.07 (m, 1H), 7.05-7.40 (m, 10H); IR (neat) ν 3060, 3030, 2970, 2930, 2900, 1600, 1580, 1490, 1450, 1370, 1320, 1180, 1120, 1090, 1030, 990, 940, 900, 760, 740, 700 cm^{-1}; HRMS Calcd for $C_{18}H_{22}O$ (M^+): 254.1670. Found: 254.1677.

1,1-Diphenyl-2-methoxybutane (**5a**): ^1H NMR ($CDCl_3$) δ 0.85 (t, *J* = 7.3Hz, 3H), 1.25-1.60 (m, 2H), 3.12 (s, 3H), 3.79 (m, 1H), 3.94 (d, *J* = 8.4Hz, 1H), 7.05-7.36 (m, 10H); IR (neat) ν 3060, 3030, 2960, 2940, 2880, 2820, 1600, 1580, 1490, 1450, 1370, 1270, 1190, 1130, 1100, 1080, 1030, 940, 750, 740, 700 cm^{-1}; HRMS Calcd for $C_{17}H_{20}O$ (M^+): 240.1513. Found: 240.1517.

1,1-Diphenyl-2-ethoxybutane (**5b**): ^1H NMR ($CDCl_3$) δ 0.90 (t, *J* = 7.3Hz, 3H), 0.95 (t, *J* = 7.0Hz, 3H), 1.27-1.60 (m, 2H), 3.08 (m, 1H), 3.39 (m, 1H), 3.86 (m, 1H), 3.96 (d, *J* = 8.1Hz, 1H), 7.08-7.42 (m, 10H); IR (neat) ν 3060, 3030, 2970, 2940, 2880, 1600, 1580, 1490, 1450, 1370, 1100, 1080, 1030, 980, 760, 740, 700 cm^{-1}; HRMS Calcd for $C_{18}H_{22}O$ (M^+): 254.1670. Found: 254.1666.

1,1-Diphenyl-2-methoxy-3-methylbutane (**6a**): ^1H NMR ($CDCl_3$) δ 0.87 (d, *J* = 6.2Hz, 6H), 1.09 (d, *J* = 7.0Hz, 1H), 2.98 (s, 3H), 3.54 (dd, *J* = 4.4, 8.4Hz, 1H), 4.00 (d, *J* = 8.1Hz, 1H), 7.03-7.51 (m, 10H).

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CHAPTER 2

Enantiodifferentiating Photocyclodimerization of 1,3-Cyclohexadiene Sensitized by Chiral Arenecarboxylates

Introduction

Enantiodifferentiating photosensitization, which necessitates only a catalytic amount of chiral sensitizer, is one of the most promising methodologies for inducing chirality into prochiral substrates through the electronically excited state.[1] Since the first report on the asymmetric photosensitization of *trans*-1,2-diphenylcyclopropane by Hammond and Cole,[2] a great deal of effort has been devoted to the study of enantiodifferentiating photosensitized isomerizations, but the reported enantiomeric excesses (ee's) have rarely exceeded 10%, until recently.[2-12,20h] The author has demonstrated that the enantiodifferentiating geometrical photoisomerization of (*Z*)-cyclooctene ,sensitized by chiral benzenepolycarboxylates gives the optically active (*E*)-isomer in exceptionally high ee's of up to 64% at -89 °C, and displays the interesting property of product chirality inversion, induced by temperature and pressure changes.[5b,h,k]

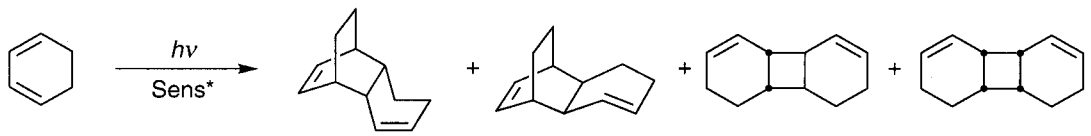
In contrast to the unimolecular enantiodifferentiating photoisomerizations, only a few attempts have been reported on bimolecular enantiodifferentiating reactions. The enantiodifferentiating [2+2] photocyclodimerizations of aryl vinyl ether and 4-methoxystylene in acetonitrile were examined in the presence of some chiral naphthalenecarboxylates to give the corresponding cyclodimers in good chemical yields, but no enantiodifferentiation occurred (ee < 1%).[13] Kim and Schuster reported that the [4+2] photocycloaddition of *trans*-β-methylstyrene with 1,3-cyclohexadiene sensitized by (–)-1,1'-bis(2,4-dicyanonaphthalene), gave the cyclodimer with 15% ee at -65 °C.[14f]

Recently the author reported that the enantiodifferentiating photoaddition of alcohols to 1,1-diphenylalkenes sensitized by chiral naphthalene(di)carboxylates gives the anti-Markovnikov adduct.[15] In this bimolecular asymmetric photosensitization, the author observed an unusual temperature affect on the enantioselectivity of the product. It was found that the

product chirality was inverted by temperature at the critical point (T_0), which enabled me to obtain both of the enantiomeric products simply by changing the irradiation temperature, also allowing higher ee's to be obtained at higher temperatures beyond T_0.[15] The author have also found that the chemical and optical yields of the product is critically controlled by the 'microenvironmental polarity' around the sensitizer chromophore, showing that the introduction of saccharide substituent(s) to the sensitizer works as a new effective strategy for overcoming the trade-off between the chemical and optical yields in such photoaddition reactions involving a radical ion intermediate. By combining the unusual temperature effect and the enhanced microenvironmental polarity by introducing saccharide substituent(s) to the sensitizer, the author obtained the optimized ee of 33%.[15]

Photocycloaddition initiated by energy or electron transfer is one of the most widely investigated photochemical reactions.[16] The photocycloadditions of 1,3-dienes to arenes have been used in the syntheses of various types of novel cyclic compounds.[14e,17-20] The photocyclodimerization of 1,3-cyclohexadiene (**1**) which gives isomeric [4+2] and [2+2] cyclodimers (**2** and **3**) (Scheme 1) has also been investigated under a variety of conditions, for which several reaction mechanisms involving different intermediates have been proposed, depending on the mode of excitation.[14b,20-22] Here, the author reports the result of my study of the enantiodifferentiating photocyclodimerization of **1** sensitized by chiral arene(poly)carboxylates. The use of chiral sensitizers with saccharide and non-saccharide substituents has enabled me to obtain definitive evidence for the cyclodimerization mechanism. Furthermore, allowing exploration into the enhancement of the microenvironmental polarity to increase the chemical yield without decreasing the ee of the product, by preventing the

Scheme 1



1 **2a*** *endo*-[4+2] **2b*** *exo*-[4+2] **3a*** *anti*-[2+2] **3b** *syn*-[2+2]

dissociation of the photochemically generated radical ion pair.

Results and Discussion

Photocyclodimerization of 1,3-Cyclohexadiene (1). The [4+2] and [2+2] cyclodimerizations of **1** have been investigated under a wide variety of thermal and photochemical conditions.[14b,20-25] The thermal dimerization requires a long reaction time and affords the *endo*- and *exo*-Diels-Alder adducts **2a** and **2b** in poor yields, with an *endo*:*exo* ratio of *ca.* 4:1.[21a,25] However, photochemical reactions of **1** lead to the formation of both [4+2] and [2+2] cyclodimers. Direct irradiation of neat **1** at 254 nm produces the *exo*-[4+2] adduct **2b** and the *anti*- and *syn*-[2+2] adducts **3a** and **3b** in 1 : 4.4 : 2.3 ratio together with other dimers,[22] whereas photosensitization with a triplet sensitizer such as phenanthrene and benzophenone gives the same products **2b**, **3a** and **3b** but in higher combined yields. The relative product ratio (**2b** : **3a** : **3b** = *ca.* 1 : 3 : 1) is appreciably different from that obtained in the direct excitation and is independent of the triplet energy and structure of the sensitizer employed.[20h] In contrast, the photoinduced electron-transfer reaction of **1** leads to the *endo*-adduct **2a** in improved yield and selectivity.[20e,h] The author performed the electron-transfer and triplet-sensitized photocyclodimerization of **1**, using 1-cyanonaphthalene (1-CN) and benzophenone (BP). As can be seen from Table 1 (runs 1 and 2), the photoinduced electron-transfer with 1-CN gave **2a** as the major product along with much smaller amounts of **2b**, **3a** and **3b** in a ratio of 27.8 : 4.2 : 3.0 : 1.0. The triplet sensitization with BP gave only **2b**, **3a** and **3b** in a ratio of 0.8 : 3.0 : 0.8, which is in good agreement with the results reported by Mattay *et al.*[20h]

In the present study, the author has employed a variety of optically active (poly)alkyl benzene- and naphthalene(poly)carboxylates (**4-12**) as chiral sensitizers for the enantiodifferentiating photocycloaddition of 1,3-cyclohexadiene **1**, as illustrated in Chart 1. Although arene(poly)carboxylates have not frequently been used as sensitizers in photoinduced electron transfer reactions of aromatic alkenes,[26,27] they are prominent and effective chiral sensitizers[15b,c] for the enantiodifferentiating photoaddition, which will allow me to examine a wide variety of chiral auxiliaries introduced into the vicinity of the chromophore.

In performing optically and chemically efficient enantiodifferentiation in a photoreaction that involves an electron transfer process and radical ionic species, one of the most important factors

is the choice of solvent. In general, the use of a polar solvent is an essential condition for high chemical yields, which however often accompanies a decreased optical yield of photoproduct as a result of the intervention of free or solvent-separated radical ion pairs between the chiral sensitizer and substrate.[5i,14f,15] The author has therefore employed nonpolar or less polar solvents in the present enantiodifferentiating photocyclodimerization of **1**.

Arenecarboxylate Sensitizers. In search of the most effective arenecarboxylate sensitizers for the photocyclodimerization of **1**, benzenepolycarboxylates (**4** and **5**) and naphthalene(poly)carboxylates (**6**-**12**) with several chiral auxiliaries (**a**-**f**) (shown in Chart 1) were examined. Using optically active arenecarboxylates (5 mmol dm^{-3}), the photosensitized cyclodimerization of **1** (100 mmol dm^{-3}) was performed in either pentane, toluene, diethyl ether or acetonitrile at -41 and +25 °C to give **2a**, **2b**, **3a** and/or **3b**. Of these four cyclodimers, **2a**, **2b** and **3a** are chiral, as indicated by an asterisk in Scheme 1. The chemical yields and the enantiomeric excesses (ee's), as determined by chiral stationary-phase gas chromatography, are

Chart 1

Chiral Sensitizers

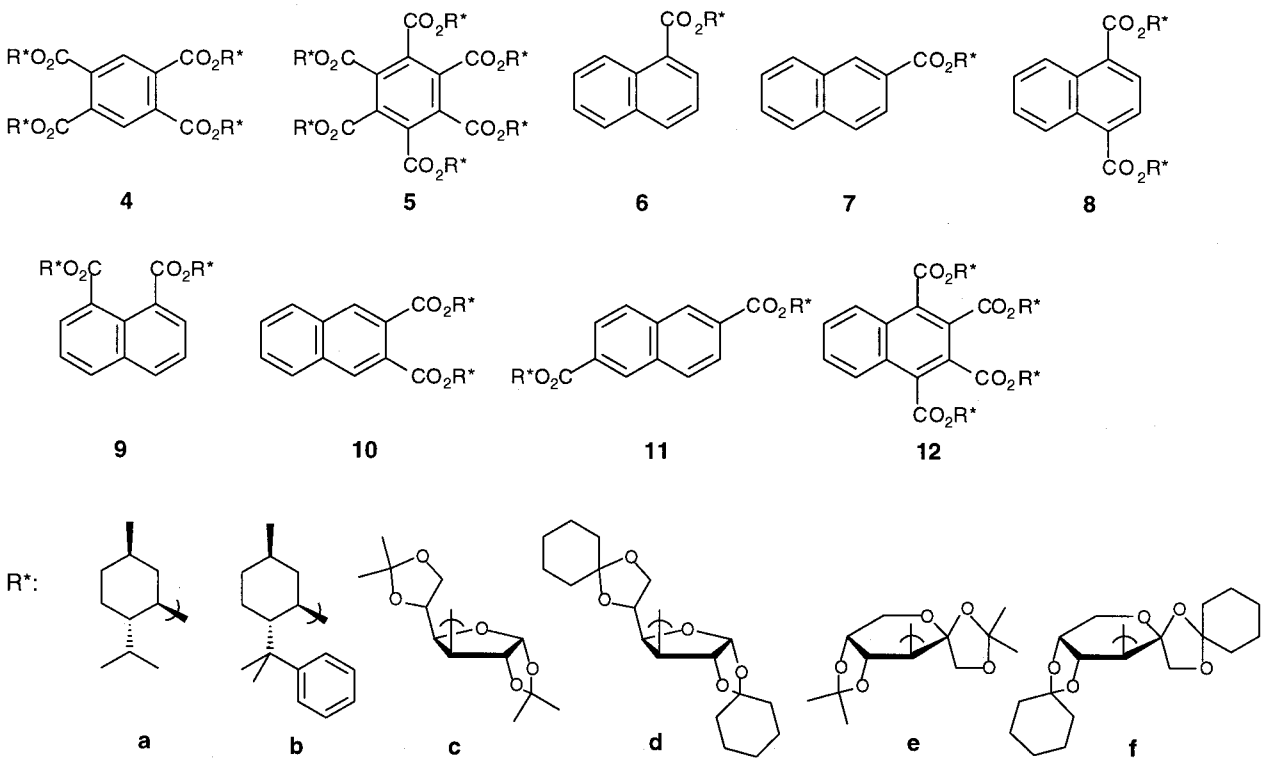


Table 1. Enantiodifferentiating photocyclodimerization of **1** sensitized by 1-cyanonaphthalene (1-CN), benzophenone (BP) and chiral arene(poly)carboxylates **4-12**[a]

entry	sensitizer	solvent	temperature /°C	irradiation time /h	conversion /%	% yield (% ee[b])							
						2a		**2b**		**3a**		**3b**	
1	1-CN	acetonitrile	25	6	61	21.3	(-0.1)	3.2	(-0.3)	2.3	(-0.3)	0.8	
2	BP	acetonitrile	25	6	>99	0		8.7	(+0.2)	30.9	(+1.0)	8.4	
3	**4a**	pentane	25	2	44	0		2.3	(+2.5)	6.0	(-0.9)	1.9	
4			-43	4	49	0		1.3	(+2.8)	3.4	(-1.5)	0.8	
5		toluene	25	2	56	0		1.7	(-0.6)	4.3	(-1.0)	1.7	
6			-41	4	22	0		1.1	(+0.3)	2.6	(-0.7)	0.6	
7	**5a**	pentane	25	2	16	0		1.6	(+0.7)	3.6	(-0.8)	1.4	
8			-41	4	17	0		2.0	(-0.1)	5.2	(-1.8)	1.1	
9		toluene	25	2	23	0		1.0	(+2.5)	2.5	(-1.1)	0.4	
10			-41	4	13	0		1.1	(+4.0)	2.6	(-1.1)	0.6	
11	**6a**	pentane	25	2	40	0		1.7	(-0.8)	4.5	(-2.0)	1.4	
12			-41	4	41	0		0.6	(-0.3)	1.7	(-1.8)	0.4	
13		toluene	25	2	21	0		1.3	(-0.1)	3.4	(-2.5)	1.1	
14			-41	4	*c*	0		1.2	(+0.7)	3.1	(-1.5)	0.8	
15	**6b**	toluene	25	2	30	0		5.1	(-0.5)	13.2	(-0.6)	4.6	
16			-41	4	24	0		2.8	(-0.2)	7.4	(-0.6)	1.5	
17	**6c**	toluene	25	2	34	0		1.7	(+0.2)	4.3	(+0.7)	1.5	
18			-41	4	35	0		1.0	(-0.2)	2.5	(+0.8)	0.6	
19	**7a**	pentane	25	2	10	0		0.2	(+1.0)	0.6	(-1.6)	0.2	
20			-34	4	49	0		0.1	(*c*)	0.3	(-0.9)	0.1	
21		toluene	25	2	11	0		<0.1	(*c*)	0.8	(+0.3)	<0.1	
22			-41	4	10	0		0.6	(+0.5)	1.5	(0.0)	<0.1	
23	**7b**	toluene	25	2	36	0		0.6	(-0.8)	1.7	(+0.6)	0.6	
24			-41	4	29	0		0.8	(-0.1)	2.2	(+0.4)	0.5	
25	**7c**	toluene	25	2	23	0		1.8	(-0.1)	4.8	(-0.2)	1.7	
26			-41	4	24	0		1.8	(0.0)	4.7	(-0.1)	1.2	
27	**8a**	pentane	25	2	92	0		17.9	(0.0)	47.5	(-1.9)	15.9	
28			-43	4	36	0		1.6	(+0.8)	4.0	(-1.4)	1.0	
29		toluene	27	2	76	0		15.6	(+0.1)	41.4	(-0.9)	14.0	
30			-41	4	59	0		3.8	(+0.9)	10.0	(+0.1)	2.4	

31		ether	25	2	16	0		2.1	(+1.4)	5.4	(-0.3)	1.8
32			-41	4	13	0		1.5	(+0.4)	3.8	(-0.2)	0.9
33		aceto-	25	2	78	26.4	(-0.1)	5.0	(+0.2)	7.8	(-1.1)	1.9
		nitrile										
34	**8b**	tolu-	25	2	65	0		4.4	(+1.4)	11.2	(-1.4)	4.2
35		ene	-41	4	48	0		3.5	(+3.0)	8.8	(-1.5)	2.2
36	**8c**	pen-	25	2	51	0		7.3	(+0.4)	18.1	(-1.3)	5.4
		tane										
37		tolu-	25	2	64	0.5	(*c*)	4.5	(-5.3)	10.8	(0.0)	4.1
38		ene	-41	4	17	0.9	(*c*)	3.2	(-2.2)	7.1	(-0.6)	2.1
39		ether	25	2	*c*	0.3	(*c*)	2.8	(-4.6)	6.3	(-0.3)	2.0
40			-41	4	*c*	0.5	(*c*)	1.3	(-6.4)	2.7	(-0.4)	0.6
41	**8d**	tolu-	25	2	21	0.4	(*c*)	5.3	(-2.8)	11.9	(-0.8)	4.8
42		ene	-41	4	38	1.1	(+0.8)	3.0	(-2.0)	6.7	(-0.4)	2.0
43		ether	25	2	*c*	0.3	(*c*)	3.1	(-2.9)	7.7	(0.0)	2.4
44			-41	4	*c*	0.6	(*c*)	2.5	(-3.6)	5.9	(-0.2)	1.3
45	**8e**	tolu-	25	2	52	0.5	(*c*)	3.8	(-7.6)	8.1	(-0.3)	3.1
46		ene	-41	4	49	0.6	(*c*)	1.4	(-0.2)	3.2	(-0.4)	0.5
47		ether	25	2	*c*	0.4	(*c*)	2.3	(-4.1)	4.7	(+0.3)	1.4
48			-41	4	*c*	0.5	(*c*)	1.1	(-2.5)	2.3	(-0.7)	0.6
49	**8f**	tolu-	25	2	31	0.6	(*c*)	5.0	(-5.1)	10.8	(-0.3)	4.2
50		ene	25[d]	2	42	1.3	(*c*)	8.8	(-2.8)	15.5	(-0.7)	5.8
51			25[e]	2	78	4.8	(*c*)	17.9	(+0.2)	25.1	(-0.7)	6.6
52			25[f]	2	96	10.5	(*c*)	22.5	(+0.4)	26.2	(-0.3)	3.7
53			-41	4	24	0.8	(*c*)	4.1	(-2.4)	9.7	(-0.8)	1.2
54		ether	25	2	*c*	0.3	(*c*)	2.0	(-6.7)	4.6	(+0.3)	1.3
55			-41	4	*c*	0.3	(*c*)	0.8	(-8.2)	1.8	(-1.3)	0.4
56		aceto-	25	2	54	21.1	(0.0)	1.9	(+0.4)	1.4	(+0.7)	0.4
57		nitrile	-41	4	36	20.0	(-0.1)	2.5	(+0.1)	4.1	(-0.1)	1.1
58	**9a**	pen-	27	2	71	0		7.6	(-0.2)	19.9	(-1.2)	6.1
59		tane	-43	4	54	0		7.1	(+0.1)	18.1	(-0.1)	4.3
60		tolu-	27	2	95	0		21.4	(+0.4)	56.8	(-1.4)	20.4
61		ene	-41	4	>99	0		19.6	(-0.4)	53.6	(-0.3)	13.0
62	**9b**	tolu-	25	2	>99	0		9.7	(+0.7)	26.2	(+1.0)	9.7
63		ene	-41	4	95	0		11.3	(+0.4)	30.8	(+0.2)	7.5
64	**9c**	tolu-	25	2	>99	0		8.8	(+1.3)	22.3	(-1.3)	7.1
65		ene	-41	4	>99	0		8.2	(+0.2)	21.2	(-0.3)	5.1
66	**10a**	pen-	25	2	*c*	0		0.6	(+1.9)	1.4	(-1.0)	0.4

67		tane	-39	3	21	0	0.3	(+1.2)	0.8	(-0.7)	0.2
68		tolu-	25	2	23	0	2.0	(+1.6)	5.0	(+1.1)	1.8
69		ene	-41	3	52	0	1.3	(+0.1)	3.3	(-1.0)	0.9
70	**10b**	tolu-	25	2	23	0	2.5	(+0.8)	6.6	(-0.3)	2.5
71		ene	-41	4	36	0	1.5	(+0.9)	3.8	(-0.5)	1.0
72	**10c**	tolu-	25	2	*c*	0	2.1	(-0.2)	5.4	(+0.6)	2.0
73		ene	-41	4	39	0	1.9	(+0.3)	5.0	(-1.4)	1.2
74	**11a**	pen-	25	2	12	0	0.4	(-2.3)	1.0	(-1.3)	0.3
75		tane	-41	4	18	0	0.2	(*c*)	0.5	(-1.2)	0.1
76		tolu-	28	2	16	0	2.8	(+0.9)	7.0	(+0.8)	2.6
77		ene	-41	4	52	0	1.5	(-0.2)	3.5	(-0.3)	1.0
78	**11b**	tolu-	25	2	30	0	1.3	(-0.1)	3.2	(-0.2)	1.0
79		ene	-41	4	62	0	1.0	(-1.4)	2.8	(+0.7)	0.7
80	**11c**	tolu-	25	2	26	0	2.4	(+0.2)	6.3	(0.0)	2.3
81		ene	-41	4	61	0	2.3	(-1.5)	6.0	(+0.7)	1.7
82	**12a**	tolu-	25	2	53	0	1.7	(+0.4)	4.3	(-0.8)	1.6
83		ene	-41	4	55	0	1.6	(+0.2)	4.2	(-1.0)	1.1

[a] [**1**] = 100 mmol dm^{-3}; [Sens*] = 5 mM unless noted otherwise. [b] Enantiomeric excess determined by chiral GC. [c] Not determined. [d] [**1**] = 50 mmol dm^{-3}. [e] [**1**] = 20 mmol dm^{-3}. [f] [**1**] = 10 mmol dm^{-3}.

summarized in Table 1. Since the enantiomers of the cyclodimers could not be isolated in a preparative scale, the sign of the reported ee value is just a tentative one representing the order of elution from the Supelco β-Dex 120 and 325 columns, and therefore may not coincide with the direction of the optical rotation of the product. Thus, a positive value means the predominant formation of the first-eluted enantiomer.

The photocyclodimerization sensitized by chiral arene(poly)carboxylates possessing (–)-menthyl and (–)-8-phenylmenthyl auxiliaries were performed in pentane and toluene at 25 and -41 °C. Polymenthyl benzenepolycarboxylates which were used as singlet energy-transfer sensitizers for photoisomerization of cycloalkenes[5] were examined first. As can be seen from Table 1, the singlet sensitization with benzenetetracarboxylate **4a** (runs 3-6) and benzenehexacarboxylate **5a** (runs 7-10) gave cyclodimers **2b**, **3a** and **3b** in low chemical yields but never produced the *endo*-dimer **2a**. Irrespective of the solvent and sensitizer used, effectively the same product ratio was obtained at 25 °C, *i.e.* **2b** : **3a** : **3b** = 1.2 : 3.0 : 1.0,

which is slightly different from that observed for triplet sensitization with BP, *i.e.* **2b** : **3a** : **3b** = 0.8 : 3.0 : 0.8. However, the product distribution was affected by the irradiation temperature, with the ratio of **3b** decreasing at lower temperatures, while the **2b** : **3a** ratio stayed constant. The ee of **2b** was generally low (<2.5%) at 25 °C but was appreciably enhanced to 4.0% in toluene at -41 °C, upon sensitization with **5a**. Conversely, low ee's (<2%) were obtained for **3a** at 25 °C and were not improved even at -41 °C.

The author further examined chiral naphthalene(poly)carboxylates, which are often used in photoinduced electron-transfer reactions.[15] Photosensitized cyclodimerization of **1** using naphthalenecarboxylates **6a** and **7a** (runs 11-14 and 19-22, respectively) gave **2b**, **3a** and **3b** in low chemical yields (**2b** and **3b** in <2%, **3a** in <5%), these yields were slightly enhanced in toluene, however no **2a** was formed in either pentane or toluene. The product ratios **2b** : **3a** : **3b** were 1.2 : 3.0 : 1.0 and 1.2 : 3.0 : 0.7 at 25 and -41 °C respectively, which are exactly the same as those obtained in the benzenepolycarboxylate sensitizations described above. This agreement suggests that the photocyclodimerizations of **1** sensitized by benzenecarboxylates **4a** and **5a**, and by naphthalenecarboxylates **6a** and **7a** proceed through a common intermediate such as a singlet biradical. Unfortunately, the photosensitizations with the naphthalenemonocarboxylates **6a-c** and **7a-c** gave practically racemic **2b** and **3a** in both pentane and toluene even at the low temperature.

Chemical yields were greatly improved upon sensitization with 1,4- and 1,8-naphthalenedicarboxylates **8a** and **9a** (runs 27-30 and 58-61), up to 14-20% for **2b** and **3b** and 41-57% for **3a**. But sensitization with 2,3- and 2,6-naphthalenedicarboxylates **10a** and **11a** (runs 66-69 and 74-77, respectively) was ineffective in enhancing the chemical yields, resulting in low ee's (< 2.5%) in all cases. In general, the use of toluene as solvent slightly enhanced the chemical yields but did not improve the products' ee. Judging from the facts that the product ratios obtained upon sensitization with **8a-11a** agree with those obtained with the benzenepolycarboxylates **4a** and **5a**, and that the *endo*-adduct **2a** was not formed under these conditions, the author deduces that the photosensitization with the naphthalenedicarboxylates in non-polar solvents proceeds through the singlet energy-transfer mechanism involving a singlet biradical or other common intermediate, as is the case with the benzenepolycarboxylates. The

ee's were not enhanced by using the (–)-8-phenylmenthyl naphthalenedicarboxylates **8b-11b** (runs 34-35, 62-63, 70-71 and 78-79, respectively). Neither chemical yield nor ee's were improved upon by using the highly substituted tetramenthyl naphthalenetetracarboxylate **12a** in toluene (runs 82-83). Based on these results the author may conclude that the product ratio is independent of the energy and structure of sensitizers in non-polar solvents, and also that the simple singlet energy-transfer sensitization is ineffective in inducing chirality in the cyclodimers.

In order to elucidate the origin of the sensitizer-dependent chemical yields, the author calculated the Rehm-Weller free energy change (ΔG_{et})[28] from the oxidation potential of **1** (E_{ox} = 1.15 V)[20c], the reduction potentials (E_{red}) and fluorescence 0-0 bands ($\lambda_{0\text{-}0}$) of sensitizers **4a-12a**. The relevant data are listed in Table 2. The observed differences in photoreactivity are well accounted for in terms of the calculated ΔG_{et} values. Apart from the highly hindered 1,2,3,4-naphthalenetetracarboxylate **12a**,[29] the 1,4- and 1,8-naphthalenedicarboxylates **8a** and **9a** gave

Table 2. Reduction potentials and calculated free energy change (ΔG_{et}) for electron transfer interaction of 1,3-cyclohexadiene **1** with chiral arene(poly)carboxylates **4-12a**

sensitizer	E_{red} [a] / V	$\lambda_{0\text{-}0}$ [b] / nm	ΔG_{et} [c] / kJ mol^{-1}
4a	*d*	315	–
5a	*d*	309	–
6a	-2.30	334	-5.2
7a	-2.39	339	8.8
8a	-1.84	371	-13.9
9a	-2.22	334	-12.9
10a	-2.30	341	2.2
11a	-2.02	357	-9.1
12a	-1.89	345	-33.7

[a] Reduction potentials estimated from the half-wave potentials measured using a platinum electrode, relative to the Ag/AgCl electrode using 0.1 mol^{-1} dm^3 tetrabutylammonium perchlorate as the electrolyte in acetonitrile. [b] Fluorescence maxima of highest energy emission in frozen EPA (diethyl ether:isopentane:ethanol = 5:5:2) glass at 77 K. [c] Based on Weller equation: ΔG_{et} = 23.06 ($E_{ox}(D^+/D) - E_{red}(A/A^-)$) – $\Delta G_{0\text{-}0} - w_p$; oxidation potential of **1** (E_{ox}) estimated as 0.028V before the peak potential (E_p = 1.33 V[14a]); Coulombic attraction term (w_p) taken to be -5.4 kJ mol^{-1}. [d] Not determined due to low solubility of **4a** and **5a** in acetonitrile.

the most negative ΔG_{et} values among the sensitizers examined, which is the primary reason for the high chemical yields obtained upon sensitization with **8** and **9**. As the singlet energies of naphthalene(poly)carboxylates **6a-12a** are significantly lower than those of benzenepolycarboxylates **4a** and **5a**, the simple singlet energy transfer mechanism cannot rationalize the photoreactivity, consequently the author may conclude that the photocyclodimerization of **1** sensitized by naphthalene(poly)carboxylates (at least with **8** and **9**) proceeds through the electron transfer mechanism which involves an exciplex with high charge-transfer character or a contact ion pair even in the nonpolar solvents.

Effect of Saccharide Auxiliary. In my recent study,[15b] the author demonstrated that the use of protected saccharides as chiral auxiliaries of the photosensitizer can enhance both the chemical and optical yields in the enantiodifferentiating photoaddition of alcohols to 1,1-diphenylalkene, through the increased 'microenvironmental polarity' around the sensitizer chromophore. In this context it is interesting to examined the effects of saccharide derivatives (**c-f**). The photocyclodimerizations of **1** sensitized by naphthalene(di)carboxylates **6c-11c**, which possess diacetone glucose (DAG) auxiliaries were first examined in pentane and in toluene (runs 17-18, 25-26, 36-38, 64-65, 72-73 and 80-81 respectively). Unexpectedly, the DAG ester chiral sensitizers **6c**, **7c**, **9c**, **10c** and **11c** did not particularly improve the chemical or optical yields, and the product ratios obtained were very similar to those for the menthyl esters **6a-11a**. However, the photosensitization with 1,4-naphthalenedicarboxylates with saccharide auxiliaries **8c-8f** (runs 36-57) showed distinctly different behavior in toluene. The *endo*-adduct **2a** which is derived from the radical cation intermediate usually generated in polar solvent under the electron transfer conditions was obtained in low but appreciable yield, along with the slightly enhanced formation of **2b** (the average product ratio of **2b** : **3a** : **3b** is 1.3 : 3.0 : 1.1 and 1.3 : 3.0 : 0.7 at 25 and -41 °C, respectively). The ee of **2b** was increased to 7.6% upon sensitization with **8e** in toluene at 25 °C (run 45), whereas the **3a** obtained was practically racemic in any solvent and at any temperature examined. Unfortunately in most cases the ee of **2a** could not be determined by chiral GC as a result of low chemical yields, though **2a** obtained from toluene at -41 °C (run 42) was racemic .

In order to investigate the influence of solvent polarity, photosensitization by **8c-f** was

performed in diethyl ether (runs 39-40, 43-44, 47-48, 54-55) and in acetonitrile (runs 56-57). In diethyl ether, the yield of **2a** relative to **3a** was slightly enhanced for all saccharide sensitizers and the highest ee (8.2%) was obtained for **2b** upon sensitization with **8f** in ether at -41 °C (run 55), although the ee of **3a** was not improved in polar solvents. In contrast, the photosensitization with menthyl ester **8a** in ether gave no *endo*-adduct **2a**, and the resulting product ratio is comparable to that obtained in non-polar solvent (runs 31 and 32). Hence, the formation of **2a** and the altered product ratios obtained upon sensitizations with saccharide esters are attributable to the enhanced microenvironmental polarity around the sensitizer chromophore. Under such conditions, the charge-transfer interaction is encouraged by the enhanced microenvironmental polarity, and the dissociation of the resulting radical ion pair is discouraged by the low bulk polarity. The combined effects keep the stereochemical interaction between chiral sensitizer and the substrate more intimate, resulting in increased ee's. Judging from the fact that the highest ee was obtained in ether, the enhancement of the microenvironmental polarity is not canceled by ethers lower bulk polarity. In acetonitrile the effect of the saccharide auxiliaries seems to disappear completely, as the photosensitization with both the methyl ester **8a** and the saccharide ester **8f** gave the electron-transfer product **2a** as the main product, and all of the chiral products obtained were racemic.

Effect of Substrate Concentration. The product ratio of the electron-transfer dimerization of **1** is known to be sensitive to the reaction conditions, *e.g.* solvent,[19,20c,f,30] concentration of **1**,[20c,e,f,24] wavelength[20c,22] and sensitizer.[20c] Upon sensitization with 1,4-dicyanonaphthalene or chloranil in acetonitrile the product ratio depends critically on the concentration of the substrate **1**, with the *endo*-isomer **2a** more favored at lower concentrations. This has been accounted for in terms of the involvement of differently solvated radical ion pairs. At high concentration of **1**, the polarized exciplex or contact ion pair (CIP), which is formed after (partial) electron transfer from **1** to excited sensitizer, is efficiently quenched by a second molecule of **1** to afford *exo*-adduct **2b**. At low concentration of **1**, the CIP dissociates to solvent-separated ion pairs (SSIP), which in turn gives *endo*-adduct **2a**.[20c,e] In the present study, the author observed considerable concentration effects on the product distribution upon photosensitization with **8f** in diethyl ether (runs 49-52). Thus, on decreasing the concentration

of **1** from 100 to 10 mmol dm^{-3}, the *endo/exo* ratio (**2a/2b**) increased from 0.12 to 0.47. Since these results coincide exactly with the reported observations,[20c,e,24] it can be concluded that the electron-transfer mechanism operates in this reaction, and that the mechanism involves differently solvated radical-ion pairs. On the other hand, the ee of **2b** was reduced with decreasing concentration of **1**, and eventually no enantiodifferentiation was observed at concentrations less than 20 mmol dm^{-3} (runs 51 and 52), where the *endo*-isomer **2a** is favored. It has been shown that a contact ion pair or exciplex with high charge-transfer character shows different selectivities in the photoinduced electron-transfer dimerization of **1**,[19,20b,c,d] compared to a solvent-separated ion pair or free radical cation. The *endo*-dimer **2a** is formed from the solvent-separated ion pair or free radical cation. Since the insufficiently cationic **1** in the contact ion pair or exciplex is not efficiently trapped by ground-state **1** at low concentrations, it thus tends to form a solvent-separated ion pair for which effective enantiodifferentiation is not expected to occur.

Quenching of Sensitizer Fluorescence. In order to elucidate the excited state and mechanism involved in the photosensitized cyclodimerization, fluorescence quenching experiments were performed with the menthyl esters **6a-12a** in aerated pentane and acetonitrile. The fluorescence of sensitizers was efficiently quenched upon the addition of **1** up to 100 mmol dm^{-3}. Representative quenching behavior of **8a** in pentane is shown in Fig. 1. Even at high concentrations of **1** no emission attributable to exciplex or triplex intermediates was observed for any sensitizer.

Using the conventional Stern-Volmer treatment of the quenching data (eqn. 1), the relative fluorescence intensity (I_F/I_F^0) was plotted as a function of the concentration of **1** added, and an excellent straight line was obtained for each sensitizer, as exemplified in Fig. 2. From the Stern-Volmer constant ($k_Q\tau^0$) obtained from the slope of the plot and the fluorescence lifetime (τ^0) determined independently by using the single photon counting technique, the quenching rate constant (k_Q) for each sensitizer was calculated. The results are summarized in Table 3.

$$I_F^0/I_F = 1 + k_Q\tau^0\,[Q] \qquad (1)$$

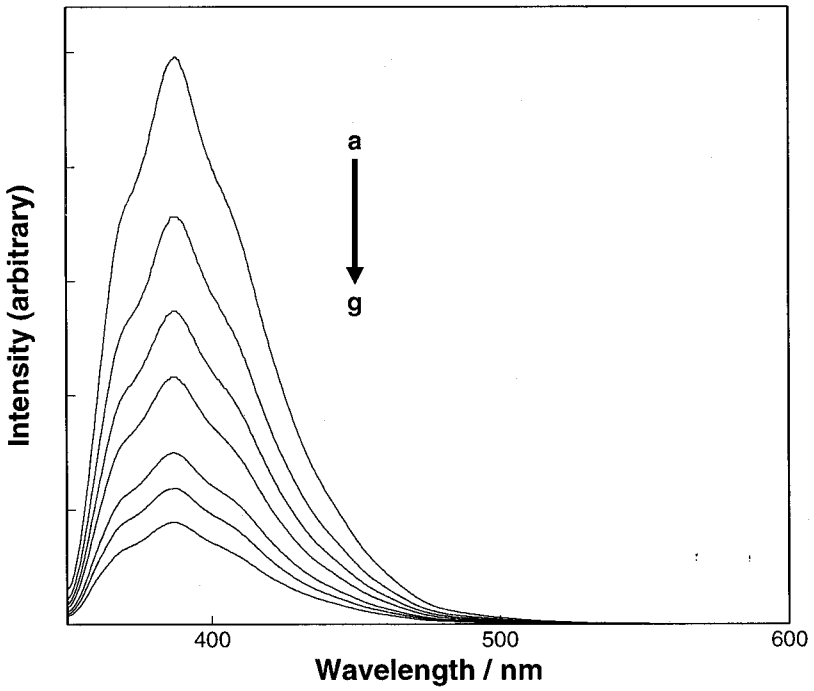


Fig. 1. Quenching of fluorescence of **8a** (1 mmol dm^{-3} in pentane), excited at 340 nm, by **1** at various concentrations: (a) 0, (b) 5, (c) 10, (d) 16, (e) 26, (f) 37, and (g) 52 mmol dm^{-3}.

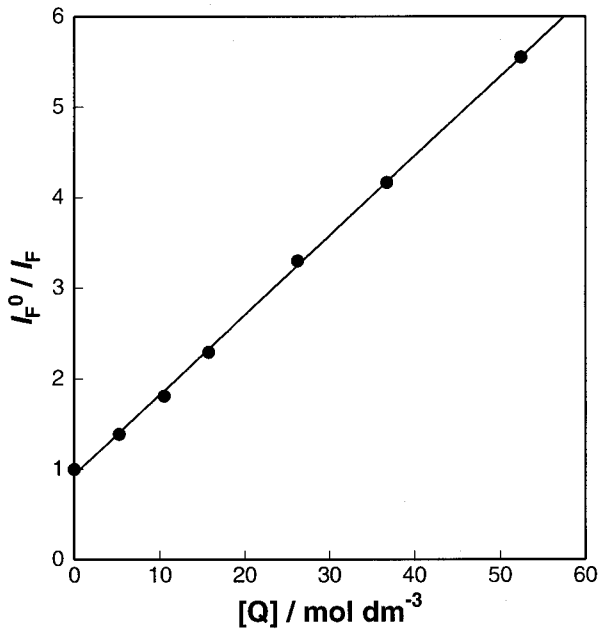


Fig. 2. Stern-Volmer plot for fluorescence quenching of **8a** by **1** in pentane.

Table 3. Fluorescence quenching of chiral sensitizers by 1,3-cyclohexadiene **1**[a]

sensitizer	solvent	$k_Q\tau$ /mol^{-1} dm^3	τ^b /ns	k_Q /10^{10} mol^{-1} dm^3 s^{-1}
6a	pentane	21	0.78	2.7
7a	pentane	87	8.0	1.1
8a	pentane	88	3.6	2.4
	acetonitrile	92	8.2	1.1
9a	pentane	21	1.5	1.4
10a	pentane	78	6.6	1.2
11a	pentane	121	9.9	1.2
12a	pentane	30	2.9	1.1

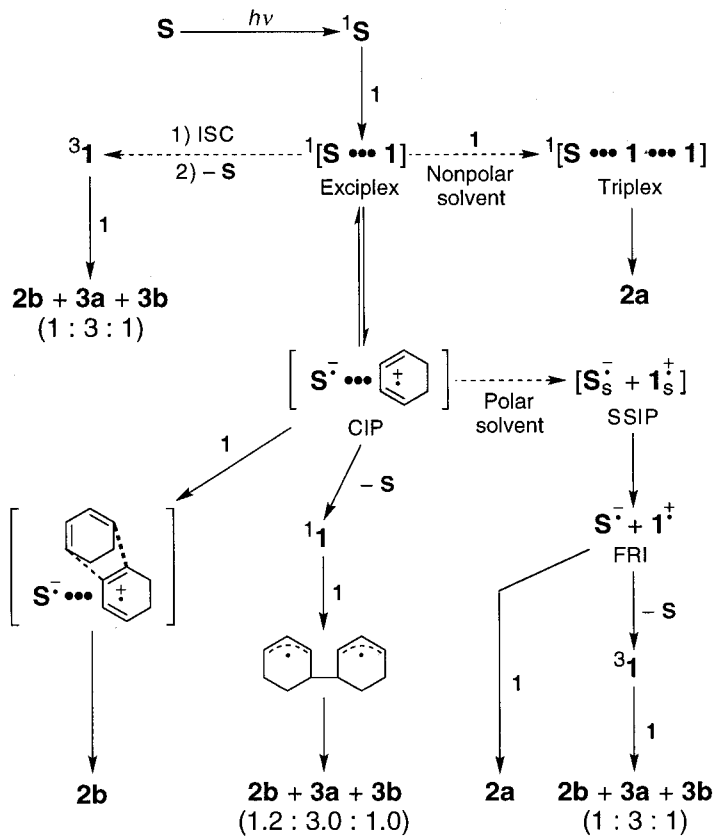
[a] Measured with 0.01 mmol dm^{-3} aerated solution of sensitizers at 25 °C. [b] Fluorescence lifetime of sensitizers in aerated solution at 25 °C.

The quenching of sensitizer singlet by **1** proceeds very efficiently at rates of 1.1-2.7 x 10^{10} mol^{-1} dm^3 s^{-1}, which are almost comparable to the diffusion controlled rate in pentane (k_{diff} = 4.4 x 10^{10} mol^{-1} dm^3 s^{-1})[31] and acetonitrile (k_{diff} = 2.9 x 10^{10} mol^{-1} dm^3 s^{-1}).[31] Although no exciplex emission was observed, it is inferred that the quenching leads to an exciplex intermediate with high charge-transfer character, or directly to a contact radical ion pair in nonpolar solution. If the ΔG_{et} value is not sufficiently negative to develop a positive charge on **1**, the subsequent attack of the second **1** (forming a dimer biradical) should be decelerated, which should account for the low chemical yields obtained upon sensitization with **6a**, **7a**, **10a** and **11a**. Contrary to this, the much higher chemical yields obtained upon sensitization with **8a** and **9a** are attributable to the highly negative ΔG_{et} values for **8a** and **9a** and the accompanying development of positive charge on **1**, which accelerates the subsequent attack of **1**.

Mechanism. On the basis of the mechanism reported previously,[14b,19,20] the author proposes a modified mechanism illustrated in Scheme 2, which is compatible with the previous and present results. In view of the relatively low concentrations of **1** (10-100 mmol dm^{-3}) employed in this study, The author may exclude the serious contribution of the triplex intermediate,[14a-d,30] intervention of which has been proposed at much higher concentrations of 0.2-2 mol dm^{-3} in non-polar or less polar solvents.[14a-d]

Although the enantiodifferentiating photocyclodimerization of **1** sensitized by various

Scheme 2



(ISC: intersystem crossing; CIP: contact ion pair; SSIP: solvent separated ion pair; FRI: free radical ions)

chiral sensitizers can potentially give four isomeric cyclodimers **2a**, **2b**, **3a** and **3b** as described above, significant ee's were obtained exclusively for the *exo*-[4+2]-cyclodimer **2b** upon sensitization with saccharide esters **8c-8f** in pentane or ether. This means that in addition to the biradical and radical ionic routes illustrated in Scheme 2, there is an independent cyclodimerization pathway that involves either the exciplex or contact ion pair of **1** with chiral sensitizer and affords preferentially **2b**. In the case of saccharide esters **8c-8f**, the highly negative ΔG_{et} values and the enhanced microenvironmental polarity around the chromophore may stabilize such an exciplex or contact ion pair intermediate in nonpolar solvents, allowing the transfer of chiral information from the sensitizer to the cyclodimer. Because the product ratios obtained in nonpolar solvents do not greatly deviate from the average value (**2b** : **3a** : **3b** = 1.15 : 3.00 : 1.02 and 1.17 : 3.00 : 0.74 at 25 and -41 °C, respectively) for most of the naphthalene(di)carboxylate sensitizers, except for the saccharide esters **8c-8f**. Then, the author

may estimate the 'net' ee of **2b** produced through this 'independent' exciplex route by assuming that **2b**, **3a** and **3b** formed through the singlet biradical intermediate are racemic (or inherently achiral), and their ratio is fixed at 1.15 : 3.00 : 1.02, irrespective of the sensitizer and solvent used. Also that **2b** is produced exclusively through either the exciplex or singlet biradical mechanism, as demonstrated in the literature.[20,32] In the case of the photosensitization by **8e** in toluene at 25 °C, 19% of **2b** is estimated to be formed via the exciplex, with a 'net' ee of 40%. In the case of the photosensitization by **8f** in ether at 25 and -41 °C, 10 and 12% of **2b** is similarly estimated to be formed via the exciplex, and the 'net' ee's are 65% and 70%, respectively.

Finally, the author would like to emphasize that although the overall ee's are not very high (<8%) in the present case as a result of the contamination from the racemic product of other route, the introduction of polar saccharide moieties into the sensitizer can raise the ee of the product through the enhancement of the microenvironmental polarity around the sensitizer chromophore.

Experimental Section

General. Melting points were measured with a YANACO MP-300 apparatus and are uncorrected. ^{1}H NMR spectra were obtained on a JEOL GX-400 or GSX-270 spectrometer in [$^2H_2$]-chloroform ($CDCl_3$). Infrared spectra were obtained on a JASCO FT/IR-230 instrument. Electronic absorption and fluorescence spectra were recorded on JASCO V-550 and FP-777 instrument, respectively. Optical rotations were determined at 589 nm in a thermostated conventional 10 cm cell, using a JASCO DIP-1000 polarimeter.

Fluorescence lifetimes were measured with 1 x 10^{-5} mol dm^{-1} solution of sensitizers in aerated pentane or toluene by means of the time-correlated single-photon-counting method on a Horiba NAES-1100 instrument equipped with a pulsed H_2 light source. The radiation from the lamp was made monochromatic by a 10-cm monochromator, and the emission from sample solution was detected through a Toshiba UV-33, 35 or 37 filter.

Enantiomeric excesses of **2a**, **2b** and **3a** were determined by gas chromatography over a 30 m chiral capillary column (SUPELCO β-Dex325 and/or 120) at 100 °C, using a Shimadzu

GC-14B instrument connected to a Shimadzu C-R6A integrator. Calibrations with racemic **2a**, **2b** and **3a** indicated that the GC analysis gave a systematic error of ±0.8% ee.

Materials. Pentane used as solvent was stirred over concentrated sulfuric acid until the acid layer no longer turned yellow, washed with water, neutralized with aqueous sodium hydrogen carbonate, dried over sodium sulfate, and then distilled fractionally. Toluene was fractionally distilled from melting sodium. Diethyl ether was refluxed with potassium hydroxide and then fractionally distilled from sodium. Spectrograde acetonitrile (Dojin) was used without further purification. 1,3-Cyclohexadiene **1** (Aldrich) was purified by fractional distillation, followed by column chromatography on activated aluminum oxide (ICN Biomedicals).

Optically active alcohols used in the preparation the sensitizers were commercially available: (–)-menthol from TCI; (–)-8-phenylmenthol from Aldrich.

Sugar derivatives were prepared from D-glucose and D-fructose according to the procedures reported by Kartha *et al.*[33] and Kang *et al.*,[34] respectively.[15b] 1,2:5,6-Di-*O*-cyclohexylidene-α-D-glucofuranose and 1,2:4,5-Di-*O*-cyclohexylidene-β-D-fructopyranose were prepared in a similar manner. 1,2:5,6-Di-*O*-cyclohexylidene-α-D-glucofuranose: $[\alpha]_D^{31}$ +3.51° (*c* 2.15, $CHCl_3$) (lit.[35] $[\alpha]_D^{31}$ +1.65° (*c* 2.10, $CHCl_3$)); mp 139-140°C; $\delta_H(CDCl_3)$ 1.24-1.87 (m, 20H), 2.60 (d, *J* = 2.9 Hz, 1H), 3.96 (dd, *J* = 2.9, 5.9 Hz, 1H), 4.06 (dd, *J* = 2.4, 4.9 Hz, 1H), 4.14-4.18 (m, 1H), 4.33-4.34 (m, 1H), 4.52 (d, *J* = 3.4 Hz, 1H), 5.95 (d, *J* = 3.4 Hz, 1H). 1,2:4,5-Di-*O*-cyclohexylidene-β-D-fructopyranose: $[\alpha]_D^{25}$ -108.3° (*c* 0.52, $CHCl_3$); mp 130-131°C; $\delta_H(CDCl_3)$ 1.59-1.79 (m, 20H), 3.64 (dd, *J* = 6.8, 8.3 Hz, 1H), 3.96 (d, *J* = 8.8 Hz, 1H), 4.01-4.05 (m, 2H), 4.10 (t, *J* = 2.4 Hz, 2H), 4.12-4.22 (m, 2H).

1-Cyanonaphthalene (TCI) and Benzophenone (Wako) used as achiral sensitizers were purified by recrystallization from methanol. Optically active benzenepolycarboxylates employed as chiral sensitizers were prepared as reported previously.[36] Chiral naphthalene(di)carboxylates were prepared from the corresponding alcohols and acid chlorides, which were prepared from the corresponding carboxylic acids or anhydrides.[15b] While most of carboxylic acids and anhydrides were commercially available: 1-, 2- and 1,4-naphthalene(di)carboxylic acid from Wako, 1,8- and 2,3-naphthalenedicarboxilic anhydride from TCI, 2,6-naphthalenedicarboxilic acid dipotassium salt from Aldrich, 1,2,3,4-naphthlenetetracarboxylic acid was obtained by the

hydrolysis of tetramethyl ester, which was prepared according to the procedures reported by Cadogan *et al.*[37]

(–)-1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl 1-naphthalene-carboxylate (6c). (Found: C, 66.41; H, 6.33. Calc. for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32%); $[\alpha]_D^{26}$ -36.1° (*c* 1.03, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2989, 1724, 1512, 1377, 1242, 1134, 1076, 849, 783, 509; λ_{max}(methylcyclohexane)/nm 211.6 (ε/dm^3 mol^{-1} cm^{-1} 37500), 218.4 (38700), 298.2 (7100); δ_H($CDCl_3$) 1.31 (s, 3H), 1.35 (s, 3H), 1.45 (s, 3H), 1.58 (s, 3H), 4.12 (m, 2H), 4.38 (m, 2H), 4.74 (d, *J* = 3.9 Hz, 1H), 5.59 (d, *J* = 2.9 Hz, 1H), 5.97 (d, *J* = 3.9 Hz, 2H), 7.48-7.66 (m, 3H), 7.90 (d, *J* = 7.8 Hz, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 8.16 (dd, *J* = 1.5, 7.3 Hz, 1H), 8.93 (d, *J* = 8.3 Hz, 1H); *m/z* 414 (M^+, 7%), 399 (43), 272 (11), 255 (11), 172 (42), 155 (100), 127 (26), 101 (43).

(–)-1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl 2-naphthalene-carboxylate (7c). m.p. 106.0-107.0°C (Found: C, 66.14; H, 6.05. Calc. for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32%); $[\alpha]_D^{26}$ -54.8° (*c* 1.02, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2989, 1724, 1631, 1462, 1377, 1269, 1200, 1095, 953, 872, 837, 764, 517; λ_{max}(methylcyclohexane)/nm 238.8 (ε/dm^3 mol^{-1} cm^{-1} 69700), 272.0 (7360), 280.6 (9110), 291.0 (6500), 320.0 (1480), 326.2 (1280), 334.8 (1980); δ_H($CDCl_3$) 1.27 (s, 3H), 1.34 (s, 3H), 1.43 (s, 3H), 1.58 (s, 3H), 4.14 (m, 2H), 4.41 (m, 2H), 4.69 (d, *J* = 3.4 Hz, 1H), 5.58 (d, *J* = 2.9 Hz, 1H), 6.01 (d, *J* = 3.4 Hz, 1H), 7.59 (m, 2H), 7.88-8.05 (m, 4H), 8.58 (s, 1H); *m/z* 414 (M^+, 1%), 399 (14), 326 (32), 172 (14), 155 (100), 127 (40), 101 (18).

(–)-Bis(1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranosyl) 1,4-naphthal-enedicarboxylate (8d). m.p. 152.0-153.0°C (Found: C, 66.93; H, 6.97. Calc. for $C_{48}H_{60}O_{14}$: C, 66.96; H, 7.02%); $[\alpha]_D^{27}$ -23.7° (*c* 1.01, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2938, 1725, 1514, 1453, 1368, 1248, 1166, 1119, 1027, 927, 848, 779; λ_{max}(methylcyclohexane)/nm 212.2 (ε/dm^3 mol^{-1} cm^{-1} 40100), 243.4 (27400), 318.0 (7800); δ_H($CDCl_3$) 1.35-1.77 (m, 40H), 4.09 (m, 4H), 4.34 (m, 4H), 4.73 (d, *J* = 3.9 Hz, 2H), 5.67 (m, 2H), 5.97 (d, *J* = 3.4 Hz, 2H), 7.67 (dd, *J* = 3.4, 6.8 Hz, 2H), 8.06 (s, 2H), 8.83 (dd, *J* = 3.4, 6.3 Hz, 2H); *m/z* 860 (M^+, 74%), 831 (11), 817 (66), 762 (14), 538 (16), 521 (100), 495 (22), 423 (9), 239 (17), 199 (86), 181 (10), 154 (13), 141 (41).

(–)-Bis(1,2:4,5-di-*O*-cyclohexylidene-β-D-fructopyranosyl) 1,4-naphthalenedicarboxylate (8f). m.p. 187.0-188.0°C (Found: C, 67.70; H, 7.30. Calc. for $C_{48}H_{60}O_{14}$: C, 66.96; H, 7.02%); $[\alpha]_D^{27}$ -180.5° (*c* 1.00, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2935, 1724, 1514, 1454, 1244, 1105, 933, 779; λ_{max}(methylcyclohexane)/nm 212.0 (ε/dm^3 mol^{-1} cm^{-1} 36400), 243.8 (25500), 320.2 (7430); δ_H($CDCl_3$) 1.39-1.89 (m, 40H), 4.04 (m, 4H), 4.20 (m, 4H), 4.31 (m, 2H), 4.50 (dd, *J* = 4.9, 8.3 Hz, 2H), 5.50 (d, *J* = 8.3 Hz, 2H), 7.66 (dd, *J* = 3.4, 6.8 Hz, 2H), 8.18 (s, 2H), 8.87 (dd, *J* = 3.4, 6.8 Hz, 2H); *m/z* 860 (M^+, 27%), 817 (6), 538 (18), 521 (96), 424 (9), 239 (8), 216 (10), 199 (100), 154 (12), 110 (9).

(+)-Bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl) 1,8-naphthalenedicarboxylate (9c). m.p. 169.0-170.0°C (Found: C, 61.49; H, 6.15. Calc. for $C_{36}H_{44}O_{14}$: C, 61.71; H, 6.33%); $[\alpha]_D^{26}$ +55.3° (*c* 1.01, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2989, 1724, 1381, 1269, 1207, 1157, 1076, 1018, 845, 779, 640, 513; λ_{max}(methylcyclohexane)/nm 225.2 (ε/dm^3 mol^{-1} cm^{-1} 35900), 294.0 (7940); δ_H($CDCl_3$) 1.41 (s, 6H), 1.42 (s, 6H), 1.44 (s, 6H), 1.55 (s, 6H), 4.09 (m, 2H), 4.23-4.37 (m, 4H), 4.54 (m, 2H), 5.07 (d, *J* = 3.4 Hz, 2H), 5.45 (d, *J* = 2.9 Hz, 2H), 6.03 (d, *J* = 3.9 Hz, 2H), 7.56 (m, 2H), 8.02 (m, 4H); *m/z* 700 (M^+, < 1%), 685 (100), 443 (15), 441 (16), 401 (17), 243 (20), 213 (12), 199 (47), 185 (64), 155 (28), 127 (56), 113 (49), 101 (97).

(–)-Bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl) 2,3-naphthalenedicarboxylate (10c). m.p. 178.5-179.5°C (Found: C, 61.80; H, 5.87. Calc. for $C_{36}H_{44}O_{14}$: C, 61.71; H, 6.33%); $[\alpha]_D^{26}$ -61.9° (*c* 1.04, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2989, 1736, 1462, 1377, 1257, 1211, 1072, 852, 783, 513; λ_{max}(methylcyclohexane)/nm 239.4 (ε/dm^3 mol^{-1} cm^{-1} 54200), 271.8 (5320), 281.4 (5120), 323.2 (1160), 336.2 (1480); δ_H($CDCl_3$) 1.34 (s, 6H), 1.38 (s, 6H), 1.44 (s, 6H), 1.57 (s, 6H), 4.08 (m, 4H), 4.35 (m, 4H), 4.85 (d, *J* = 3.4 Hz, 2H), 5.50 (m, 2H), 5.99 (d, *J* = 3.9 Hz, 2H), 7.67 (dd, *J* = 2.9, 6.4 Hz, 2H), 7.93 (dd, *J* = 3.4, 5.9 Hz, 2H), 8.24 (s, 2H); *m/z* 700 (M^+, < 1%), 685 (81), 569 (11), 459 (11), 441 (26), 401 (25), 283 (28), 325 (15), 213 (15), 199 (43), 185 (41), 155 (30), 127 (53), 113 (71), 101 (100).

(–)-Bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl) 2,6-naphthalenedicarboxylate (11c). m.p. 106.5-107.5°C (Found: C, 61.88; H, 6.76. Calc. for

$C_{36}H_{44}O_{14}$: C, 61.71; H, 6.33%); $[\alpha]_D^{26}$ -71.7° (*c* 1.03, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2989, 1720, 1377, 1261, 1219, 1173, 1084, 1022, 845, 768, 636, 513; λ_{max}(methylcyclohexane)/nm 224.8 (ε/dm^3 mol^{-1} cm^{-1} 24900), 244.4 (82800), 274.4 (8950), 284.0 (14000), 294.6 (13800), 335.0 (2330), 351.0 (2970); δ_H($CDCl_3$) 1.27 (s, 6H), 1.34 (s, 6H), 1.43 (s, 6H), 1.58 (s, 6H), 4.14 (m, 4H), 4.38 (m, 4H), 4.69 (d, *J* = 3.9 Hz, 2H), 5.90 (d, *J* = 2.9 Hz, 2H), 6.01 (d, *J* = 3.9 Hz, 2H), 8.03 (d, *J* = 8.3 Hz, 2H), 8.12 (d, *J* = 8.3 Hz, 2H), 8.61 (s, 2H); *m/z* 700 (M^+, < 1%), 685 (75), 541 (14), 441 (88), 199 (40), 154 (18), 101 (100).

(–)-Tetramenthyl 1,2,3,4-naphthalenetetracarboxylate (12a). m.p. 160.0-161.0°C (Found: C, 75.60; H, 9.41. Calc. for $C_{54}H_{80}O_8$: C, 75.66; H, 9.41%); $[\alpha]_D^{26}$ -162.9° (*c* 1.02, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2954, 1732, 1454, 1373, 1215, 957; λ_{max}(methylcyclohexane)/nm 239.6 (ε/dm^3 mol^{-1} cm^{-1} 53200), 288.6 (6670), 334.4 (1130); δ_H($CDCl_3$) 0.78-0.90 (m, 28H), 0.97 (d, *J* = 6.4 Hz, 6H), 1.01 (d, *J* = 6.4 Hz, 6H), 1.14 (s, 8H), 1.41-1.75 (m, 16H), 2.02 (m, 4H), 2.35 (m, 2H), 2.53 (m, 2H), 4.80 (dt, *J* = 4.4, 10.7 Hz, 2H), 5.00 (dt, *J* = 4.4, 10.5 Hz, 2H), 7.64 (dd, *J* = 3.2, 6.6 Hz, 2H), 7.98 (dd, *J* = 3.2, 6.6 Hz, 2H); *m/z* 879 (M^+ + Na, 6%), 855 (2), 305 (50), 287 (78), 269 (21), 137 (42), 123 (13).

Photolysis. All irradiations were performed in a temperature-controlled water (25 °C), methanol/2-propanol (-40 °C) bath. The light sources employed were a conventional 300W high-pressure mercury lamp for irradiations at 25 °C and an equivalent lamp fitted with a transparent Pyrex vacuum sleeve designed for low-temperature irradiation (Eikosha). A solution (4 cm^3), containing 1,3-cyclohexadiene **1** (100 mmol dm^{-3}), optically active sensitizer **4-12** (5 mmol dm^{-3}), and n-dodecane (5 mmol dm^{-3}) added as an internal standard, was irradiated at > 300 nm under an argon atmosphere in a Pyrex tube (1 cm i.d.) placed near the lamp surface or in an annular Pyrex vessel surrounding the lamp, the whole system being immersed in the cooling bath.

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CHAPTER 3

Enantiodifferentiating Photocyclodimerization of Cyclohexene Sensitized by Chiral Benzenecarboxylates

Introduction

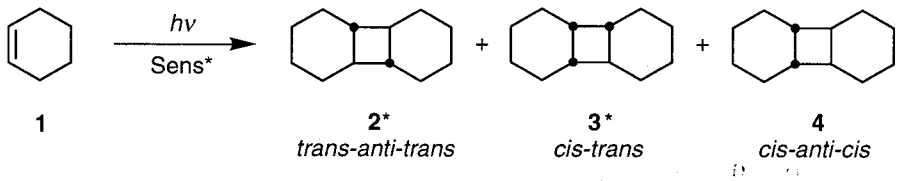
Enantiodifferentiating photosensitization, which necessitates only a catalytic amount of optically active compound as chiral sensitizer, provides us with the most chiral source-efficient photochirogenetic methodology for transferring and multiplying chirality through the electronically excited state.[1] For that reason, a considerable amount of efforts have 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, the author has shown that the enantiodifferentiating geometrical photoisomerization of (*Z*)-cyclooctene sensitized by chiral benzenepolycarboxylates gives the optically active (*E*)-isomer in fairly high enantiomeric excesses (ee's) of up to 64%, and unprecedentedly the product chirality is inverted by changing temperature[5d-i] and also by applying hydrostatic pressure.[5j] 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 ee of 77% at -80 °C.[5k]

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 the 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 ether 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 with extremely low ee's (<

1%).[14] Kim and Schuster reported the first successful asymmetric photochemical study on the [4+2] photocycloaddition of (*E*)-β-methylstyrene with 1,3-cyclohexadiene, sensitized by (–)-1,1'-bis(2,4-dicyanonaphthalene), which gave the [4+2]-cycloadduct of 15% ee at -65°C.[15] Recently, the author has reported that the enantiodifferentiating polar addition of alcohols to 1,1-diphenyl-1-alkenes sensitized by optically active naphthalene(di)carboxylates gives the optically active anti-Markovnikov adduct with the optimized ee's 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 ee's at higher temperatures.[16a,b]

The enantiodifferentiating photocyclodimerization of 1,3-cyclohexadiene 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 sorted out the mechanistic ambiguity.[16c] 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 the competing concerted and stepwise mechanisms have been proposed to be involved in the photocyclodimerization.[18-20] It is also interesting to examine the effect of its smaller ring size, reduced steric hindrance, an less flexible skeleton upon both the photosensitization and enantiodifferentiation processes, by comparing the asymmetric photochemical behavior of **1** with that of cyclooctene[5a-j] and cycloheptene.[5k] Here, the author report the results of the study on the enantiodifferentiating photocyclodimerization of

Scheme 1



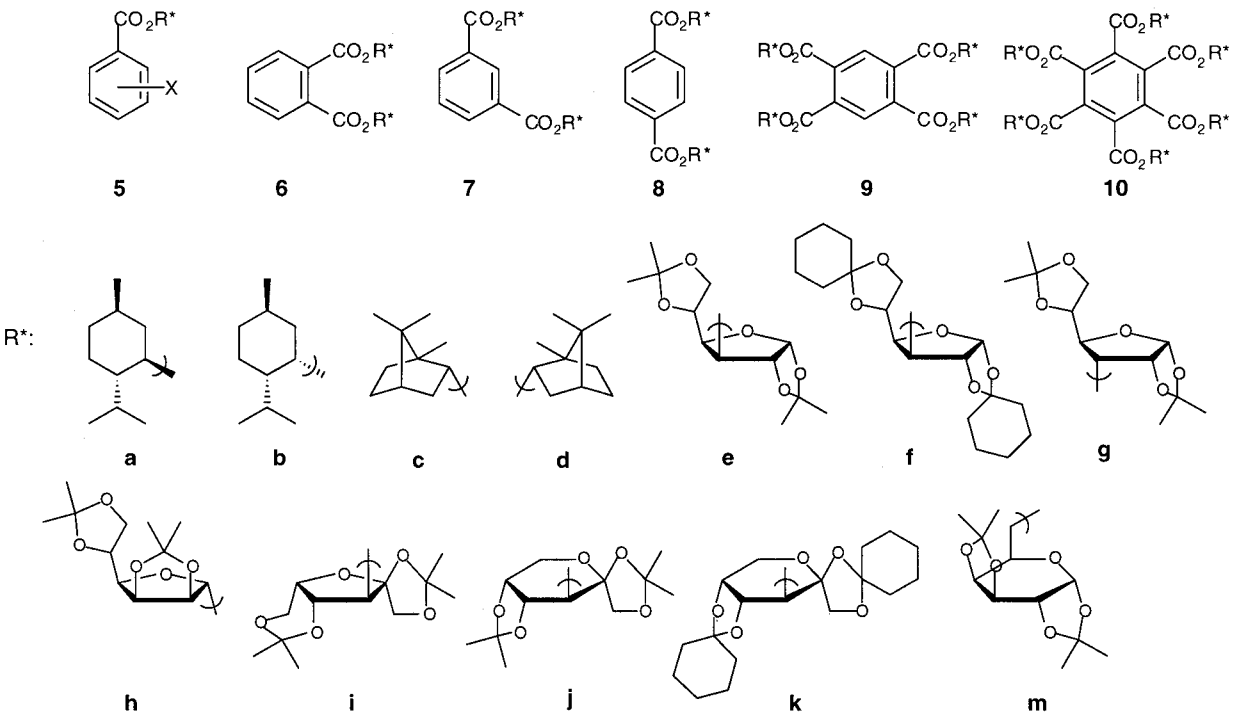
cyclohexene sensitized by optically active benzene(poly)carboxylates, and the author will discuss the detailed mechanism and intermediates involved in the enantiodifferentiation and subsequent cyclodimerization processes.

Results and Discussion

The photocyclodimerization of **1** has been investigated under the direct excitation and triplet sensitization conditions.[18-20] The direct irradiation of **1** in pentane produces a mixture of three [2+2]-cyclodimers, *i.e. trans-anti-trans* (**2**), *cis-trans* (**3**), and *cis-anti-cis* (**4**), in a ratio of 2.0 : 2.6 : 1.0. The *p*-xylene-sensitization of **1** in aprotic media also affords a mixture of cyclodimers **2**-**4**, product ratio of which is different from that obtained in the direct excitation and varies appreciably with solvent and temperature used.[18c] Thus, the xylene-photosensitization gives **2**, **3** and **4** in ratios of 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 decreases with lowering temperature.

Chart 1

Chiral Sensitizers



In the present study, the author 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.

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**-**m**) 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 ℃ 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 ee's, determined by the gas chromatographic analysis over chiral stationary phase, are summarized in Tables 1 and 2. No other peaks were found in the 'dimer region' of GC retention time, and the formation of bicyclohexyl was clearly ruled out by the direct comparison on GC with the authentic sample. Furthermore, the relative ratio of **2** : **3** : **4** was not affected by the catalytic hydrogenation of the irradiated solution over Pd/C, which clearly indicates the absence of any unsaturated product overlaying on the GC 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 the preparative GPC separation. Although the GPC column used was achiral, the ee of the product was checked to be the same before and after the isolation procedure. The isolated *trans-anti-trans* isomer **2** afforded a negative optical rotation (α = –0.0038 ± 0.0006°) at 589 nm. In Tables 1 and 2, the sign of the ee value for **2** represents the direction of optical rotation, *i.e.* the 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 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.* the positive value means the predominant formation of the first-eluting enantiomer.

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

entry	sensitizer			conversion	% yield (% ee[c])		
		X	E_S[b]	/%	**2**	**3**	**4**
1	**5a**	H	102.3	69	4.9 (-5.3)	9.0 (-0.2)	4.0
2		2-CF_3	106.3	38	0.2 (+0.1)	0.3 (+1.2)	0.1
3		3-CF_3	102.9	56	2.3 (-3.4)	4.3 (-0.4)	1.9
4		4-CF_3	101.7	44	0.7 (-5.7)	1.2 (+0.6)	0.5
5		3,5-$(CF_3)_2$	103.4	49	1.6 (-1.7)	2.9 (-0.4)	1.3
6		4-CN	98.5	20	0	0	0
7		2-OH	95.0	15	0	0	0
8	**6a**		101.6	31	0	0	0
9	**7a**		99.4	51	1.1 (-4.7)	2.1 (-0.8)	0.9
10	**8a**		97.1	40	0.1 (+2.3)	0.2 (-1.1)	0.1
11	**9a**		97.9	33	0	0	0
12	**10a**		94.4	29	0	0	0

[a] [**1**] = 20 mmol dm^{-3}; [Sens*] = 5 mmol dm^{-3}; irradiation time 24 h, unless noted otherwise. [b] Singlet energy of sensitizer in kcal/mol, estimated from the absorption 0-0 band in pentane (ref. 5g). [c] Enantiomeric excess determined by chiral GC.

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 8-12). 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 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 menthoxycarbonyl groups at the 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 elongated 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 2-7 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 higher E_S, trifluoromethyl-substituted benzoates (X = 2-, 3-, 4-CF_3 and 3,5-$(CF_3)_2$) gave the cyclodimers only in much decreased chemical yields. Thus, the introduction of both electron-donating and withdrawing groups equally diminishes the product yield dramatically, which is rationalized by the increased steric hindrance and/or lower E_S induced by the substitution. The ee's of **2** obtained upon sensitization with the substituted benzoates were much lower than that obtained with unsubstituted benzoate (5.3% ee), except for 4-trifluoromethylbenzoate which gave **2** of 5.7% ee.

In sharp contrast to the cyclooctene and cycloheptene cases investigated under the 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 **2**, **3** and **4** upon sensitization with **5e** as 2.9 x 10^{-3}, 5.3 x 10^{-3} and 2.4 x 10^{-3}, respectively. The combined quantum yield is 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 the 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 homologues, since the vertical, or Franck-Condon, singlet of 1,2-dialkylethylene (*ca.* 130 kcal mol^{-1})[5b] is higher than that of 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] the author could not detect these radical dimers in significant amounts on GC analysis. Instead, the GPC analysis revealed the presence of a considerable amount of polymeric products in the irradiated solution. These polymers account for *ca.* 25% of cyclohexene consumed at 25 °C but amount to *ca.* 40% of the conversion at temperatures lower than -40 °C. The average molecular weight, 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, as a product from the Paternó-Büchi reaction of sensitizer with cyclohexene, was detected on GC-MS analysis, but further search for such oxetane derivatives from the chiral benzoates was unsuccessful, 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 severe 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, the author has 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-m** as chiral sensitizers in pentane and 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 a 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 the experimental error

Table 2. Enantiodifferentiating photodimerization of cyclohexene **1** sensitized by chiral benzoates **5a-m**[a]

entry	sensi-tizer	solvent	temper-ature /°C	irradi-ation time /h	conver-sion /%	% yield (% ee[b])		
						2	**3**	**4**
1	**5a**	pentane	25	4	42	3.6 (-5.0)	6.8 (-0.2)	3.1
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		ether	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		ether	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	**5c**	pentane	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		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	**5d**	pentane	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		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	**5e**	pentane	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		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			-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		aceto-	25	4	40	2.0	(-9.8)	2.9	(-0.1)	0.8
49		nitrile	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		methanol	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	**5f**	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		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	**5g**	pentane	25	4	36	2.2	(+7.0)	4.1	(+0.5)	1.5
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		ether	25	4	41	2.3 (+7.5)	4.1 (+0.6)	1.6
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
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		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		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
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
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
95		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		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	**5m**	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		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] [**1**] = 20 mmol dm^{-3}; [Sens*] = 5 mmol dm^{-3}, unless noted otherwise. [b] Enantiomeric excess determined by chiral GC. [c] [**1**] = 200 mmol dm^{-3}. [d] [**1**] = 25 mmol dm^{-3}. [e] [**1**] = 15 mmol dm^{-3}. [f] [**1**] = 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] [Sens*] < 5 mmol dm^{-3} due to low solubility.

(±0.8% ee) over the irradiation period, as exemplified by runs 42 and 45 in 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 the product **2** is not subjected to any further reactions under the irradiation conditions. The product ratios 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**.

The singlet sensitization with benzoates **5a**-**m** gave cyclodimers **2**, **3** and **4** in the same ratio of 1.2 : 2.2 : 1.0 in pentane at 25 °C, irrespective of the sensitizer used. However, the product ratio was affected significantly by the irradiation temperature, although the same product ratios were obtained for all sensitizers at each temperature. The relative ratio of **2** : **3** : **4** obtained in pentane was 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 the temperature. The use of ether as a solvent also led to a slightly different ratio (**2** : **3** : **4** = 1.4 : 2.5 : 1.0 at 25 °C), which is independent of the sensitizer used at each temperature but is 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** 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 temperature up to 18.7% at -78 °C in pentane (runs 1-5). The ee's in 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 ee's (< 3%) even at low temperatures, but the product chirality was switched within the experimental temperature range in both pentane and ether; *i.e.* the (+)-**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] 1,3-cyclooctadiene[5i] and cycloheptene[5k] and the photosensitized enantiodifferentiating polar addition of alcohols to 1,1-diphenyl-1-alkenes.[16b] This apparently unusual phenomenon has been reasonably rationalized in terms of the entropy term.[1b,c,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 ether, although the ee obtained in pentane was higher than that in ether at each temperature, reaching 30% at -78 °C.

The author further examined the saccharide derivatives, which was used as effective chiral auxiliaries of the sensitizers for the enantiodifferentiating photoaddition of alcohol to 1,1-diphenyl-1-alkenes [16b] and photocyclodimerization of 1,3-cyclohexadiene.[16c] A series of furanose **5e-i** and pyranose derivatives **5j-m** were employed in this study. The photosensitization with benzoate **5e**, which possesses a diacetone glucose auxiliary, was first examined in ether (runs 42, 45-47). The ee of **2** obtained at 25 °C was 10.9% on average but was enhanced by lowering 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 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** is better at lower concentrations, the net amount of cyclodimers produced increases with the substrate concentration and is saturated above 20 mmol dm^{-3}. In contrast, both the product ratio 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 the photochemical production of highly reactive (*E*)-cyclohexene followed by the 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 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 ee's 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 accompanying any 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 the studies on the photoisomerization of cycloheptene and 1-phenylcyclohexene, which clearly demonstrate the intervention of 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 ee's 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 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 homologues.[1b,c,5]

The author 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 ee's 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 carbons 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 carbons 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 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 the 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

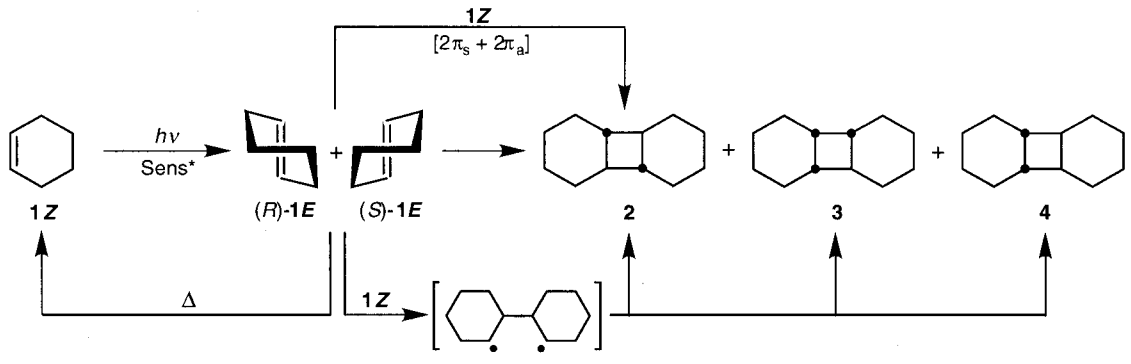
saccharide **m** with a primary hydroxyl group (Chart 1). The fact that the photosensitization with **5m** failed to give appreciable enantiodifferentiation at any temperatures (runs 108-113) not only supports this theory but also indicates that the stereogenic center should be directly attached to the ester oxygen of the arenecarboxylate sensitizers. In other words, primary alcohols are poor chiral auxiliaries for this type of photosensitizers 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's, whereas *cis-trans*-cyclodimer **3** obtained is always racemic. In view of the consistent product ratios 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.

Mechanism. On the basis of the mechanism reported perviously[18-20] and the facts obtained in this study, the author proposes a modified 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 that is anticipated for the concerted $[2\pi_s + 2\pi_a]$ cycloaddition of **1E** to **1Z** from the Woodward-Hoffmann rule,[25] assuming the (*E*)-isomer reacts suprafacially.[26] The copper(I)-sensitized photodimerization of **1**

Scheme 2



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 ratio did not depend on the sensitizer used. These facts indicate that the sensitizer is not directly 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 process 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 ratio of **2**-**4** does not change throughout the irradiation period, the interconversion among **2**-**4** through photoepimerization, which has been reported for the triplet ketone-sensitized photodimerization,[19,20] is clearly ruled out. Alternatively, cyclodimer **3** would 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 light intensity or by lowering temperature.[18c] Eventually, this possibility is completely eliminated by the result that no appreciable enantiodifferentiation was observed for **3**, under the conditions that gave good ee's for **2**. It is concluded that cyclodimer **3**, and probably **4**, are produced through the non-stereospecific stepwise cycloaddition of **1E** to **1Z** in the ground state, affording 1,4-biradical with a loss of the optical activity of **1E** induced photochemically. The formation of polymeric products may 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 ratio (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 curvature for each sensitizer and the apparent slope increases with decreasing temperature, as shown in Figure 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 significant contribution from the non-concerted cyclodimerization path to racemic **2**, and the dramatic enhancement of ee at the low temperatures is achieved by the predominant contribution of the concerted [$2\pi_s + 2\pi_a$] process to the formation of **2**.

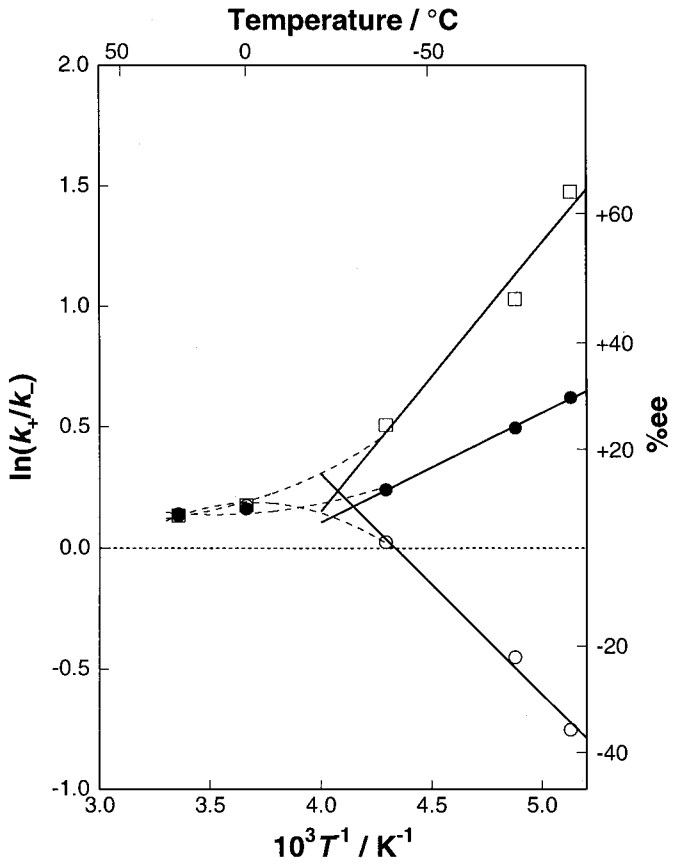


Fig. 1. Temperature dependence of enantiomeric excess (ee) of **2**: the logarithm of relative rate constant (k_+/k_-) plotted as a function of reciprocal temperature in enantiodifferentiating photocyclodimerization of **1** sensitized by **5d** (●), **5g** (○) and **5i** (□) in pentane.

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

$$\ln (k_+/k_-) = -\Delta E/RT + \ln (A_+/A_-)$$
$$= -\Delta\Delta H^{\ddagger}/RT + \Delta\Delta S^{\ddagger}/R \qquad (1)$$

where ΔE represents the 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, the plot of ln (k_+/k_-) value against the 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 the low temperatures, where the contribution of the non-concerted path can be neglected , the ee of initially formed **1E** is completely transferred to cyclodimer **2**. Hence the linear fit of the plot was carried out by using the ee's obtained at the temperatures lower than -40 °C to give a good straight line, as exemplified in Figure 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 summarized 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 materialized only when the chiral recognition is governed exclusively by the enthalpic factor and 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 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 Figure 2, all of the $\Delta\Delta S^{\ddagger}$ values obtained are plotted

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] / cal mol^{-1} K^{-1}	A_+/A_- [d]	T_0 [e] / °C
5a	pentane	0.52	1.96	2.68	-7
	ether	0.26	0.82	1.51	41
5c	pentane	0.80	2.81	4.12	10
	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
	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
	ether	1.06	4.80	11.2	-53
5i	pentane	-2.22	-8.56	0.013	-14
	ether	-1.81	-7.22	0.026	-23
5j	pentane	2.75	11.1	270	-26
	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.

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_{iso} = 249 K, which is in good agreement with those reported for cyclooctene and cycloheptene.[5g,l] The comparable T_{iso} obtained for all of the cycloalkenes indicate 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

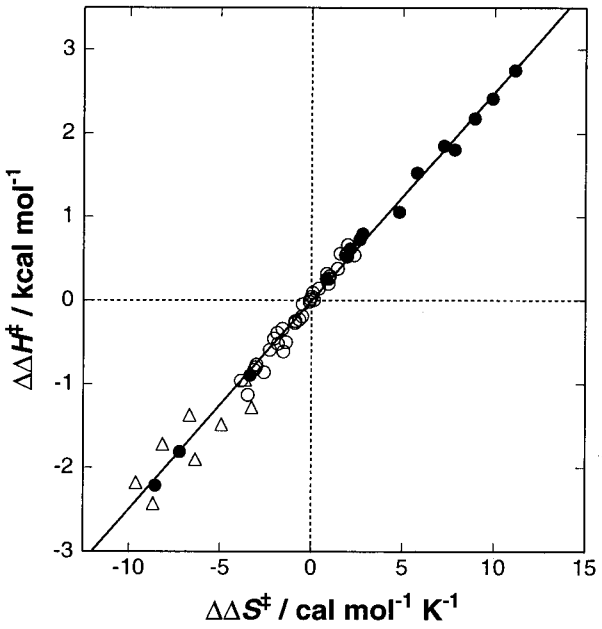


Fig. 2. Enthalpy-entropy compensation plot for the differential activation parameters obtained in the enantiodifferentiating photocyclodimerization of cyclohexene (●) and photoisomerization of cycloheptene (Δ) and cyclooctene (○) sensitized by chiral benzene(poly)carboxylates.

mechanism involves the concerted and non-concerted paths in the formation of the three cyclodimers.

Experimental Section

General. Melting points were measured with a Yanaco MP-300 apparatus and were uncorrected. ^{1}H and ^{13}C NMR spectra were obtained on a JEOL GX-400 or GSX-270 spectrometer in $CDCl_3$. Infrared 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 thermostated conventional 10 cm cell, using a JASCO DIP-1000 polarimeter.

Enantiomeric excesses of **2** and **3** were determined by gas chromatography 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 yield 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 300 x 7.5 mm PLgel 5μm Mixed-C column (Polymer Laboratories) using a JASCO GPC-900 instrument.

Materials. Pentane used as solvent was stirred over concentrated sulfuric acid until the acid layer no longer turned yellow, washed with water, neutralized with aqueous 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 aluminum oxide (ICN Biomedicals).

Optically active alcohols and some saccharide derivatives used in the preparation the sensitizers were commercially available: (–)-menthol and (–)-borneol from TCI; 1,2:5,6-Di-*O*-cyclohexylidene-α-D-glucofuranose 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-glucofuranose, 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; $\delta_H(CDCl_3)$ 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 $C_{17}H_{22}O_2$: C, 79.03;

H, 8.58%); $[\alpha]_D^{30}$ +45.0° (*c* 1.02, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2954, 2879, 1716, 1602, 1452, 1273, 1176, 1117, 1068, 1026, 980, 712; λ_{max}(ether)/nm 227.2 (ε/dm^3 mol^{-1} cm^{-1} 13100), 270.2 (898); δ_H($CDCl_3$) 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).

(–)-1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl benzoate (5e). (Found: C, 63.20; H, 6.84. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[\alpha]_D^{30}$ -50.1° (*c* 1.01, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2970, 2870, 1720, 1610, 1460, 1380, 1270, 1170, 1080, 1040, 960, 890, 860, 730; λ_{max}(ether)/nm 228.4 (ε/dm^3 mol^{-1} cm^{-1} 15100), 272.0 (1180); δ_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).

(–)-1,2:5,6-Di-*O*-cyclohexylidene-α-D-glucofuranosyl benzoate (5f). m.p. 116 °C (Found: C, 67.52; H, 7.21. Calc. for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26%); $[\alpha]_D^{30}$ -33.2° (*c* 1.00, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2935, 1716, 1450, 1367, 1273, 1165, 1115, 1074, 1012, 941, 930, 715; λ_{max}(ether)/nm 228.4 (ε/dm^3 mol^{-1} cm^{-1} 16000), 271.6 (1340); δ_H($CDCl_3$) 1.25-1.80 (m, 20H), 4.00-4.20 (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).

(+)-1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranosyl benzoate (5g). m.p. 76 °C (Found: C, 62.56; H, 6.48. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[\alpha]_D^{30}$ +124.3° (*c* 1.04, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2985, 2893, 1724, 1454, 1377, 1277, 1115, 1030, 864, 717; λ_{max}(ether)/nm 228.4 (ε/dm^3 mol^{-1} cm^{-1} 15500), 272.0 (1070); δ_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). m.p. 128 °C (Found: C, 62.55; H, 6.43. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[\alpha]_D^{30}$ +40.5° (*c* 1.01, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2989, 2940, 1724, 1454, 1377, 1292, 1255, 1209, 1084, 968, 849, 712; λ_{max}(ether)/nm 228.6 (ε/dm^3 mol^{-1} cm^{-1} 14000), 271.4 (1260); δ_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).

(–)-1,2:4,6-Di-*O*-isopropylidene-α-L-sorbofuranosyl benzoate (5i). (Found: C, 61.81; H, 6.78. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[\alpha]_D^{30}$ -48.0° (*c* 1.00, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2993, 2935, 1728, 1454, 1377, 1269, 1115, 1072, 937, 852, 714; λ_{max}(ether)/nm 228.2 (ε/dm^3 mol^{-1} cm^{-1} 15200), 271.8 (1080); δ_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).

(–)-1,2:4,5-Di-*O*-isopropylidene-β-D-fructopyranosyl benzoate (5j). m.p. 111 °C (Found: C, 62.61; H, 6.54. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[\alpha]_D^{30}$ -162.1° (*c* 1.02, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2940, 1684, 1585, 1454, 1371, 1300, 1186, 1115, 1028, 910, 854, 773, 709; λ_{max}(ether)/nm 228.8 (ε/dm^3 mol^{-1} cm^{-1} 16800), 271.8 (1240); δ_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).

(–)-1,2:4,5-Di-*O*-cyclohexylidene-β-D-fructopyranosyl benzoate (5k). m.p. 116 °C (Found: C, 67.49; H, 7.22. Calc. for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26%); $[\alpha]_D^{30}$ -146.1° (*c* 1.02, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2931, 2860, 1724, 1448, 1263, 1101, 916, 708; λ_{max}(ether)/nm 228.6 (ε/dm^3 mol^{-1} cm^{-1} 16500), 271.6 (1260); δ_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).

(–)-1,2:3,4-Di-*O*-isopropylidene-D-galactopyranosyl benzoate (5m). (Found: C, 62.48; H, 6.60. Calc. for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64%); $[\alpha]_D^{30}$ -59.4° (*c* 1.04,

$CHCl_3$); ν_{max}(KBr)/cm^{-1} 2989, 2931, 1724, 1454, 1380, 1272, 1214, 1173, 1107, 1072, 1007, 895, 714; λ_{max}(ether)/nm 227.4 (ε/dm^3 mol^{-1} cm^{-1} 13200), 271.8 (950); δ_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/2-propanol (-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 cm^3), 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 i.d.) 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 cm^3), the photolyzed solution of **1** was first subjected to preparative TLC on silica gel with an ethyl acetate/hexane (1:99) 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 were detected on GC or NMR in the isolated products.

***trans-anti-trans*-Tricyclo[6.4.0.0^{2,7}]dodecane (2).** δ_C($CDCl_3$) 26.7, 31.2, 50.5 (lit.[20] δ_C 26.5, 31.0, 50.3); HRMS calcd for $C_{12}H_{20}$ (M^+): 164.1564. Found: 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).** δ_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 resonance), 37.2, 39.3, 41.6, 44.2); HRMS calcd for $C_{12}H_{20}$ (M^+): 164.1564. Found: 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).** δ_C($CDCl_3$) 23.2, 27.3, 34.4 (lit.[20] δ_C 23.1, 27.1, 34.3); HRMS calcd for $C_{12}H_{20}$ (M^+): 164.1564. Found: 164.1570; *m/z* 164 (M^+, 21%), 135 (8), 121 (6), 107 (4), 96 (8), 82 (100), 67 (75).

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CHAPTER 4

Photochirogenesis:
Multidimensional Control of Asymmetric Photochemistry

Introduction

Asymmetric synthesis is an area of vital importance in current chemistry, to which a considerable amount of effort have been devoted in recent years.[1-9] Thus, enantio- and diastereoselectivity are the principal objective or prerequisite when developing a new asymmetric catalyst or synthetic methodology,[1-3] as well as in synthesizing chiral compounds such as naturally occurring and pharmaceuticals.[4-9] The stereochemical outcome of these asymmetric reactions has been discussed in terms of the empirical rules using the models of Cram,[10] Felkin-Anh[11,12] and others.[4,13] These models are based primarily on the relative steric bulk of the aligned substituents near the reaction center, which are oriented by steric hindrance, dipole interactions or metal chelation. Obviously, the chiral discrimination mechanism based on these empirical rules can assess only the enthalpic contributions attributable to the steric/stereoelectronic interaction between the substituent and attacking reagent, while the entropic contribution arising from the conformational changes and re-positioning of the solvent molecules during the transition state has not been discussed explicitly for thermal and enzymatic asymmetric syntheses. Nevertheless, these empirical rules, which only take the enthalpy term into account, are generally successful and are frequently employed in interpreting and/or predicting the dominant stereoisomer formed, and also the trend in optical yield obtained in a variety of asymmetric induction and asymmetric catalysis processes. Consequently, the entropic contribution has not been discussed globally, or experimentally examined as a factor in the mechanism of most thermal asymmetric reactions until recently,[14] in spite of some early observations of small to moderate temperature effects on enantio- or diastereoselectivity, *e.g.* in the addition of alcohols or amines to ketenes in the presence of acetylquinine,[15] in the $LiAlH_4$ reduction of acetophenone in the presence of quinine,[16] and in the oxidation of sulfides with optically active peracids.[17] That entropy plays an important role does not seem unreasonable,

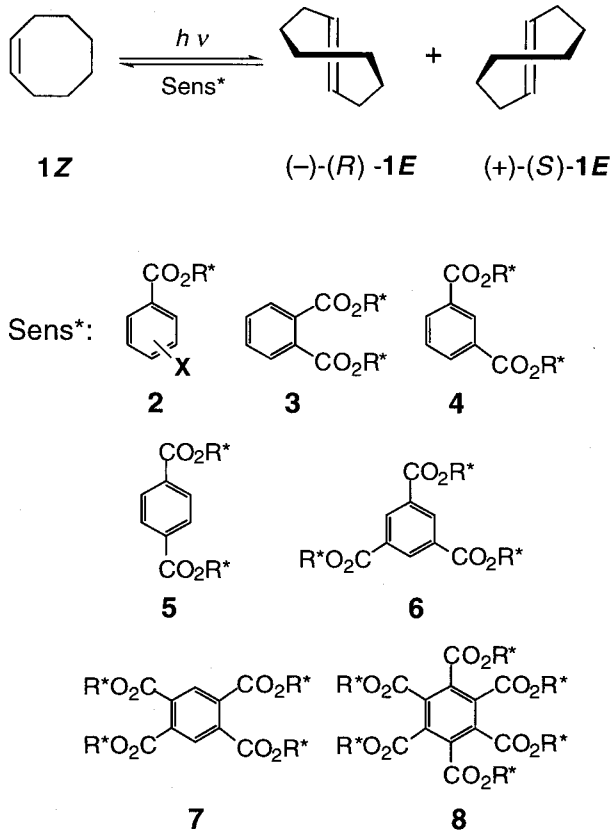
since the temperature range available is rarely wide enough to thoroughly survey the effect of this variable, and the possible incorporation of different reaction mechanisms or a switch in intermediates resulting from a change in temperature is not rigorously ruled out in many thermal asymmetric reactions.

In contrast, photochemical reactions are driven by the absorption of high-energy photons and proceed through the excited state, which renders them inherently free from temperature restrictions, and they are, therefore, advantageous for investigating the effect of the entropy factor upon stereoselectivity over a wide temperature range without undergoing any essential changes in reaction mechanism or intermediates formed. However, the temperature effect has been rarely and only recently explored in the rather short history of asymmetric photochemistry.[18,19] Thus, in the diastereodifferentiating Paternò-Büchi photocycloaddition of optically active phenylglyoxylic esters with several alkenes,[20] Scharf *et al.* showed that the diastereoselectivity of the oxetane produced not only depends on the irradiation temperature, but also gives a bent Eyring plot as a consequence of the alteration of the rate limiting step that determine the diastereoselectivity. In the enantiodifferentiating *Z-E* photoisomerization of cyclooctene sensitized by optically active sensitizers,[21] the author demonstrated that the antipodal (*E*)-cyclooctenes, *i.e.* (*S*)-(–)- and (*R*)-(+)-enantiomers, can be obtained simply by changing the irradiation temperature from -88 to +50 °C, and that the enantiomeric excess (ee) of the product increases with increasing temperature, an observation that conflicts with the belief that lowering the temperature will generally enhance the ee. This unprecedented temperature dependence and the switching of the major enantiomer produced was revealed to be exclusively entropic in origin through an analysis of the Eyring plot of the enantioselectivity of the reaction. A similar 'unusual' temperature dependence of stereoselectivity, which leads to the switching of product chirality and/or higher selectivity at higher temperature, has been observed in many enantio[22-25] and diastereodifferentiating photoreactions[26-31] over the last decade. More recently, the author has revealed that the product chirality can be controlled, and in some cases, actually switched by changing the pressure from atmospheric to 400 MPa in the photosensitized enantiodifferentiating isomerization of cyclooctene.[32]

In this paper, the author wishes to present a global view of recent advances in 'photochirogenesis', particularly in enantiodifferentiating photosensitization reactions. The author will also demonstrate how the entropic and enthalpic factors share the roles in manipulating the stereochemical outcome of these enantiodifferentiating photoreactions. Finally, the author will show that the combined use of entropy-related factors, such as temperature, pressure and solvent, provides us with a new method for the control of asymmetric photochemistry. Indeed, the basic concepts revealed here by asymmetric photochemistry should also be applicable to thermal and biological asymmetric reactions.

Results and Discussion

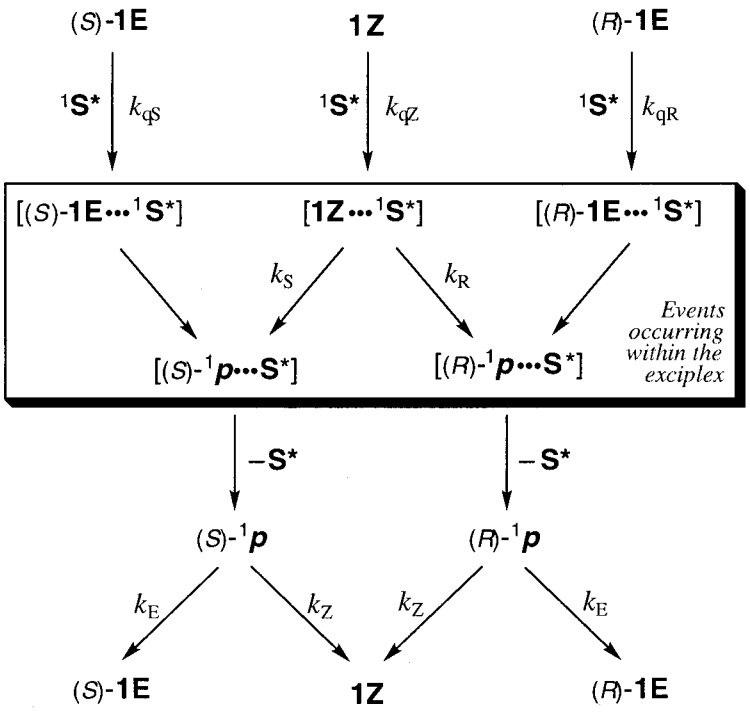
Temperature effect. In this study, which aims to devise methods for highly efficient photochemical generation, transfer and multiplication of molecular chirality,



Scheme 1 Enantiodifferentiating *Z-E* photoisomerization of cyclooctene sensitized by chiral benzene(poly)carboxylates (Sens*).

the author has chosen the enantiodifferentiating geometrical photoisomerization of (*Z*)-cyclooctene (**1Z**) sensitized by optically active aromatic esters as one of the most promising processes for development (Scheme 1), simply because this photosensitization was known to give chiral (*E*)-cyclooctene (**1E**) in high chemical and quantum yields and was also found to involve a singlet exciplex between the substrate and sensitizer (S*).[33] The involvement of a structurally well-defined exciplex intermediate, which enables efficient transfer of chiral information in the excited state, is an essential condition for obtaining high optical yield in an enantiodifferentiating photosensitization.

Taking into account the simultaneous formation of the two enantiomers of **1E**, the original sensitization mechanism[33] was modified to include chirality, as shown in Scheme 2.[22a] The photosensitization is initiated by the formation of an encounter complex [**1Z/E**•••^{1}**S***] between the excited sensitizer (^{1}**S***) and **1Z** or one of enantiomers of **1E**. Energy transfer within the



Scheme 2 Enantiodifferentiating mechanism for photosensitized isomerization of cyclooctene (**1**) via exciplex, where **S*** and ^{1}**S*** are the chiral sensitizer in the ground and excited singlet states, and ^{1}***p*** is the twisted, excited singlet of **1**.

exciplex intermediate and the subsequent rotation around the C=C bond of **1Z/1E** to a dihedral angle of *ca.* 90° afford a relaxed exciplex [^{1}***p***•••**S***], which in turn releases the perpendicular singlet (^{1}***p***), regenerating the ground-state sensitizer (**S***). It should be noted that chirality is induced in ^{1}***p*** during the rotational relaxation step. The subsequent decay of ^{1}***p*** to **1Z** or **1E** concludes the photoisomerization cycle.

There are two steps in this mechanism that are potentially enantiodifferentiating: (i) the quenching of ^{1}**S*** by enantiomeric **1E** and (ii) rotational relaxation within the exciplex [**1Z**•••^{1}**S***]. Thus, the rate constants for quenching (k_{qS}, k_{qR}) and/or rotation (k_S, k_R) may be different from one another. Experimentally, no appreciable optical rotation was detected in **1E** recovered during the initial stages of the enantiodifferentiating photosensitization of racemic **1E**, and the ee of product **1E** did not show any conversion dependency in the enantiodifferentiating photosensitization of **1Z**,[22b] both of which rule out the possibility of enantiodifferentiation in the quenching process, and thus $k_{qS} = k_{qR}$. Hence, the rotational relaxation of **1Z** to ^{1}***p*** within the exciplex intermediate can be the only enantiodifferentiating step in this asymmetric photosensitization, and the ee of **1E** is determined exclusively by the relative rate, k_S/k_R. This seems quite reasonable, since intimate interaction, which leads to efficient chiral recognition, is more likely to occur in the long-lived exciplex intermediate that possesses a more defined structure than during the collisional quenching stage.

In order to discuss quantitatively the temperature dependence of the ee's observed for this asymmetric photosensitization, the rate constants k_S and k_R were analyzed according to the Arrhenius, or Eyring equation. The relative rate constant, k_S/k_R, can then be expressed by the following equations:

$$\ln(k_S/k_R) = -\Delta E_{S\text{-}R}/RT + \ln(A_S/A_R) \quad (1a)$$

$$= -\Delta\Delta H^{\ddagger}_{S\text{-}R}/RT + \Delta\Delta S^{\ddagger}_{S\text{-}R}/R \quad (1b)$$

where $\Delta E_{S\text{-}R}$ represents the differential energy of activation, A_S/A_R is the relative frequency factor, and $\Delta\Delta H^{\ddagger}_{S\text{-}R}$ and $\Delta\Delta S^{\ddagger}_{S\text{-}R}$ denote the differential enthalpy and entropy of activation, respectively.

The enantiodifferentiating photosensitizations of **1Z** were performed in several solvents at temperatures ranging from +50 to -90 °C, using a variety of optically pure (poly)alkyl benzene(poly)carboxylates as chiral sensitizers.[22] Interestingly, the product chirality switched at a specific, or equipodal temperature, T_0, upon sensitization with most *ortho*-substituted benzenepolycarboxylates, whereas no chirality inversion was observed for non-*ortho* sensitizers; typical examples are shown in Fig. 1. This is the first observation of an enantiodifferentiating reaction where the ee of the product is not only inverted by temperature, but also raised with increasing temperature above T_0. It is also important that both enantiomers

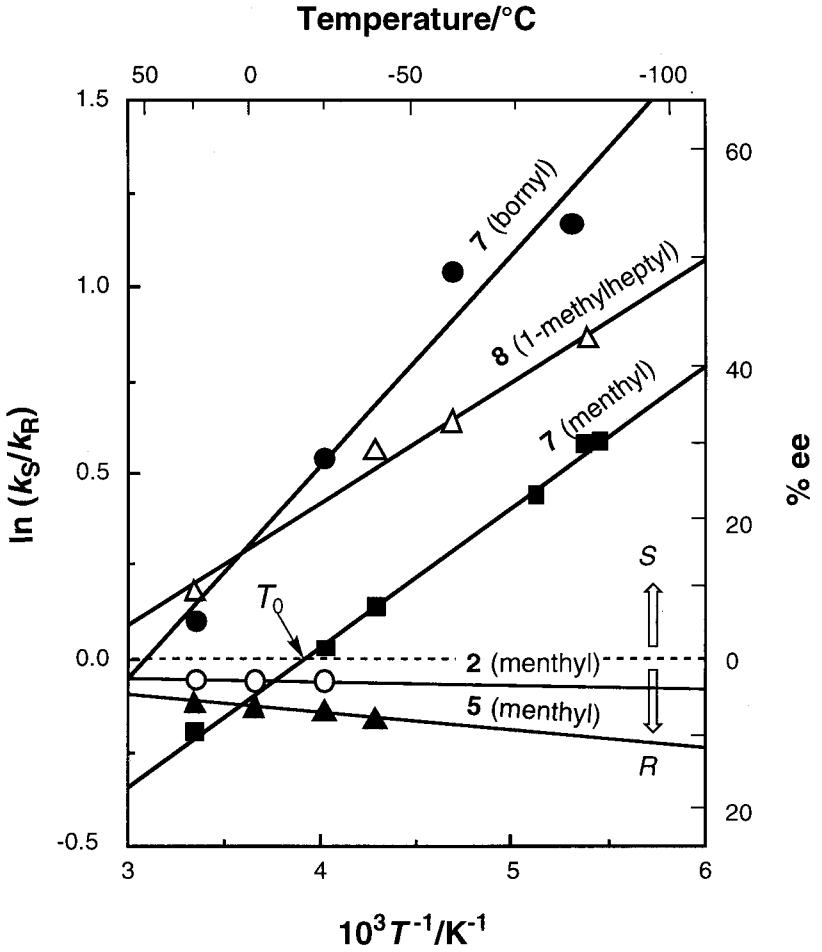


Fig. 1 Temperature dependence of the ee of the product in enantiodifferentiating photoisomerization of cyclooctene (**1Z**) sensitized by (–)-menthyl benzoate **2** (○) and terephthalate **5** (▲), (–)-menthyl and (–)-bornyl 1,2,4,5-benzenetetracarboxylate **7** (■ and △), and (–)-1-methylheptyl benzenehexacarboxylate **8** (●) in pentane. The chirality of product **1E** is switched at the equipodal temperature, T_0.

Table 1 Activation parameters at 25 °C, determined from the temperature and pressure dependence of the ee of **1E** obtained in enantiodifferentiating photoisomerization of cyclooctene (**1Z**), sensitized by chiral benzenepolycarboxylates **2-5**, **7** and **8** in pentane

Sensitizer		$\Delta\Delta H^{\ddagger}_{S-R}$ [a]	$T\Delta\Delta S^{\ddagger}_{S-R}$ [a]			$\Delta\Delta V^{\ddagger}_{S-R}$ [b]
Compound	R*	/kcal mol^{-1}	/kcal mol^{-1}	A_S/A_R	T_0/°C	/kcal mol^{-}
2	(–)-Menthyl	+0.014	-0.039	0.99	*c*	-0.13
3	(–)-Menthyl	-0.19	-0.51	0.90	100	+0.83
	(–)-Bornyl	-0.50	-1.38	0.74	91	+1.48
4	(–)-Menthyl	+0.08	+0.15	1.16	530	+0.07
5	(–)-Menthyl	+0.09	+0.08	1.02	940	+0.36
7	(–)-Menthyl	-0.77	-3.00	0.52	-15	-3.71
	(–)-Bornyl	-0.61	-1.55	0.71	123	+0.29
	(–)-1-Methylheptyl	-0.54	-1.93	0.67	8	-1.44
8	(–)-Menthyl	-0.96	-3.85	0.43	-23	+3.50
	(–)-Bornyl	-0.86	-2.60	0.56	60	-5.56
	(–)-1-Methylheptyl	-1.13	-3.48	0.47	51	+0.56

[a] Reference 22b. [b] Reference 32. [c] T_0 does not exist.

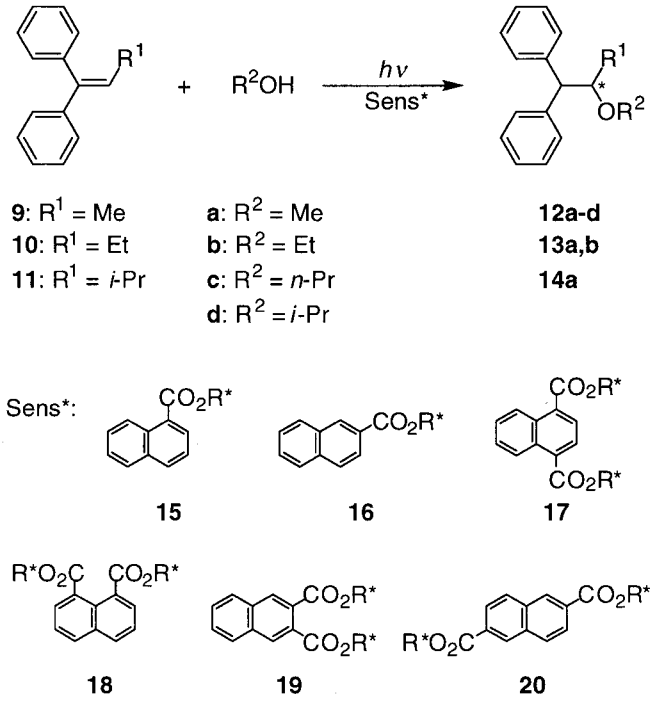
can be prepared simply by changing the temperature without using antipodal sensitizer.

From eqns. 1a and 1b and the experimental plots exemplified in Fig. 1, the activation parameters were determined for these enantiodifferentiating photoisomerizations using various chiral benzenecarboxylate sensitizers; the relevant activation parameters and equipodal temperatures obtained for several sensitizers are listed in Table 1.

By examining eqn. 1, it is apparent that this temperature switching behavior of product chirality is attributable to the non-zero differential entropy of activation ($\Delta\Delta S^{\ddagger}_{S-R} \neq 0$) or the unequal frequency factor ($A_S \neq A_R$). Thus, the entropy factor is shown to play a decisive role in the enantiodifferentiation process. It should be emphasized that the *ortho*-substituted benzenepolycarboxylates, such as phthalate, benzenetetracarboxylate and benzenehexacarboxylate, afford very large deviations from unity for the ratio A_S/A_R, while benzoate and terephthalate show almost equal frequency factors for the (*R*)- and (*S*)-isomers, as can be seen in Table 1. This tendency is not incidental, but implies that the rotational motion of the double bond of **1** in the exciplex causes simultaneous global conformational changes of the closely situated *ortho*-alkoxycarbonyl groups of the sensitizer. Such dynamic changes during

rotational relaxation in the exciplex inevitably produce large differences in the activation entropy of enantiodifferentiation.

Although the author has hitherto concentrated on the enantiodifferentiating photoisomerization of **1**, similar chirality inversion phenomena have been observed in the enantiodifferentiating photosensitizations of 1-methylcyclooctene[22f] and 1,3-cyclooctadiene,[24] as well as in the enantiodifferentiating *anti*-Markovnikov photoaddition of methanol to 1,1-diphenylpropene (**9**).[25b] Of these, the diphenylpropene case is particularly interesting, since this is the first bimolecular enantiodifferentiating photoreaction that affords the *anti*-Markovnikov adduct (**12**) upon sensitization with chiral 1,4-naphthalenedicarboxylates (**17**), with moderate ee's of up to 33% observed (see Scheme 3 and Fig. 2). In this photosensitized polar addition, the use of *ortho* aromatic esters is no longer required to cause the inversion of product chirality by altering the temperature, probably because the termolecular interaction of the attacking methanol with the initially formed sensitizer-substrate exciplex exaggerates the influence of the conformational differences on the enantiodifferentiating process.



Scheme 3 Enantiodifferentiating photoaddition of alcohols to 1,1-diphenyl-1-alkenes (**9-11**) sensitized by chiral naphthalene(di)carboxylates (**15-20**).

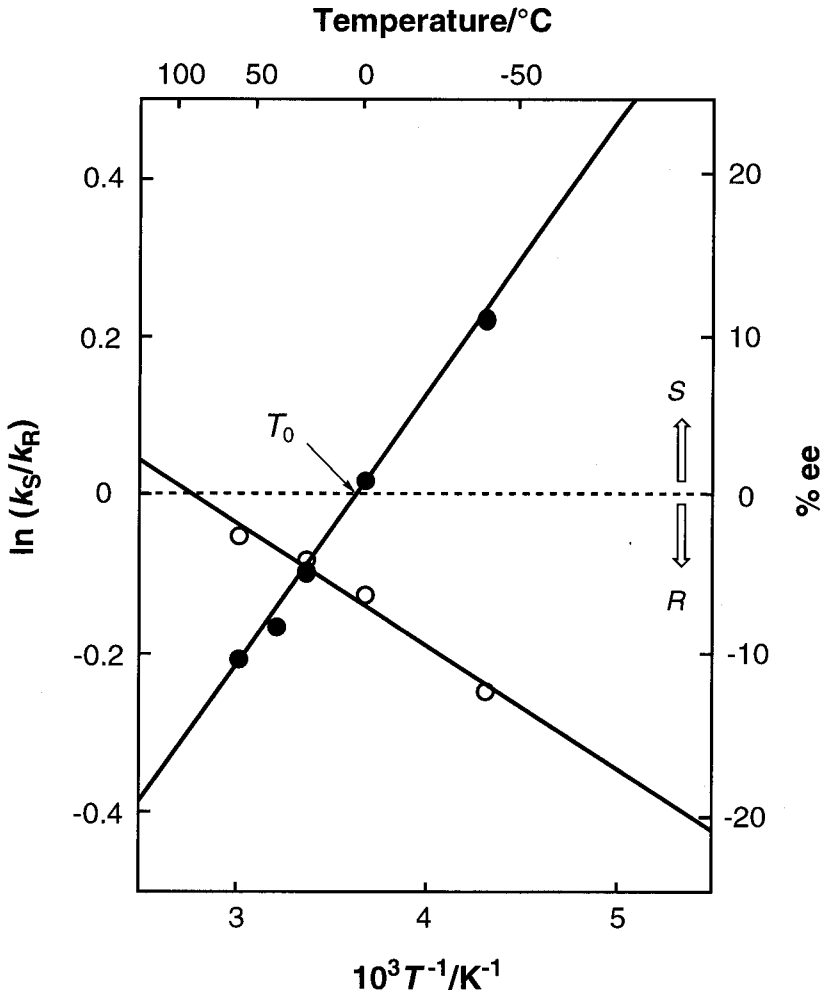


Fig. 2 Temperature dependence of the ee of the product in the enantiodifferentiating addition of methanol to **10**, sensitized by **17** with R* = (–)-menthyl (○) and 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (●) in methylcyclohexane.

The roles of entropy and enthalpy. The contributions of the enthalpy and entropy factors to the enantiodifferentiating process can be discussed in terms of eqn. 1b, or using the Gibbs-Helmholtz equation for the differential activation free energy:

$$\Delta\Delta G^{\ddagger}_{S\text{-}R} = \Delta\Delta H^{\ddagger}_{S\text{-}R} - T\Delta\Delta S^{\ddagger}_{S\text{-}R} \qquad (2)$$

As can be seen from eqn. 2, T_0 is the critical point, at which the enthalpic and entropic contributions balance with each other ($\Delta\Delta H^{\ddagger}_{S\text{-}R} = T_0\Delta\Delta S^{\ddagger}_{S\text{-}R}$), affording no enantiodifferentiation. Below T_0, the enthalpy difference, $\Delta\Delta H^{\ddagger}_{S\text{-}R}$, controls the

enantiodifferentiating process, while the entropic term, $T\Delta\Delta S^{\ddagger}_{S\text{-}R}$, is dominant at temperatures higher than T_0. If both $\Delta\Delta H^{\ddagger}_{S\text{-}R}$ and $\Delta\Delta S^{\ddagger}_{S\text{-}R}$ possess the same sign, switching of the dominant term in the enantiodifferentiation process leads to the inversion of product chirality, as exemplified above. In the enthalpy-controlled temperature region below T_0, the difference in the conformational freedom of the enantiodifferentiating transition states does not seriously affect the stereochemical consequence of the photoreaction, which is determined by the steric and stacking interactions in the exciplex intermediate. Since the π-π stacking interaction in the exciplex does not vary a great deal by changing the chiral auxiliary attached to the sensitizer, the majority of the enthalpy difference ($\Delta\Delta H^{\ddagger}_{S\text{-}R}$) may be attributed to different levels of steric interaction. In this context, it is reasonable to assume that the absolute configuration of the chiral sensitizer can be related directly and exclusively to that of photoproduct. In the following section, the author first examines the appropriateness of this simple theory and then explore its scope and limitations, using the enantiodifferentiating photoisomerization of cyclooctene as a representative system which can provide extensive information concerning the effects of temperature and chiral auxiliary on the ee of the product.

Stereochemical correlation. The chiral photosensitizers employed in the enantiodifferentiating photoisomerization of cyclooctene can be classified into two categories,[22] according to the temperature dependency of the ee of **1E** obtained. As shown in Fig. 1, non-*ortho* benzene(poly)carboxylate sensitizers give only small ee values and low gradient slopes in the Eyring plots, where the T_0 does not exist at all, or appears only at an extreme temperature. In contrast, *ortho*-benzenepolycarboxylates, such as **3**, **7** and **8**, give much higher ee's and steep slopes, and the product chirality is often switched at a readily accessible temperature. Since this contrasting behavior originates from the entropy term alone, it is probable that different enantiodifferentiation mechanism operates for the *ortho* and non-*ortho* sensitizers, from the conformational point of view.

In order to elucidate whether or not the absolute configuration of product **1E** can be correlated directly and globally to that of the stereogenic center of the relevant chiral sensitizer, the data reported for the enantiodifferentiating photoisomerization of **1Z** sensitized by chiral benzene(poly)carboxylates in different solvents at ambient and low temperatures are

summarized in Table 2.[22b,c] The sensitizers that carry phenyl group(s) in the chiral auxiliary are not included in this Table, nor in the following discussion, since they are known to form an intramolecular exciplex, to which the substrate **1Z** approaches from the phenyl side.[22c]

Firstly, the author will consider the stereochemical consequence observed upon sensitization with the non-*ortho* sensitizers (**2**, **4**, **5** and **7**). As demonstrated by several representative examples, these sensitizers do not exhibit chirality inversion behavior caused by a change in temperature. It is reasonable, therefore, to discuss the relationship between the absolute configuration of **1E** obtained at any temperature with that of the stereogenic center of the sensitizer. In examining this correlation, the author will take into account only the stereogenic center directly connected to the ester oxygen of the relevant sensitizer when the chiral auxiliary has many such centers. This approach may be justified, since the configuration around the stereogenic center nearest to the benzenecarboxylate chromophore is expected, in general, to dominate the steric interactions in the exciplex intermediate. After examining the data for 23 different non-*ortho* sensitizers in a variety of solvents, the author found a perfect stereochemical correlation between the stereogenic centers of the relevant sensitizer and product, in spite of the low ee's obtained. Thus, non-*ortho* sensitizers with *R*-configuration at the nearest stereogenic center afford (*R*)-(–)-**1E** without exception, and the opposite is true of *S*-configuration sensitizers.

Encouraged by the above result, the author made further attempts to understand the seemingly complex stereochemical outcome observed for *ortho* sensitizers (*i.e.* **3**, **7** and **8**). *Ortho* sensitizers are known to cause the chirality inversion of product through a change in the reaction temperature as a consequence of the significant contribution of the entropy term. However, the entropic contribution is minimized or made negligible at temperatures below T_0. Under these conditions, the absolute configuration of the chiral sensitizer correlates to that of **1E**. Examining the results for the *ortho* sensitizers presented in Table 1, a highly consistent stereochemical correlation was observed again. Apart from those sensitizers that possess highly congested secondary and tertiary chiral auxiliaries, *e.g.* the *endo,endo*- and *exo,exo*-3-cyclohexylmethyl-2-bornyl, cedryl, 2-dicyclohexylmethyl-5-methylcyclohexyl and isopinocamphenyl auxiliaries, the other 21 *ortho* sensitizers completely obey a rule which is

Table 2 Enantiodifferentiating Photoisomerization of **1Z** Sensitized by Chiral (Poly)alkyl Benzene(poly)carboxylates in Pentane at Ambient and Low Temperatures

sensitizer					product **1E**	
com-pound	R* (X)	configu-ration[a]	solvent	temper-ature/°C	% ee[b]	configu-ration[c]
2	(–)-bornyl (H)	*R*	pentane	25	-1.0	*R*
	(–)-cholesteryl (H)	*R*	pentane	25	-0.04	*R*
	(–)-1,3-diphenyl-1,3-propanediyl[d] (H)	*S*	pentane	25	+1.2	*S*
	(+)-isomenthyl (H)	*S*	pentane	25	+0.96	*S*
	(–)-menthyl (H)	*R*	pentane	25	-2.7	*R*
				-25	-3.0	*R*
			cyclohexane	25	-2.7	*R*
	(–)-menthyl (2-Meo)	*R*	pentane	25	-2.1	*R*
	(–)-menthyl (4-Meo)	*R*	pentane	25	-4.3	*R*
	(–)-menthyl (2-OH)	*R*	pentane	25	-7.0	*R*
				-60	-25.3	*R*
	(–)-menthyl (2-Me)	*R*	pentane	25	-1.7	*R*
	(–)-menthyl (3-Me)	*R*	pentane	25	-4.2	*R*
	(–)-menthyl (4-Me)	*R*	pentane	25	-3.7	*R*
	(–)-menthyl (4-*t*-Bu)	*R*	pentane	25	-3.5	*R*
	(–)-menthyl (4-F)	*R*	pentane	25	-2.1	*R*
	(–)-menthyl (2-CF_3)	*R*	pentane	25	-0.7	*R*
	(–)-menthyl (3-CF_3)	*R*	pentane	25	-2.6	*R*
	(–)-menthyl (4-CF_3)	*R*	pentane	25	-3.9	*R*
				-60	-4.4	*R*
	(–)-menthyl (4-CN)	*R*	pentane	25	-3.3	*R*
	(–)-menthyl (3,5-$(CF_3)_2$)	*R*	pentane	25	-2.4	*R*
	(+)-neomenthyl (H)	*S*	pentane	25	+0.1	*S*
3	(–)-bornyl	*R*	pentane	25	+7.6	*S*
				-60	+24.0	*S*
	(–)-menthyl	*R*	pentane	25	+3.8	*S*
				-60	+10.3	*S*
	(–)-menthyl,methyl[e]	*R*	pentane	25	+3.0	*S*
				-60	+10.8	*S*
4	(–)-menthyl	*R*	pentane	25	-4.4	*R*
5	(–)-menthyl	*R*	pentane	25	-6.0	*R*
				-40	-8.2	*R*

			cyclohexane	25	-5.9	*R*
			acetonitrile	25	-7.1	*R*
				-40	-8.5	*R*
			methanol	25	-5.8	*R*
	(–)-menthyl, methyl[e]	*R*	pentane	25	-3.0	*R*
				-40	-4.0	*R*
6	(–)-menthyl	*R*	pentane	25	-3.4	*R*
7	(–)-(1*S*,2*R*,3*S*)-*endo*-3-(cyclohexylmethyl)-*endo*-2-bornyl	*R*	pentane	25	-19.5	*R*
				-40	-18.7	*R*
	(–)-(1*S*,2*R*,3*R*)-*exo*-3-(cyclohexylmethyl)-*endo*-2-bornyl	*R*	pentane	25	+13.1	*S*
				-88	+53.3	*S*
	(–)-(1*S*,2*S*,3*R*)-*endo*-3-(cyclohexylmethyl)-*exo*-2-bornyl	*S*	pentane	25	+6.9	*S*
				-88	-18.6	*R*
	(–)-(1*S*,2*S*,3*S*)-*exo*-3-(cyclohexylmethyl)-*exo*-2-bornyl	*S*	pentane	25	+22.9	*S*
				-88	+51.4	*S*
	(–)-bornyl	*R*	pentane	25	+11.5	*S*
				-88	+40.6	*S*
	(+)-cedryl	*R*	pentane	-86	-22.5	*R*
	(+)-1-cyclohexylethyl	*S*	pentane	25	+1.8	*S*
				-86	-11.4	*R*
	(–)-(1*R*,2*S*,5*R*)-8-cycrohexylmenthyl	*R*	pentane	25	+49.2	*S*
				-89	+63.5	*S*
	(–)-(1*R*,2*S*,5*R*)-2-(dicyclohexylmethyl)-5-methylcyclohexyl	*R*	pentane	-40	+3.3	*S*
				-86	-14.8	*R*
	(+)-1,2-dimethylpropyl	*S*	pentane	25	+3.1	*S*
			pentane	-87	-16.1	*R*
	(–)-fenchyl	*S*	pentane	25	-0.9	*R*

			pentane	-86	-8.0	*R*
	(+)-isomenthyl	*S*	pentane	25	+6.0	*S*
			pentane	-88	-4.5	*R*
	(+)-isopinocampheyl	*S*	pentane	25	+4.2	*S*
			pentane	-87	+4.4	*S*
	(–)-menthyl	*R*	pentane	25	-9.6	*R*
				-90	+28.5	*S*
			heptane	25	-8.8	*R*
				-87	+30.7	*S*
			decane	25	-8.7	*R*
				-30	+7.1	*S*
			hexane	-85	+3.8	*S*
			isooctane	25	-14.2	*R*
				-87	+5.4	*S*
			isopentane	25	-13.1	*R*
				-87	+10.0	*S*
	(+)-1-(methoxycarbonyl)ethyl	*S*	acetonitrile	25	-5.7	*R*
				-40	-13.2	*R*
	(+)-1-methylheptyl	*S*	pentane	25	+1.5	*S*
				-85	-24.3	*R*
	(–)-1-methylheptyl	*R*	pentane	25	-1.2	*R*
				-86	+24.0	*S*
			acetonitrile	25	-0.8	*R*
				-40	+5.6	*S*
			methanol	25	-0.03	*R*
				-86	+13.2	*S*
	(+)-1-methylnonyl	*S*	pentane	25	+1.2	*S*
				-87	-27.0	*R*
	(+)-1-methylpentyl	*S*	pentane	25	+1.8	*S*
				-90	-26.3	*R*
	(+)-1-methylpropyl	*S*	pentane	25	-0.01	*R*
				-80	-13.4	*R*
	(+)-neomenthyl	*S*	pentane	25	-8.4	*R*
				-88	-6.2	*R*
	(+)-1,2,2-trimethylpropyl	*S*	pentane	25	+11.6	*S*
			pentane	-86	-15.6	*R*
8	(–)-bornyl	*R*	pentane	25	+7.7	*S*

			-86	+47.0	*S*
(–)-menthyl	*R*	pentane	25	-16.8	*R*
			-86	+28.3	*S*
(–)-1-methylheptyl	*R*	pentane	25	+5.1	*S*
			-87	+52.7	*S*
(–)-1-(methoxycarbonyl)ethyl	*S*	acetonitrile	25	-4.9	*R*
			-40	-20.1	*R*

[a] Absolute configuration of the stereogenic center connected directly to the ester oxygen. [b] Enantiomeric excess of **1E**. Positive and negative signs for ee correspond to the formation of (*S*)-(+)- and (*R*)-(–)-isomers, respectively. [c] Absolute configuration of **1E**. [d] Dibenzoate. [e] Mixed ester.

opposite to that observed for the non-*ortho* sensitizers, *i.e.* *ortho* sensitizers with *R*-configuration afford (*S*)-(–)-**1E**.

These two mutually opposing stereochemical correlations, which are separately applicable to non-*ortho* and *ortho* sensitizers, urged us to derive plausible models which are compatible with them. A similar attempt to derive an exciplex model for a non-*ortho* sensitizer has already been carried out for (–)-menthyl benzoate, where an interaction of the ester carbonyl of excited benzoate with the C=C bond of **1Z** was proposed.[22b] This model is based on the fact that the ee values obtained upon sensitization with (–)-menthyl methyl terephthalate are exactly half of the values obtained with the (–)-dimenthyl analogue at all temperatures examined, and that a semiempirical MNDO calculation for methyl benzoate indicates a good match between the MO lobes of the ester carbonyl and the C=C bond of **1Z**.[22b] In the present study, the author carried out the MO recalculations on methyl benzoate and phthalate in the excited singlet state, using the PM3 program (MOPAC). The results are mostly consistent with the previous ones,[22b] except for the highly developed antibonding lobes on the carbonyl and the different pattern of the aromatic lobes in HSOMO. However, steric interactions in (–)-menthyl benzoate and phthalate are better evaluated by MM2 calculations to give the optimized conformations shown in Fig. 3. As can be seen from the front view (Fig. 3a, bottom), the lower side of menthyl benzoate is covered by the menthyl isopropyl group preventing the approach of cyclooctene molecule to the ester carbonyl. If the top view is considered, it appears that the interaction of **1Z** with the C=O

bond from the front side and the subsequent rotation of the C=C bond to the open side in the exciplex affords (*R*)-**1E**, in accord with the experimentally observed configuration. In the dimenthyl phthalate case (Fig. 3b), the optimized conformation is substantially different from that of the benzoate due to steric hindrance between the adjacent menthoxycarbonyl groups. Thus, the two ester groups are non-equivalent, with one carbonyl orientated inside and the other outside. It is assumed that the less hindered C=O group, which is directed outwards, can interact with cyclooctene molecule from the open face, forming the exciplex (Fig. 3b). The

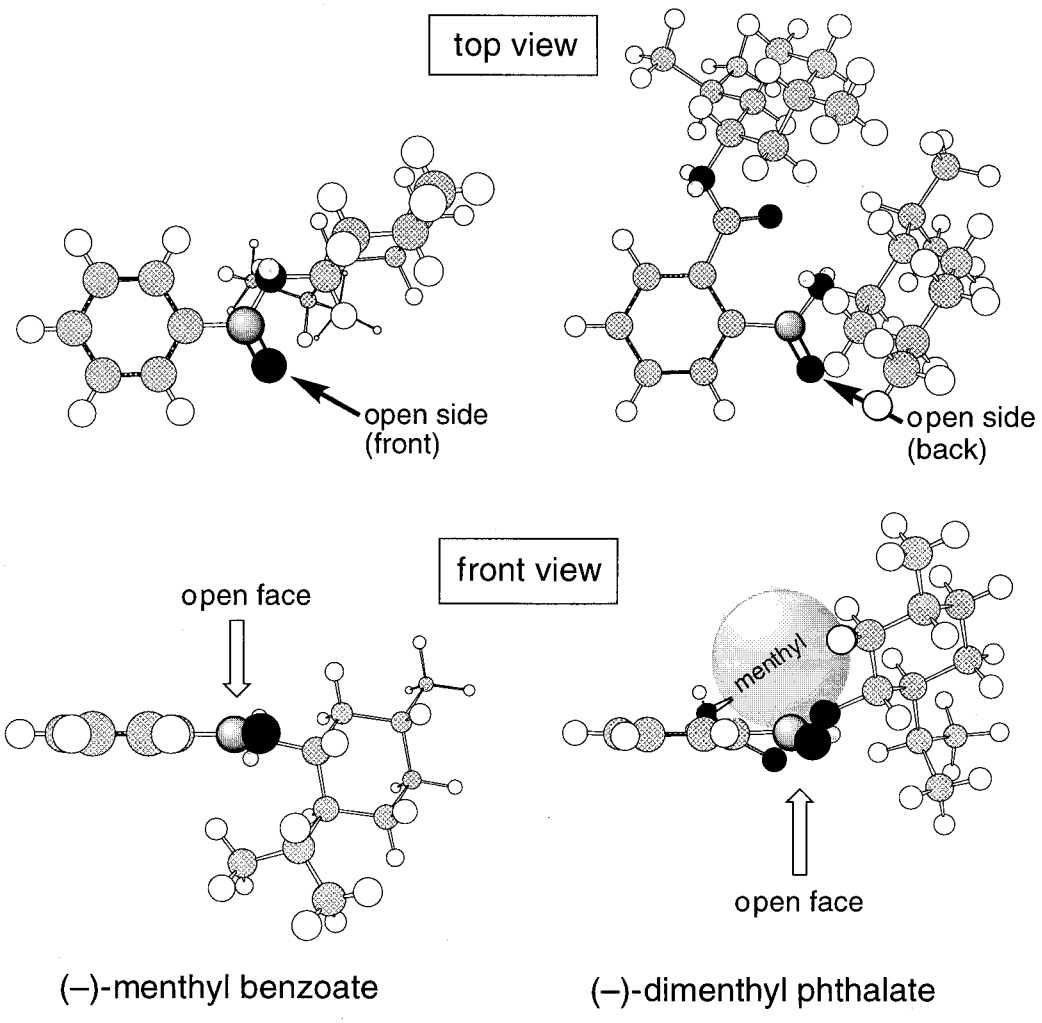


Fig. 3 Top and front views of MM2-optimized structures of (–)-menthyl benzoate **2** and phthalate **7**. In the latter structure, the shaded sphere represents the menthyl group located in the backside.

subsequent rotation in the exciplex towards the open side of the menthyl group results in the formation of (*S*)-**1E**, as observed experimentally at temperatures lower than T_0.

In view of the low ee's obtained, especially for non-*ortho* sensitizers, other rationales cannot be ruled out absolutely. However, the author could not find any other model which was compatible with all of the experimental and MO calculation data.

The effect of pressure. In the preceding sections, the author has demonstrated that weak interactions in the exciplex intermediate can be controlled by temperature as a result of the contribution of the entropy term. In this context, it is interesting to study the way in which pressure can be used as an alternative tool for controlling the weak interactions that determine the stereochemical outcome in the excited state. Although pressure effects upon thermochemical and photochemical reactions have been studied in considerable detail,[34] very little effort has been extended to enantiodifferentiating photochemical reactions until recently, probably as a result of the low ee's reported for such processes. However, the author has recently discovered that the enantiodifferentiating photoisomerization of **1Z** (shown in Scheme 1) is significantly affected by pressure, resulting in the inversion of product chirality.[32]

The pressure effect on the relative rate constant, k_S/k_R (Scheme 2), can be expressed as a linear function of pressure (P) at a constant temperature,[32]

$$\ln (k_S/k_R) = -(\Delta\Delta V^{\ddagger}_{S\text{-}R}/RT)P + C \qquad (3)$$

where $\Delta\Delta V^{\ddagger}_{S\text{-}R}$ represents the difference in activation volume and C is equal to $\ln (k_S/k_R)$ at P = 0. The effect of hydrostatic pressure of up to 400 MPa was investigated in the enantiodifferentiating photoisomerization of **1Z** sensitized by chiral benzene(poly)carboxylates.[32] According to eqn. 4, the $\ln (k_S/k_R)$ values obtained were plotted against pressure.

As can be seen from Fig. 4, variations in the reaction pressure significantly affect the ee of **1E**, and often the product chirality is switched at the equipodal pressure (P_0) upon sensitization with *ortho* benzenepolycarboxylates (**3**, **7**, **8**). However, ee's obtained for non-*ortho* sensitizers (**2**, **4**, **5**) were generally small and insensitive to pressure changes. This contrasting

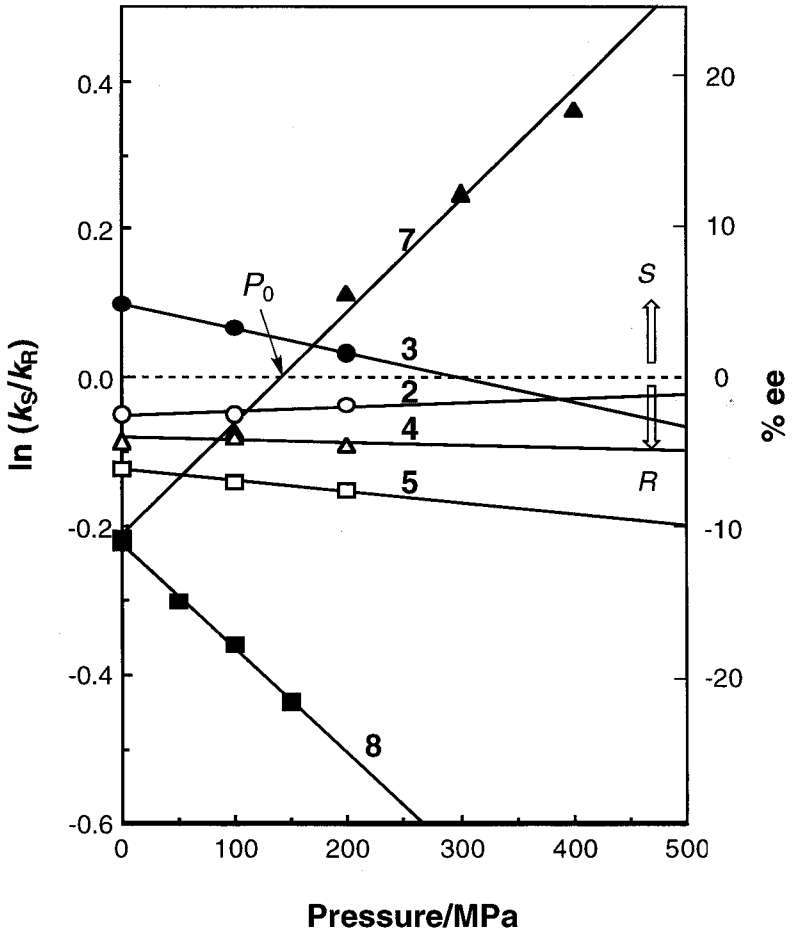


Fig. 4 Pressure dependence of the ee of the product in enantiodifferentiating photoisomerization of cyclooctene (**1Z**) sensitized by (–)-menthyl benzoate **2** (○), phthalate **3** (●), isophthalate **4** (△), terephthalate **5** (□), 1,2,4,5-benzenetetracarboxylate **7** (▲), and benzenehexacarboxylate **8** (■) in pentane at 25 °C; the chirality of product **1E** was switched at the equipodal pressure (P_0).

behavior of the *ortho* and non-*ortho* sensitizers is similar to that observed for the temperature dependency of ee, again indicating a significant contribution of the entropy factor in the enantiodifferentiating process. However, the differential activation parameters obtained from the temperature- and pressure-dependence experiments,[22b,32] which are listed in Table 1, behave quite differently. Indeed, inconsistencies become evident particularly in the parameters obtained for *ortho* esters, as sensitizers that give large $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values do not always show a strong pressure dependency, and no consistent relationship is found for the signs of $\Delta\Delta H^{\ddagger}$ or $\Delta\Delta S^{\ddagger}$ and $\Delta\Delta V^{\ddagger}$.

Multidimensional control of product chirality. The above discrepancy observed for temperature and pressure is not surprising, since both can be regarded as inherently independent variables. In order to verify this experimentally, and also to reveal the relationship between the ee of the product and these variables, the author further investigated the effect of pressure on the enantiodifferentiating photoisomerization at several different temperatures, and found that the $\Delta\Delta V^{\ddagger}$ value depends critically on the reaction temperature.[32] From the data obtained, novel three-dimensional diagrams that correlate the ee with temperature and pressure were constructed for all possible cases. Two representative cases, which show inversion of the product chirality by temperature and/or pressure, are illustrated schematically in Fig. 5. In both cases, the enantiodifferentiating event occurs exclusively on one of the two intersecting planes that correspond to the antipodal sensitizers, and these two enantiodifferentiation planes are

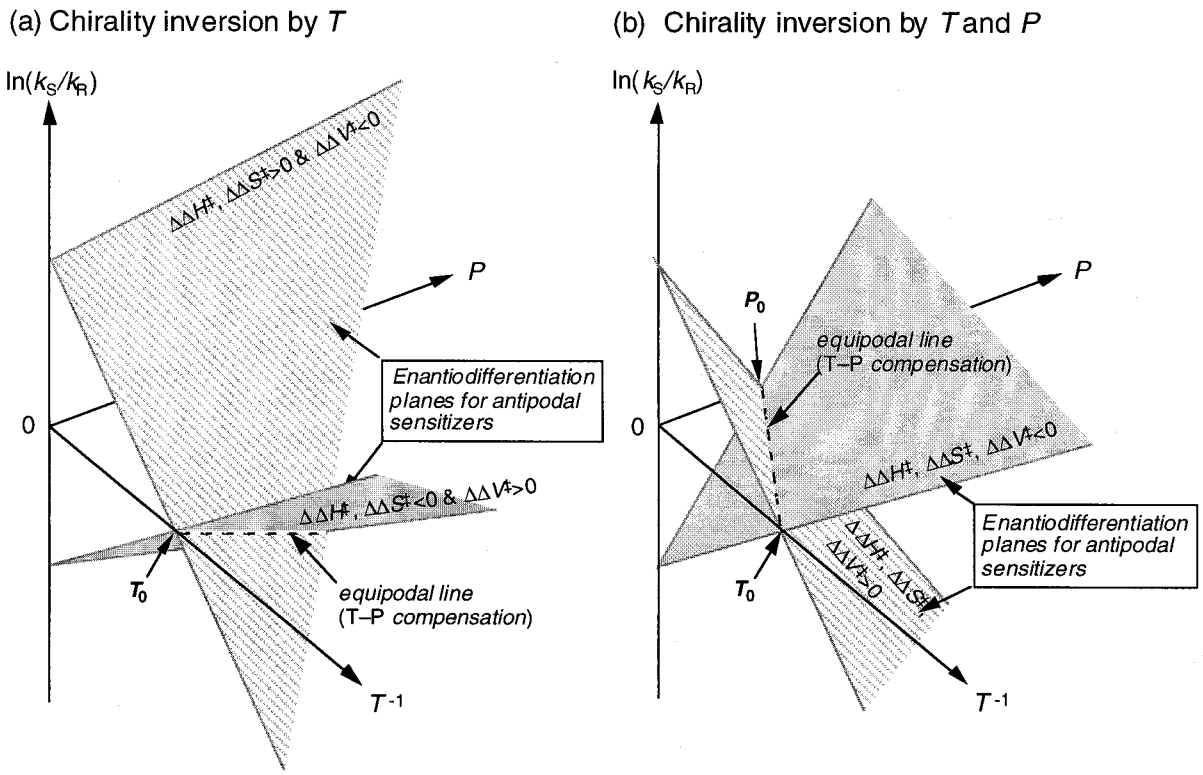


Fig. 5 Representative T^{-1}-P- $\ln(k_S/k_R)$ diagrams, correlating the ee of **1E** with temperature and pressure in the enantiodifferentiating photoisomerization of **1Z** sensitized by antipodal sensitizers; (a) the product chirality is inverted only by temperature as the signs of $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ are opposite to that of $\Delta\Delta V^{\ddagger}$; (b) the chirality is inverted by both temperature and pressure as the signs of $\Delta\Delta H^{\ddagger}$, $\Delta\Delta S^{\ddagger}$ and $\Delta\Delta V^{\ddagger}$ are all the same.

symmetrical to each other with respect to the T^{-1}–P plane. The temperature and pressure drive the product's ee in opposite directions in Fig. 5a, where they act as independent factors, or in the same direction in Fig. 5b. In spite of the limited number of sensitizers examined, a (–)-menthyl benzenetetracarboxylate sensitizer provides us with fortuitous example, in which the ee of **1E** increases with decreasing temperature and increasing pressure, ultimately affording an extrapolated ee as high as 98.3% under conditions which are practically accessible, *i.e.* -9 ℃ and 1500 MPa.[32]

Conclusions

From the extensive experiments and comprehensive analyses of a variety of enantio- and diastereodifferentiating photochemical reactions,[20-32] it has been revealed that the entropy term plays unexpectedly vital role in the stereodifferentiating processes where weak interactions determine rates and equilibria. However, it is important to emphasize that at temperatures below T_0, the stereoselectivity is dominated by the enthalpy difference arising mostly from steric and electrostatic interactions, while the dynamic behavior of stereoselectivity over the whole temperature range, including the chirality switching phenomenon, is exclusively attributable to the entropy difference.

Experimental verification that temperature and pressure can function indeed as independent, yet cooperative, factors governing the product chirality in the enantiodifferentiating photosensitization gives us the new and versatile methodology of 'multidimensional control of asymmetric photochemistry'.[32] This strategy employs several entropy-related factors, such as temperature,[35] pressure, solvent,[36] concentration[37] and substituent flexibility, as tools for controlling the stereochemistry and stereoselectivity of photoproducts more conveniently and effectively through the manipulation of the steric and electronic weak interactions involved in the exciplex intermediates. Further, the concept of multidimensional control is not necessarily restricted to the asymmetric photochemical reactions described in this paper, but may be applied in general to any thermal and biochemical reaction or equilibria where weak interactions are the principal driving force or determining factor, and therefore, where the entropy factor plays a major role.[38]

Experimental Section

Instruments. Specific rotations were determined on a Perkin-Elmer model 243B polarimeter with a temperature-controlled 10 cm cell. Gas chromatographic (GC) analyses of photolyzed samples were performed on a Shimadzu GC-6A or GC-14B instrument with a packed or chiral capillary column.

Materials. Hydrocarbon solvents were purified by treatment with concentrated sulfuric acid and subsequent fractional distillation. Acetonitrile was fractionally distilled from diphosphorus pentaoxide. Methanol was refluxed with magnesium turnings and distilled fractionally.

(*Z*)-Cyclooctene **1Z** (Nakarai) was purified by silver nitrate treatment followed by fractional distillation. 1,1-Diphenyl-1-alkenes **9-11** were synthesized by dehydration of the corresponding 1,1-diphenyl-1-alkanols which were prepared by the Grignard reactions of the corresponding ketones with the appropriate alkyl bromides.[25b]

The chiral benzene(poly)carboxylates **2-7** and chiral naphthalene(di)carboxylates **15-17**, **19**, **20** were prepared from the corresponding acid chlorides and optically pure alcohols in pyridine.[25b,39] The highly congested benzenehexacarboxylates **8** and 1,8-naphthalenedicarboxylates **18** were synthesized in reactions of corresponding acid chloride with potassium alkoxides in the presence of 18-crown-6.[39] The mixed esters **3** and **5** (R = (–)-menthyl, methyl) were synthesized by esterification in pyridine of acid chloride of respective hydrogen methyl esters.

Photoisomerization of cyclooctene. All irradiations were conducted in a thermostated water or methanol bath. A solution containing **1Z** (200 mM) and an optically active sensitizer (2-5 mM) was irradiated under an argon atmosphere in an annular quartz vessel using 30 W low-pressure mercury lamp fitted with a Vycor sleeve. After irradiation, **1E** was extracted from the solution with three portions of 20% aqueous silver nitrate at 0 °C.[40] The combined aqueous extracts were washed with three portions of pentane and then added dropwise into concentrated ammonium hydroxide at 0 °C to liberate **1E**, which was in turn

extracted with three portions of pentane. Upon evaporation of the solvent at a reduced pressure > 150 Torr, a crude product was obtained and subjected to bulb-to-bulb distillation in vacuo to yield **1E** of chemical purity up to 95-99%.

Optical rotation of the isolated **1E** was measured in methylene chloride, corrected for the purity, and compared with the literature value: $[\alpha]_D^{25}$ -426° (CH_2Cl_2).

Photoaddition of alcohol to 1,1-diphenylalkene. All irradiations were carried out in a temperature-controlled water (25 °C), methanol/2-propanol (-40 °C) and methanol/ethanol (-68 °C) bath. The light sources employed were a conventional 300 W high-pressure mercury lamp for irradiations at 25 °C and an equivalent lamp fitted with a transparent Pyrex vacuum sleeve designed for low-temperature irradiation (Eikosha). A solution (4 or 300 mL), containing 1,1-diphenylalkene **9-11** (20 mM), alcohol (0.5 mM), optically active sensitizer (3 mM), and cyclododecane (3 mM) added as an internal standard, was irradiated at >300 nm under an argon atmosphere in a Pyrex tube (1 cm i.d.) placed near the lamp surface or in an annular Pyrex vessel surrounding the lamp, the whole system being immersed in the cooling bath.

Enantiomeric excesses of **12a-d**, **13a-b** and **14a** were determined by gas chromatography over a 15 m chiral capillary column (TCI Chiraldex B-DA) at 145 °C.

Photoisomerization of cyclooctene under high pressure. All irradiations were conducted in a pressure vessel HKP-921208 designed and manufactured by Hikari Koatsu Co., which was equipped with a sapphire window (5 mm i.d.) for external irradiation, and also with a coolant circulation system in the body of the reactor. A solution (11 cm^3) of (*Z*)-cyclooctene (5 mM), containing optically active sensitizer (0.2-1.0 mM) and cycloheptane added as an internal standard, was placed in the vessel, and pressurized up to 400 MPa with a high-pressure pump KP5B, thermostated at a constant temperature between +25 to -10 °C by circulating water or water-methanol coolant through the reactor body. The solution was then irradiated for a given period of time with a 250 W high-pressure mercury arc (Ushio UI-501C). The collimated incident beam from lamp housing was focused with a quarts lens (f 16.5 cm) which was placed in front of the sapphire window, allowing an efficient irradiation.

(*E*)-isomer **1E** was selectively extracted from the irradiated solution with 2 cm^3 portion of 20% aqueous silver nitrate at <5 °C. The aqueous extract was washed with two 1 cm^3 portion of

pentane and then added to concentrated ammonium hydroxide (1 cm^3) at 0 °C to liberate a chemically pure sample of **1E** (>99%), which was in turn extracted with a small portion (0.1-0.5 cm^3) of pentane. Enantiomeric excess of **1E** was determined by gas chromatography over a 30 m chiral capillary column (Supelco β-DEX 120) at 60 °C.

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General Conclusions

In contrast to the relatively widely explored unimolecular enantiodifferentiating photochemical reactions, only a few attempts have been reported on the bimolecular enantiodifferentiating photochemical reactions, giving very low optical yields. The major purpose of this study is to find a general strategy for obtaining high chemical and optical yields and also to elucidate the factors and mechanism that govern the uni- and bimolecular asymmetric photochemical processes. The novel findings and major conclusions presented in this thesis are summarized below.

In Chapter 1, the photosensitized enantiodifferentiating polar additions of alcohols to 1,1-diphenyl-1-alkenes were performed over a range of temperatures in the presence of chiral naphthalene(di)carboxylate photosensitizers, giving the corresponding chiral anti-Markovnikov adducts with optimized ee's of up to 33%. An unusual switching of product chirality was found to occur by changing irradiation temperature, which leads to antipodal products at different temperatures, often affording higher ee's at higher temperatures. The differential activation parameters for the enantiodifferentiation process, which were determined by the Eyring treatment of the temperature-dependent ee values obtained, clearly demonstrate that the unusual temperature switching behavior of the product chirality is entropic in origin. Factors controlling the product ee were extensively surveyed, and the steric demands and/or electronic structures of sensitizer, substrate, and alcohol, the solvent polarity, the alcohol concentration, and the irradiation temperature were all shown to play crucial roles. The detailed reaction mechanism and excited states involved and the origin of enantiodifferentiation, as well as the reaction kinetics and energetics, were fully elucidated for the first time from the fluorescence quenching and lifetime measurement of both sensitizer and exciplex in the presence/absence of added alcohol. A new strategy has also be developed to overcome the normally accepted trade-off between the chemical and optical yields in this typical radical ion-mediated photoaddition. This is accomplished by introducing polar chiral auxiliaries in sensitizer molecule, which enhance the "microenvironmental polarity" around the chromophore, keeping bulk polarity low.

In Chapter 2, the enantiodifferentiating photosensitized cyclodimerization of 1,3-cyclohexadiene was performed over a range of temperatures in the presence of chiral arene(poly)carboxylates, giving *endo*- and *exo*-[4+2] cyclodimers and *anti*- and *syn*-[2+2] cyclodimers. Among the three chiral cyclodimers, only *exo*-isomer was obtained as an optically active species with ee of up to 8.2%. The detailed reaction mechanism and the origin of the enantiodifferentiation have been elucidated. It has also been shown that the "microenvironmental polarity" around the chromophore plays a crucial role in determining the photoreactivity and the ee of the product.

In Chapter 3, the photosensitized cyclodimerization of (*Z*)-cyclohexene 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. Of the two chiral cyclodimers, only *trans-anti-trans* isomer was obtained as an optically active species with enantiomeric excesses as high as 68.3% at –78 °C, whereas *cis-trans* isomer was consistently racemic under various reaction conditions employed. The detailed reaction mechanism and the origin of enantiodifferentiation have been elucidated to involve the initial enantiodifferentiating photoisomerization of (*Z*)-cyclohexene to the highly reactive (*E*)-isomer and the subsequent stereospecific concerted cyclodimerization with (*Z*)-isomer giving optically active *trans-anti-trans* cyclodimer which is competing with the non-stereospecific stepwise cyclodimerization to racemic *trans-anti-trans* and *cis-trans* isomer.

In Chapter 4, the effect of temperature on optical yield was investigated over a wide range. The absolute configuration of photoproduct was frequently inverted at a critical temperature (T_0), above which the optical yield increased with increasing temperature. The widespread hypothesis that "lowering temperature leads to higher optical yield" was demonstrated not to be true in the photosensitized photoaddition reaction as well as in photoisomerization reactions. The Eyring treatment of the relative rate constant for the production of each enantiomer revealed that the unusual temperature dependency originates from the non-zero differential entropy of activation for the enantiodifferentiating process. In this case, the enthalpy term dominates at lower temperatures, while the entropy term becomes more important above T_0, switching the product chirality. The absolute configuration of photoproduct

obtained at temperatures lower than T_0 was correlated to that of chiral sensitizer, except for those containing extremely bulky chiral auxiliaries, and the stereochemical outcomes are discussed on the basis of the molecular model examinations. Interestingly, similar switching behavior was induced by varying the hydrostatic pressure of the irradiating solution from 0.1 to 400 MPa. The pressure effect was investigated at different temperatures to construct three-dimensional diagrams that correlate the optical yield with temperature and pressure as mutually independent factors. The combined use of temperature and pressure provides us with a convenient, powerful tool for controlling the product chirality and optical yield in asymmetric photochemistry.

Finally, the author hopes that these findings and concepts described in this thesis greatly contribute to the further development of this relatively unexplored area of photochemistry and also to the deeper and more comprehensive understanding of the roles of entropy in both thermal and photochemical enantiodifferentiation processes.

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