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Citation	大阪大学, 2008, 博士論文
Version Type	VoR
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Studies on Photochirogenesis Controlled by Clustering Effect in Supercritical Carbon Dioxide

(超臨界二酸化炭素中でのクラスタリング効果による
不斉光化学反応制御に関する研究)

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Department of Applied Chemistry
Osaka University

January, 2008

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Preface

This thesis work on photochirogenesis in near-critical and supercritical carbon dioxide (nc- and $scCO_2$) has been carried out under the supervision of Professor Yoshihisa Inoue during 2002-2008 at the Department of Applied Chemistry, Osaka University, and in part Professor Frank V. Bright at the Department of Chemistry, State University of New York at Buffalo, New York, USA during the summer of 2007 as a JSPS predoctoral fellow.

This thesis deals with the fine control of photochirogenesis by clustering in nc- and $scCO_2$. In this study, the author has demonstrated that "clustering", which is unique to these unconventional media, can be used as a crucial and effective, yet convenient, tool for critically controlling the molecular chirality in asymmetric photochemical reactions.

It is a sincere desire of the author that the present results, discussion, and conclusions described in this thesis greatly contribute to further understanding and future development of (photo)chirogenesis and (photo)chemistry in both nc- and $scCO_2$.

Yasuhiro Nishiyama

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Osaka University
January, 2008

List of Publications

1) Pressure Control of Enantiodifferentiating Polar Addition of 1,1-Diphenylpropene Sensitized by Chiral Naphthalenecarboxylates
   Masayuki Kaneda, Yasuhiro Nishiyama, Sadayuki Asaoka, Tadashi Mori, Takehiko Wada, and Yoshihisa Inoue
   Org. Biomol. Chem. **2004**, *2*, 1295-1303.
2) Enantiodifferentiating Photoaddition of Alcohols to 1,1-Diphenylpropene in Supercritical Carbon Dioxide: Sudden Jump of Optical Yield at the Critical Density
   Yasuhiro Nishiyama, Masayuki Kaneda, Ryota Saito, Tadashi Mori, Takehiko Wada, and Yoshihisa Inoue
   J. Am. Chem. Soc. **2004**, *126*, 6568-6569.
3) Mechanistic Study on the Enantiodifferentiating Anti-Markovnikov Photoaddition of Alcohols to 1,1-Diphenyl-1-alkenes in Near Critical and Supercritical Carbon Dioxide
   Yasuhiro Nishiyama, Masayuki Kaneda, Sadayuki Asaoka, Ryota Saito, Tadashi Mori, Takehiko Wada, and Yoshihisa Inoue
   J. Phys. Chem. A, **2007**, *121*, 13432-13440.
4) Critical Control by Temperature and Pressure of Enantiodifferentiating Anti-Markovnikov Photoaddition of Methanol to Diphenylpropene in Near Critical and Supercritical Carbon Dioxide
   Yasuhiro Nishiyama, Takehiko Wada, Tadashi Mori, and Yoshihisa Inoue
   Chem. Lett. **2007**, *36*, 1488-1489.
5) Enantiodifferentiating Intramolecular Photocyclization of ω-Hydroxy-1,1-diphenyl-1-alkenes Sensitized by Chiral Naphthalenecarboxylates
   Yasuhiro Nishiyama, Shigenori Shiraishi, Sadayuki Asaoka, Tadashi Mori, Takehiko Wada, and Yoshihisa Inoue
   In preparation
6) Entrainer Effect on Enantiodifferentiating Intramolecular Photocyclization in Supercritical Carbon Dioxide
   Yasuhiro Nishiyama, Takehiko Wada, Tadashi Mori, and Yoshihisa Inoue
   In preparation

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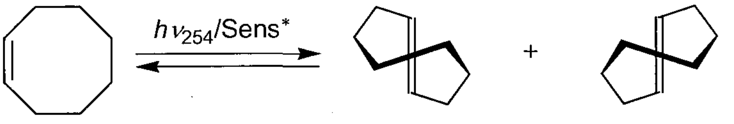
General Introduction

Recently, optically active compounds are indispensable in the fields of medical, pharmaceutical, agricultural and other chemistry-related science and technology. The most versatile way for preparing those compounds is conventional asymmetric synthesis thermally driven by chirally modified organic and transition metal catalysts and by enzymes, which were already demonstrated to give satisfactorily high enantioselectivities in several cases.[1]

Photochemical asymmetric synthesis, or photochirogenesis,[2] proceeding through the electric excited state and thus affording unique and/or highly strained photoproducts, have several advantages over the thermal counter as an alternative methodology to obtain optically active compounds. Among the several approaches to accomplish photochirogenesis, chiral photosensitization is an attractive method for efficiently transfer and multiply the molecular chirality of a chirogen to a product. Since the first example of asymmetric photosensitization reported by Hammond and Cole in 1965,[3] a considerable amount of effort has hitherto been devoted to this area of chemistry, but the enantiomer excess (ee) of the photoproduct obtained from such a process was consistently very low (<10%). However, Hoffmann and Inoue reported high ee's of up to 77% in the enantiodifferentiating *Z*-to-*E* photoisomerization of cycloheptene.[4] Furthermore, Inoue and coworkers reported a dramatic temperature dependence of the product's ee in the enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**) to (*E*)-isomer (**1E**) (Scheme 1) upon sensitization with optically active polyalkyl benzenepolycarboxylates, which often accompanies an inversion of the product's absolute configuration. They reported that this unprecedented chirality switching by temperature is induced by the difference in activation entropy between the diastereomeric transition states formed from substrate **1Z** and excited chiral sensitizer.[5] In more recent studies, they elucidated that photochirogenesis can be critically controlled by several entropy-related factors, such as temperature,[5,6] solvation,[7] and pressure,[8] which are jointly used to enhance the product's ee.[6,9]



1Z (*R*)-(−)-**1E** (*S*)-(+)-**1E**

Scheme 1. Enantiodifferentiating geometrical photoisomerization of **1Z** sensitized by chiral photosensitizer.

In recent "green" chemical and chemical engineering systems against critical global environment, supercritical fluid (SCF), in particular supercritical carbon dioxide ($scCO_2$), has been employed as environmentally benign replacement for more traditional organic solvents, because of their mild condition for achieving the supercritical state (31 °C, 7.38 MPa), nontoxicity, nonflammable, abundance, low cost, and other favorable features. In addition to the environmental advantages of $scCO_2$ itself, the use of $scCO_2$ as a reaction medium for photochirogenic reactions is of particular interest from the entropic point of view, because the chemo-, regio-, and stereochemical fates of (photo)chemical reactions can be critically manipulated[10,11] by changing the medium property (density, dielectric constant, etc.) through alteration of pressure and/or temperature in a narrow range.[12-14] The use of $scCO_2$ provides us with a rare opportunity to inspect the effects of dynamic density-fluctuation and clustering, which are unique to SCFs, on photochirogenic reactions by examining the product's ee. This was examined only briefly by Saito et al. by using the photosensitized enantiodifferentiating unimolecular isomerization of (*Z*)-cyclooctene in $scCO_2$.[15] They demonstrated that the ee of (*E*)-isomer produced is extremely pressure-dependent particularly in the low-pressure region near the unit reduced density ($d_r = 1$). This extraordinary observation was tentatively rationalized in terms of the different degrees of CO_2 clustering around the exciplex intermediate in nc- and $scCO_2$ media. Although $scCO_2$ appeared to be an interesting and unique reaction medium for photochirogenesis, this reaction system has some limitations, as the benzenepolycarboxylate sensitizers are hardly soluble in nc/$scCO_2$ at pressures lower than 8 MPa and only weakly fluorescent, both of which unabled further in-depth examinations that are needed to elucidate the special roles of nc/$scCO_2$ in photochirogenesis.

In this thesis, the author has endeavored to elucidate the factors and mechanisms that control the photochirogenic processes occurring in nc- and $scCO_2$, to comprehensively understand the roles of clustering in the critical steps of photochirogenesis, and finally to establish a method for manipulating the enantiodifferentiating processes and the product's ee by utilizing the clustering effect as a new entropy-related factor.

In Chapter 1, the enantiodifferentiating photosensitized polar addition of various alcohols to some aromatic alkenes was examined as the first bimolecular photochirogenesis in nc/$scCO_2$ media to verify the influence of clustering effect as a new entropy-related factor. The stereochemical outcomes of the present photochirogenic reaction compared with the corresponding results obtained in conventional organic solvents.[8(d),16] Detailed fluorescence spectral analyses were also performed to reveal the nature of the excited sensitizers and exciplex intermediates in both nc- and $scCO_2$. The effects of CO_2 pressure, as an entropy-related factor, were also closely examined, since the medium properties of nc/$scCO_2$ are changed dramatically by an apparently small change of pressure.

In Chapter 2, the effects of temperature, which is also a typical entropy factor, were investigated in photochirogenesis in nc/$scCO_2$ media in order to clarify the roles of temperature in determining the product's ee, which was compared with those in conventional organic solvents. Similarly, the effects of concentration of alcohol added as a reagent were examined, since the alcohol added to nc/$scCO_2$ is expected to preferentially cluster around the exciplex intermediate to alter the microenvironmental polarity, the stereochemical consequence of which was detected by the changes in product's ee.

In Chapter 3, the intramolecular enantiodifferentiating photocyclization of aromatic alkenol was examined to investigate the influence of pure CO_2 clustering on the photochirogenic processes in $scCO_2$. More interestingly, the effects of entrainer (cosolvent) added to $sc/ncCO_2$ media on an asymmetric photoreaction were elucidated for the first time to give better product's ee's in the presence of entrainer.

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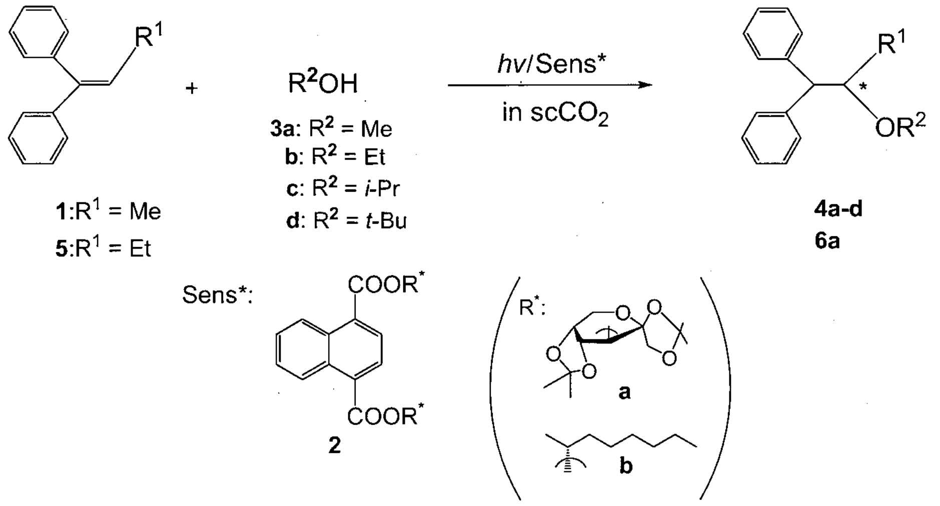
Chapter 1

Enantiodifferentiating Photosensitized Polar Addition of Alcohols to Aromatic Alkenes in ScCO$_2$: Pressure and Substituent Group Control

1-1. Introduction

In this chapter to expand the scope of photochirogenesis in SCF to bimolecular reaction system and also to elucidate the origin of the discontinuous pressure dependence of ee in scCO$_2$, the enantiodifferentiating photoaddition reaction of primary to tertiary alcohols (**3a**-**d**) to 1,1-diphenylpropene (**1**) and 1,1-diphenyl-1-butene (**5**) sensitized by chiral naphthalenedicarboxylates with saccharide (**2a**) and alkyl ester moieties (**2b**) under a variety of conditions at 45 °C (Scheme 1-1) was conducted. Furthermore, the author examined the photophysical behavior of chiral naphthalenedicarboxylate sensitizers and the exciplex intermediates derived therefrom.



Scheme 1-1. Enantiodifferentiating Photosensitized Polar Addition of Alcohols (**3**) to 1,1-Diphenylalkenes (**1** and **5**) in ScCO$_2$ at 45 °C.

This photochirogenic system is suitable for both spectral examinations and further mechanistic investigations, since the sensitizers and the exciplex intermediates are fluorescent and the product's ee is moderate to good even at ambient or higher temperatures and critically responds to the environmental factors, in particular, to the solvent polarity.[1,2] Taking these advantages, the author elucidates the vital roles of clustering in the photochirogenesis in SCF.

1-2. Results and Discussion

Effects of Alcohol's Bulk. It has been amply demonstrated that many photochirogenic reactions are critically affected by temperature and higher ee's are often obtained at lower temperatures.[3-7] In this context, SCF as a reaction medium appears to have an inherent limitation in available temperature range, which is higher than the critical point (T_c = 31 °C at P_c = 7.38 MPa for CO_2). Hence, the author should use such a chiral photoreaction system that affords reasonably high ee's at ambient and higher temperatures in order to seriously examine the effects of clustering on the photochirogenic process in SCF media. Fortunately, it is known that the product's ee increases with increasing temperature in the polar photoaddition of alcohol to 1,1-diphenylpropene (**1**) sensitized by saccharide 1,4-naphthalenedicarboxylate.[1,2] By utilizing this relatively rare case, the author can closely investigate the effects of clustering and other entropy-related factors on the photophysical and photochemical behavior of excited sensitizer and exciplex intermediate in $scCO_2$.

The author first examined the bulkiness effect of alcohol **3** on the reactivity and the ee of adduct **4** produced upon photosensitization with diacetonefructosyl (DAF) 1,4-naphthalenedicarboxylate (**2a**, R* = 1,2:4,5-di-*O*-isopropylidene-α-D-fructopyranosyl) in $scCO_2$; the results obtained are summarized in Table 1-1.

Table 1-1. Enantiodifferentiating Photoaddition of Various Alcohols to 1,1-Diphehylpropene (**1**) Sensitized by Diacetone-Fructose (DAF) 1,4-Naphthalenedicarboxylate (**2a**) in Supercritical Carbon Dioxide ($scCO_2$) at 45 °C[a]

R^2OH	pressure/MPa	irradiation time/h	conversion/%	yield/%[b]	ee/%[c]
MeOH (**3a**)	7.7	1	51	>79	-6.5
	8.0	1	25	>20	-6.8
	8.3	1	44	>21	-7.2

	9.0	1	80	>50	-8.0
	9.4	1	55	>49	-9.7
	10.0	1	34	>89	-17.5
	12.0	1	29	>84	-18.5
	18.0	1	41	>32	-20.7
EtOH (**3b**)	7.8	2	34	>15	-18.3
	8.4	2	53	>40	-15.2
	9.0	2	59	>50	-16.6
	9.5	2	52	>47	-20.7
	10.0	2	46	>44	-21.8
	10.6	2	43	>43	-23.9
	11.6	2	43	>40	-22.5
	18.0	2	31	>38	-27.6
i-PrOH (**3c**)	8.0	4	28	>26	+21.2
	8.5	4	52	>71	+22.4
	8.8	4	70	>22	+23.9
	9.0	4	58	>10	+24.9
	9.5	4	31	>63	+33.6
	10.0	4	40	>29	+39.3
	12.4	4	33	>20	+39.6
	18.0	4	36	>17	+42.3
t-BuOH (**3d**)	8.5	12	*d*		
		24	*d*		
	9.0	3	*d*		
		6	*d*		
	18.0	3	*d*		

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[a] [**1**] = 2 mM; [**2a**] = 0.3 mM; [**3a-d**] = 0.5 M. [b] Chemical yield based on the consumption of the starting material. [c] Enantiomeric excess determined by chiral GC; error <0.3% ee. Except for the **4a** case, the sign of ee does not mean the sign of optical rotation or absolute configuration, but is tentatively assigned according to the elution order on ASTEC B-PH and B-DM column for **4b** and **4c**, respectively; the first eluted enantiomer is given a positive sign. [d] Practically no reaction.

As can be seen from Table 1-1, longer periods of irradiation are needed for bulkier alcohols to obtain comparable conversions under the identical irradiation conditions, yet the less bulky alcohols **3a-c** afforded the corresponding photoadducts **4a-c** in moderate to good yields in $scCO_2$. These results prompted us to re-examine the photoaddition of the bulkiest *tert*-butanol **3d** to **1** in $scCO_2$, despite the negative results obtained for the same reaction in conventional organic solvents.1(b) In $scCO_2$ of low density and polarity, alcohols are expected to more intimately interact, forming clusters, with an exciplex intermediate of charge-transfer nature. However, the repeated experiments with prolonged irradiations up to 24 h in near critical and supercritical CO_2 region merely led to the formation of some amounts of side products such as benzophenone, without affording the *tert*-butanol adduct. This indicates that *tert*-butanol is too bulky to approach the radical cationic substrate even in near critical and supercritical CO_2 media and that the clustering effect is not sufficient to overcome the steric hindrance of the *tert*-butyl group.

The pressure-dependence profiles of the absolute ee values of **4a-c** obtained are illustrated in Figure 1-1, where the natural logarithm of relative rate constant for the formation of (*R*)- and (*S*)-**4**, i.e. $|\ln(k_R/k_S)| = \ln[(100 + |\%ee|)/(100 - |\%ee|)]$, is plotted against the CO_2 pressure (note that the signs of ee for **4b** and **4c** indicate only the elusion order on a specific chiral GC column (see Experiments), as the absolute configurations of **4b** and **4c** are not known).

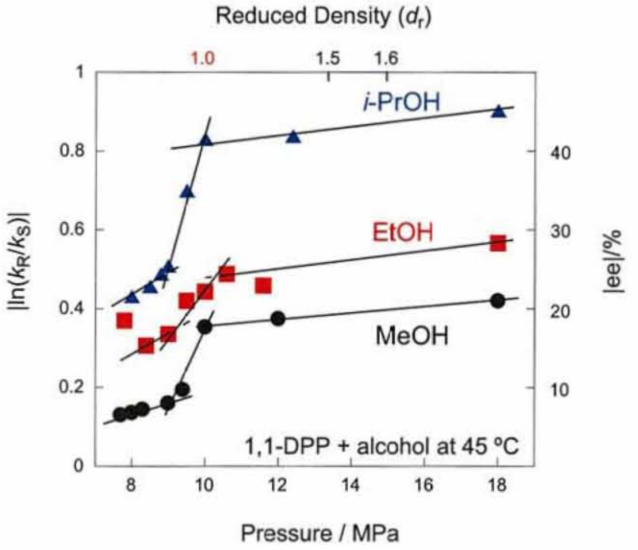

Figure 1-1. Pressure Dependence of the Relative rate Constants ($|\ln(k_R/k_S)|$) and the Absolute Ee Values of **4a-c** Obtained in the Enantiodifferentiating Photoaddition of Alcohols to **1** Sensitized by **2a** in Nc- and $ScCO_2$ at 45 °C.

As can be seen from Figure 1-1, the ee values obtained for all the adducts derived from reactive alcohols (**3a-c**) increase in general with increasing pressure, but the pressure-dependence profiles are obviously discontinuous, showing an abrupt jump at the transition region between $ncCO_2$ media and $scCO_2$ media. Similar behavior has been observed in the enantiodifferentiating photoisomerization of (*Z*)-cyclooctene in $scCO_2$,[8] where the ee profile showed a kink just above the critical density but the ee behavior at pressures lower than 8 MPa (in the $ncCO_2$ region) could not be examined due to the low solubility of the benzenepolycarboxylate sensitizers employed. In contrast, the present system allowed us to observe the ee profile over the whole pressure range starting from the near critical region, since both the sensitizer and substrate are sufficiently soluble even in near critical CO_2 media that contains 0.5 M methanol, which probably functions as a co-solvent (or so-called "entrainer") to enhance the solubility.

Obviously, the abrupt ee leap observed in the transition region (from the near critical to the supercritical region) indicates a sudden change in the surroundings of the sensitizer and/or the exciplex intermediate, probably the structure and properties of cluster around the exciplex that determines the stereochemical outcome of the alcohol attack. The scattered ee plot in the near critical region may be related not to the partial deposition of substrate or sensitizer but rather to the fluctuation of alcohol clustering since the product's ee is not appreciably affected by the concentration of substrate or sensitizer.[1,2] To more quantitatively analyze this unique pressure dependence behavior of ee, we calculated the differential activation volume ($|\Delta\Delta V^{\ddagger}_{R\text{-}S}| = |\Delta V^{\ddagger}_{R} - \Delta V^{\ddagger}_{S}|$) at $T = 318$ K (or 45 °C) for each of the near critical, transition, and supercritical region by using eq 1-1:[2]

$$\ln(k_R/k_S) = -(\Delta\Delta V^{\ddagger}_{R\text{-}S}/RT)P + C \qquad (1\text{-}1)$$

where R stands for the gas constant and C for the intrinsic enantiodifferentiation at zero pressure, i.e. the $\ln(k_R/k_S)$ value at $P = 0$. The $|\Delta\Delta V^{\ddagger}_{R\text{-}S}|$ values calculated from the data obtained in the near critical (7.7-9 MPa), transition (9-10 MPa) and supercritical (10-18 MPa) regions are shown in Table 1-2. It is noted that, apart from the extraordinarily large values (290-850 $cm^3\ mol^{-1}$) tentatively assigned for the transition region, the $|\Delta\Delta V^{\ddagger}_{R\text{-}S}|$ values for the supercritical region (22-26 $cm^3\ mol^{-1}$) and for the near critical region (60-210 $cm^3\ mol^{-1}$) are one to two orders of magnitude larger than those (1-2 $cm^3\ mol^{-1}$) obtained for the same photoreaction performed in conventional organic solvents under pressure.[2] These results indicate that the difference in volume between the diastereomeric transition states, leading to (*R*)- and (*S*)-**4**, are much larger in the supercritical region and specifically in the near critical region than in organic solvents, which is probably one of the unique features of near and supercritical media originating from the clustering effect. This means that the product's ee is more efficiently controlled by pressure in the order: near critical >supercritical>>conventional organic media. In this connection, Kim and co-worker have reported that the activation volume and the ratio of the local versus bulk density are correlated to the compressibility of SCFs,[9] and Ikushima and co-workers have also observed similar behavior near the critical density in the Diels-Alder reaction of isoprene with methyl acrylate.[10] Such unique behavior has been attributed to the density fluctuation of SCF.[11]

Table 1-2. Differential Activation Volumes ($\Delta\Delta V^{\ddagger}_{\text{R-S}}$) for the Enantiodifferentiating Photoaddition of Various Alcohols to **1** Sensitized by **2a** in Carbon Dioxide Media in the Near Critical (<9 MPa), Transition (9-10 MPa), and Supercritical (>10 MPa) Regions

R^2OH	$\lvert\Delta\Delta V^{\ddagger}_{\text{R-S}}\rvert$/cm^3 mol^{-1}		
	7.7-9 MPa	9-10 MPa	10-18 MPa
MeOH (**3a**)	60	(530)	22
EtOH (**3b**)	130	(290)	26
i-PrOH (**3c**)	210	(850)	25

Supercritical CO_2 versus Conventional Solvents. It is interesting to further examine the medium effects on the present photochirogenesis by comparing the results obtained in scCO_2 with those in conventional organic solvents. The chemical and optical yields of alcohol adducts **4a-c** obtained upon photosensitizations with DAF 1,4-naphthalenedicarboxylate (**2a**) in scCO_2 at 18 MPa and in conventional solvents are listed in Table 1-3. As reported previously,[1] the product's ee increases with increasing solvent polarity from methylcyclohexane (MCH) to toluene and then to ether. It should be noted however that the use of more polar solvents, such as methanol and acetonitrile, leads to a dramatic decrease of ee as a result of dissociation of the intervening exciplex to a solvent separated radical ion pair. Hence, the precise manipulation of solvent polarity is extremely crucial to overcome the trade-off relationship between the chemical and optical yields.

The steric bulk of attacking alcohol plays another important role in determining the product's ee. Thus, in MCH and toluene solutions, the product's ee consistently increases with increasing bulkiness of alcohol to reach the highest values of 25% (MCH) and 32% (toluene) for **4c** upon irradiation with 2-propanol (Table 1-3). In ether solutions, the ee was similarly enhanced from 27% (**4a**) to 34% (**4b**) by increasing the alcohol's bulk from methanol to ethanol. However, the use of bulkier 2-propanol did not further improve the ee but simply afforded comparable 35% ee for **4c**, as if there is an apparent ceiling value of ee in organic solvents. In this context, it is interesting that the ee obtained in $scCO_2$ media (18 MPa) smoothly increases with increasing bulkiness of alcohol from 21% (**4a**) to 28% (**4b**) and then to the highest value of 42% for **4c**, without encountering such a ceiling phenomenon (Table 1-3). As demonstrated for alcohols used as an entrainer in $scCO_2$ extraction,[12] tight clustering and appreciably increased nucleophilicity of alcohol to the exciplex intermediate in $scCO_2$ would be responsible for the continued enhancement of ee throughout the alcohol series up to 2-propanol.

Table 1-3. Enantiodifferentiating Photoaddition of Various Alcohols to 1,1-Diphehylpropene **1** Sensitized by DAF 1,4-Naphthalenedicarboxylate **2a** in $ncCO_2$[a] and $scCO_2$[a] and Organic Media[b]

R^2OH	medium	pressure /MPa	tempera ture/°C	irradiation time/h	conver-sion/%	yield/%[c]	ee/%[d]
MeOH (**3a**)	MCH	0.1	25	24	82	54	-4.7
	toluene	0.1	25	24	75	47	-15.7
	ether	0.1	25	24	82	32	-27.0
	$scCO_2$	18.0	45	1	41	>32	-20.7
EtOH (**3b**)	MCH	0.1	25	24	84	52	-9.5
	ether	0.1	25	24	80	23	-34.0
	$scCO_2$	18.0	45	2	31	>38	-27.6
i-PrOH (**3c**)	MCH	0.1	25	24	64	30	+24.9
	toluene	0.1	25	24	57	27	+31.6
	ether	0.1	25	24	65	43	+35.0
	$scCO_2$	18.0	45	4	36	>17	+42.3

[a] [**1**] = 2 mM; [**2a**] = 0.3 mM; [**3a-c**] = 0.5 M. [b] [**1**] = 20 mM; [**2a**] = 3 mM; [**3a-c**] = 0.5 M. [c] Chemical yield based on the consumption of the starting material. [d] Enantiomeric excess determined by chiral GC; error <0.3% ee.

It is notable that, while serving as an environmentally benign reaction medium, $scCO_2$ enables us to overcome the apparent limitation of conventional organic solvents in enhancing the product's ee. To explore the general validity of such unique pressure dependence and also to obtain a better ee, the author employed a higher homologue, 1,1-diphenyl-1-butene (**5**), as a new substrate in the following experiments.

Effects of Vinylic Substituent's Bulk. In the previous studies,[1] Asaoka and co-workers demonstrated that 1,1-diphenyl-1-butene **5**, possessing a larger ethyl substituent at the vinylic C-3, consistently affords higher ee's than 1,1-diphenylpropene **1** under the comparable conditions. This prompted the author to examine the effects of the substituent's bulk on the enantiodifferentiating photoaddition in $scCO_2$ at varying pressure by using **5** as a bulkier substrate and saccharide and 1-methylheptyl naphthalenedicarboxylates **2a** and **2b** as chiral sensitizers. The chemical and optical yields of photoproduct **6a**, determined by chiral GC, are summarized in Table 1-4, along with the conversion.

The optical yields of methanol adduct **6a** (34% ee) obtained from **5** upon photosensitization with **2a** in $scCO_2$ media (18 MPa) are significantly larger than those of methanol adduct **4a** (5-27% ee) obtained from **1** in both $scCO_2$ media (18 MPa) and conventional organic solvents (Table 1-3). The ee values of **6a** obtained by using **2a** and **2b** are plotted as a function of pressure in Figures 1-2 and 1-3, respectively. Again, abrupt changes are clearly seen near the critical density, indicating that this phenomenon is a rather general feature of the photochirogenesis in near and supercritical media. However, the original ability of chiral sensitizers does not appear to be significantly changed by the medium employed and hence the saccharide sensitizer **2a** consistently affords better ee's than the chiral alkyl sensitizer **2b**.

Table 1-4. Enantiodifferentiating Photoaddition of Methanol **3a** to 1,1-Diphenyl-1-butene **5** Sensitized by Chiral Naphthalenedicarboxylates **2a** and **2b** in $scCO_2$ at 45 °C[a]

sensitizer	pressure/MPa	conversion/%	yield/%[b]	ee/%[c]
1,4-$Np(DAF)_2$ (**2a**)	8.0	59	*d*	-10.3
	8.6	35	>17	-13.3
	9.2	44	>36	-19.2
	9.7	33	>35	-24.7
	10.2	32	>28	-31.8
	12.0	17	>25	-32.5
	18.3	5	>77	-33.5
1,4-$Np(Oct)_2$ (**2b**)	8.1	31	>51	+0.5
	8.5	43	>33	+1.5
	9.1	30	>28	+0.6
	9.6	15	>34	+2.5
	10.0	12	>28	+3.7
	10.2	10	>34	+3.8
	12.0	2	>35	+5.1
	18.0	3	>10	+8.0

[a] [**5**] = 2 mM; [Sens*] = 0.3 mM; [MeOH] = 0.5 M; irradiated for 2 h. [b] Chemical yield based on the consumption of the starting material. [c] Ee determined by chiral GC; error <0.3% ee. [d] Not determined.

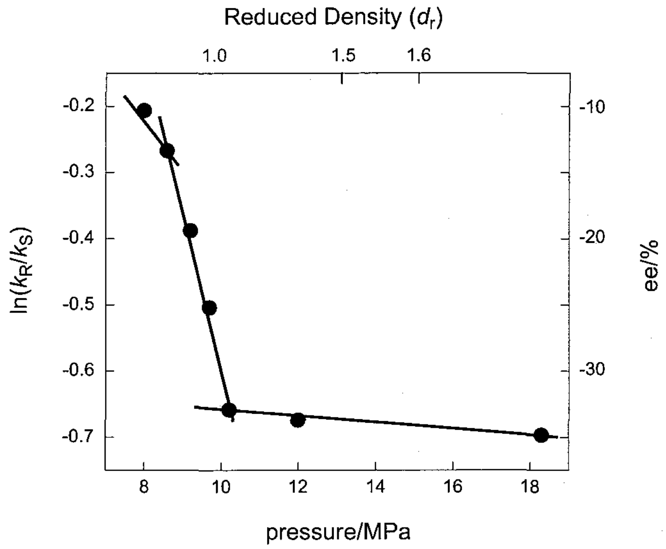

Figure 1-2. Pressure Dependence of the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photoaddition of **3a** to **5** Sensitized by **2a** in $ScCO_2$ at 45 °C.

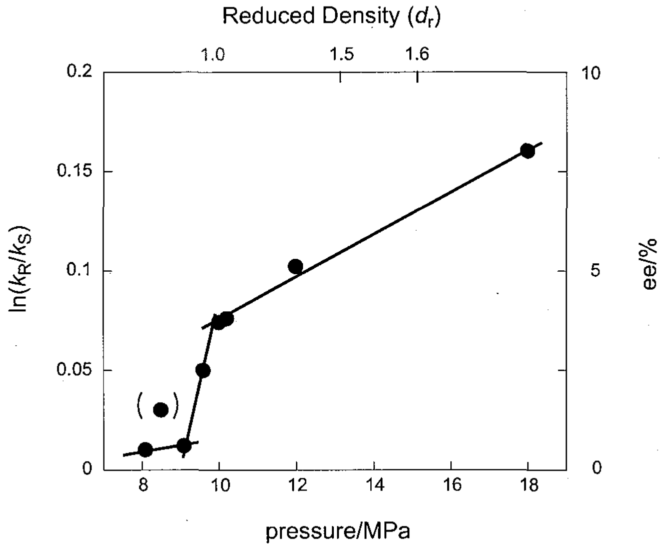

Figure 1-3. Pressure Dependence of the Relative rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photoaddition of **3a** to **5** Sensitized by **2b** in $ScCO_2$ at 45 °C.

To more quantitatively analyze the pressure dependence behavior, the differential activation volume ($|\Delta\Delta V^{\ddagger}_{\text{R-S}}|$) were calculated from the slope of the plots in Figures 1-2 and 1-3, by using the equation 1-1 derived in the previous report.[2] Due to the discontinuous nature of the plots, we determined the $|\Delta\Delta V^{\ddagger}_{\text{R-S}}|$ values for the near critical and supercritical regions but only as tentative values for the transition area. The $|\Delta\Delta V^{\ddagger}_{\text{R-S}}|$ values in $scCO_2$, shown in Table 1-5, are comparable to those obtained with substrate **1** (Table 1-2), but much (at least one order of magnitude) larger than those reported for organic solvents. Although no $|\Delta\Delta V^{\ddagger}_{\text{R-S}}|$ value is calculated for the near critical region due to the limited number of data points available, the tentative $|\Delta\Delta V^{\ddagger}_{\text{R-S}}|$ values calculated for the transition region are also extremely large. It may be concluded therefore that the sudden jump of ee near the critical density is a fairly common phenomenon observed for uni- and bimolecular photochirogenic reactions and enables one to obtain the best ee in $scCO_2$ rather than conventional organic media.

Table 1-5. Differential Activation Volumes ($|\Delta\Delta V^{\ddagger}_{\text{R-S}}|/\text{cm}^3\ \text{mol}^{-1}$) Calculated for the Enantiodifferentiating Photoaddition of Methanol **3a** to 1,1-Diphenyl-1-butene **5** Sensitized by **2a** and **2b** in Near Critical, Transition, and Supercritical Pressure Regions of CO_2

sensitizer	$\|\Delta\Delta V^{\ddagger}_{\text{R-S}}\|/\text{cm}^3\ \text{mol}^{-1}$		
	8-9 MPa	9-10 MPa	10-18 MPa
2a	*a*	(610)[b]	10
2b	*a*	(150)[b]	28

[a] Not calculated due to the limited number of available data points. [b] Tentative values due to the transition nature of this pressure region between the near critical and supercritical states.

Fluorescence Spectral Behavior of Chiral Sensitizers in $scCO_2$. As demonstrated in previous studies[8] and mentioned above, the abrupt change of product's ee near the critical density is a feature common to both uni- and bimolecular enantiodifferentiating photoreactions performed in CO_2 media. Thus, the nature of intervening excited species and also the detailed enantiodifferentiation mechanism can be appreciably different in $ncCO_2$ versus $scCO_2$. It is well known that fluorescence spectrum is a good measure of the charge-transfer nature of relevant species,[13] and the local polarity around solute molecule or complex can be deduced from the fluorescence measurement.[13-20] Hence, the author investigated the fluorescence spectral behavior of saccharide and chiral alkyl ester sensitizers **2a** and **2b** in near critical (9 MPa) and supercritical (10 MPa) CO_2 media at 45 °C in the presence and absence of methanol. The results are presented in Figure 1-4 and in Table 1-6; note that a direct comparison of fluorescence intensity between the spectra taken in near and supercritical CO_2 is not appropriate due to the difference in sample solubility (concentration) in near and supercritical CO_2.

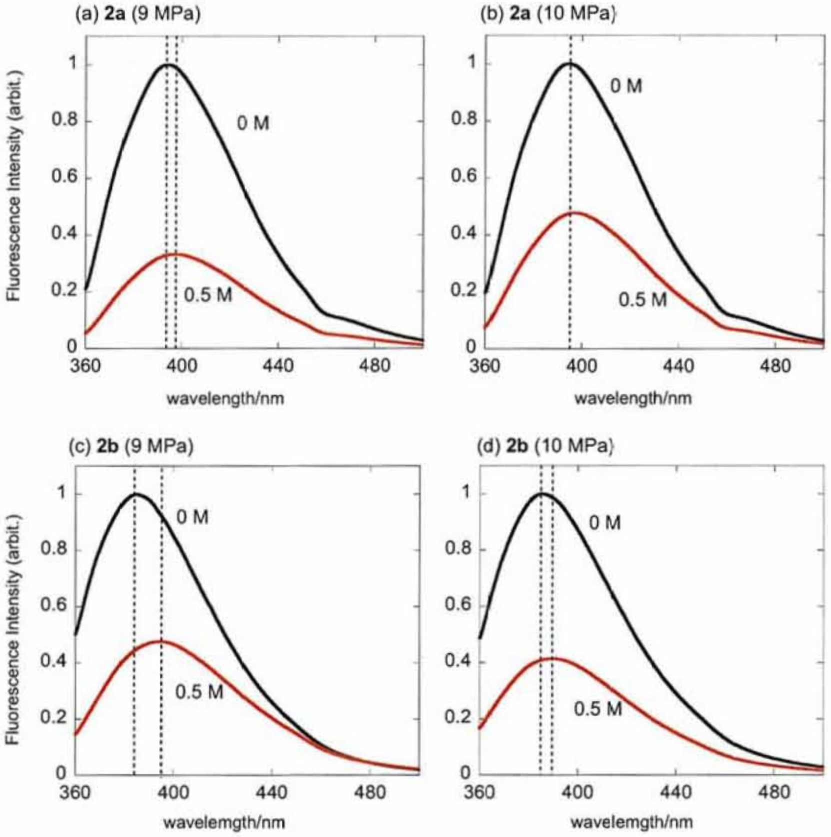

Figure 1-4. Fluorescence Spectra of DAF and 1-Methylheptyl 1,4-Naphthalenedicarboxylates **2a** (0.01 mM) and **2b** (0.035 mM) Excited at 340 nm in the Presence and Absence of Methanol **3a** (0, 0.5 M) in (a) and (c) Near Critical (9 MPa), (b) and (d) Supercritical (10 MPa) CO_2 Media at 45 °C.

Table 1-6. Fluorescence Maxima (λ_{max}) and Full Width at Half Maxima (fwhm) for DAF and 1-Methylheptyl 1,4-Naphthalenedicarboxylates (**2a** and **2b**) Excited at 340 nm in Near Critical (9 MPa) and Supercritical (10 MPa) CO_2 Media at 45 °C in the Presence and Absence of Methanol

sensitizer	[MeOH]/M	near critical CO_2 (9 MPa)		supercritical CO_2 (10 MPa)	
		λ_{max}/nm	fwhm/nm	λ_{max}/nm	fwhm/nm
2a	0	394	60	394	61
	0.5	398 (+4)[a]	65 (+5)[a]	396 (+2)[a]	61 (±0)[a]
2b	0	385	61	385	63
	0.5	395 (+10)[a]	67 (+6)[a]	391 (+6)[a]	66 (+3)[a]

[a] Changes in λ_{max} and fwhm induced by the addition of 0.5 M methanol.

Upon addition of 0.5 M methanol, the fluorescence peak position (λ_{max}) and width (fwhm) showed only negligible changes (0-2 nm) in supercritical CO_2 region, but exhibited a larger peak shift (by 4 nm) and broadening (by 5 nm) in ncCO_2 region, as shown in Figure 1-4 and Table 1-6. These results reveal that the clustering of polar methanol around excited **2a** is relatively weak in supercritical CO_2 region and only slightly influence the fluorescence behavior. In contrast, the methanol clustering is rather strong in more gaseous near critical CO_2 region enough to induce the appreciable shift and broadening of the fluorescence peak. Such distinction in sensitizer photophysics is probably related to the completely different photochirogenic behavior observed in near critical versus supercritical CO_2 region, and therefore the author further investigated the fluorescence spectral behavior of exciplex intermediate in the presence and absence of added methanol to obtain more direct evidence for the active role of methanol clustering particularly in near critical CO_2 region.

Fluorescence spectral behavior of alkyl naphthalenedicarboxylate **2b** is more interesting, displaying larger changes in λ_{max} and fwhm upon addition of methanol. Thus, the original fluorescence of **2b** appears at 385 nm in both near and supercritical CO_2 media, which is shorter in wavelength by 7 nm than that of **2a** (392 nm). Addition of 0.5 M methanol caused bathochromic shifts of 10 nm and 6 nm with accompanying band broadening of 6 nm and 3 nm in near and supercritical CO_2 media, respectively. The induced peak shift and broadening are appreciably larger for alkyl ester **2b** than for saccharide ester **2a**, indicating that the saccharides in **2a**, working as built-in dipoles, enhance the microenvironmental polarity around the naphthalene fluorophore to induce the bathochromic shift even in the absence of methanol. However, the fluorescence maxima of **2a** and **2b** become closer in position upon addition of 0.5 M methanol; i.e., λ_{max} = 395-398 nm in near critical CO_2 media and 391-396 nm in supercritical CO_2 media. Irrespective of the ester moiety attached, the bathochromic shifts caused by the addition of the same concentration of methanol are consistently larger by 4 nm (or 0.7 kcal mol^{-1} in energy) in near critical CO_2 media than in supercritical CO_2 media, which may be rationalized by stronger clustering of methanol in near critical CO_2 media.

Fluorescence Spectral Behavior of Exciplex in $scCO_2$. Fluorescence behavior of exciplex has rarely been investigated in SCF. Inomata and co-workers reported that the fluorescence intensity of a pyrene–*N*,*N*-dimethylaniline exciplex decreases with increasing pressure in near and supercritical CO_2 media.[16] A few photophysical studies on other systems have also been done more recently.[19,21] In this photochirogenic system, the exciplex intermediate, rather than the excited sensitizer, plays the key role in determining the reactivity and selectivity of the enantiodifferentiating photoaddition.[1,2] Hence, the author tried to elucidate the nature of exciplex species by examining and comparing the fluorescence spectral behavior in near and supercritical CO_2 media.

First, the fluorescence spectra of sensitizer **2a** was measured in the presence and absence of substrate **1** in near critical (9 MPa) and supercritical (10 and 18 MPa) CO_2 at 45 °C without adding methanol. As shown in Figure 1-5a, the fluorescence intensity of **2a** was increased with increasing pressure, probably reflecting the solubility enhancement. The addition of substrate **1** (35 mM) to the same solution dramatically quenched the fluorescence of **2a** at all pressures examined with accompanying development of a new peak (shoulder) at longer wavelengths, which is assignable to the exciplex fluorescence, as illustrated in Figure 1-5b. Subtraction of the normalized fluorescence spectrum of **2a** (Figure 1-5a) from the obtained spectrum (Figure 1-5b) affords the exciplex fluorescence spectrum at each pressure. The results are shown in Figure 1-6 and summarized in Table 1-7, along with the relevant data in conventional solvents.[1(b)]

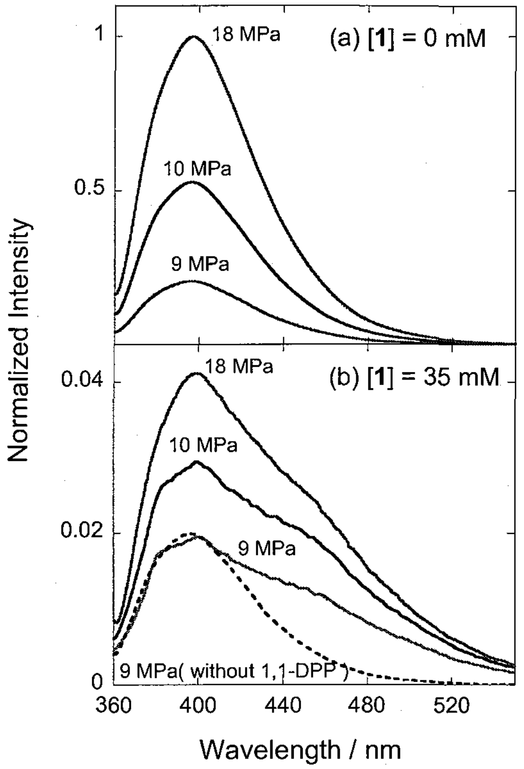

Figure 1-5. Fluorescence Spectra of DAF 1,4-Naphthalenedicarboxylate **2a** (0.065 mM) Excited at 340 nm (a) in the Absence and (b) in the Presence of 1,1-Diphenylpropene **1** (35 mM) in Near Critical (9 MPa) and Supercritical (10 and 18 MPa) CO_2 at 45 °C; the Dotted Line in the Bottom Figure (b) Indicates the Normalized Spectrum of **2a** in the Absence of **1** at 9 MPa.

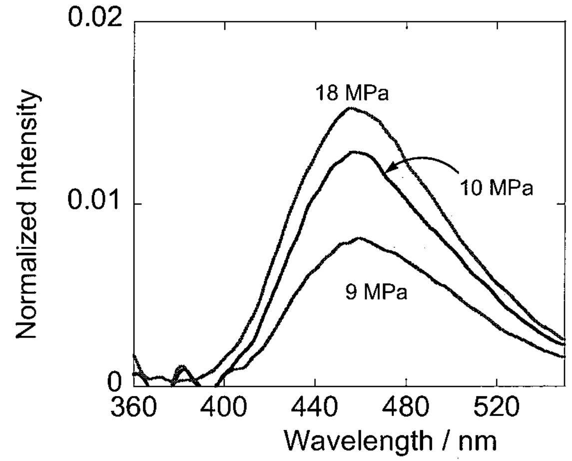

Figure 1-6. Exciplex Fluorescence Spectra Obtained by Subtraction of the Spectra of **2a** in the Presence (Figure 1-5b) and Absence (Figure 1-5a) of Substrate **1** at the Same Pressure.

Table 1-7. Fluorescence Maxima (λ_{max}) of Sensitizer **2a** and its Exciplex with Substrate **1** upon Excitation at 340 nm, as well as the Peak Shift ($\Delta\lambda_{max}$) and Energy Difference (ΔE) Caused by Exciplex Formation, in Near Critical (9 MPa) and Supercritical (10 and 18 MPa) CO_2 at 45 °C and in Conventional Solvents at 25 °C

media	temperature /°C	pressure /MPa	λ_{max}/nm		$\Delta\lambda_{max}$/nm	ref
			sensitizer	exciplex[a]	(ΔE/kcal mol^{-1})[b]	
near critical CO_2	45	9	394	459	65 (10.4)	*c*
supercritical CO_2	45	10	394	457	63 (10.1)	*c*
		18	396	456	60 (9.6)	*c*
methylcyclohexane	25	0.1	396	459	63 (10.0)	*d*
diethyl ether	25	0.1	405	463	58 (9.0)	*e*
acetonitrile	25	0.1	418	*f*	*f*	*e*
toluene	25	0.1	420	462	42 (6.2)	*d*

[a] Exciplex fluorescence obtained by spectrum subtraction; error <2 nm. [b] $\Delta\lambda_{max} = \lambda_{max}$(exciplex) - λ_{max}(sensitizer); $\Delta E = \Delta E$(sensitizer) - ΔE(exciplex). [c] This work. [d] Reference 1(a). [e] Reference 1(b). [f] Exciplex emission not observed.

As can be seen from Table 1-7, the sensitizer fluorescence is insensitive to pressure, but the exciplex fluorescence is more or less affected by the pressure in CO_2 media. Thus, appreciably better stabilization of up to 0.8 kcal mol^{-1} (or 1.4 kcal mol^{-1} if ether is taken as a reference solvent) is achieved upon exciplex formation in near critical CO_2 than in supercritical CO_2 or conventional organic solvents (although the direct comparison of the spectral data in organic solvents at a different temperature would be risky). However, the observed effect is rather small in the absence of methanol that is expected to cluster more strongly. Hence, the author further attempted to measure the exciplex fluorescence in the presence of added methanol, but unfortunately failed to detect any meaningful signal beyond the noise level. The complete loss of fluorescence in the presence of methanol would be attributable to the very strong methanol clustering in near and supercritical CO_2 of low polarity. Asaoka and co-workers have previously demonstrated that the fine tuning of solvent polarity is essential in optimizing the product's ee in this photochirogenic reaction and the best ee's are obtained in moderately polar solvents such as dialkyl ether,[1] where the substrate moiety of exciplex is sufficiently electron-deficient to accept the nucleophilic attack of alcohol but the charge-transfer character of exciplex is not enough to give a solvent-separated (or free) radical ion pair which is totally useless in view of chirality induction. Similarly, the author speculate that the strong clustering of methanol particularly in near critical CO_2 (as demonstrated in the fluorescence spectral examinations mentioned above) ruptures the exciplex at least in part to give generally lower ee's.

Stern-Volmer Study: Fluorescence Quenching of 2a by 1 in CO_2 Media. It is of particular interest to examine the fluorescence quenching in such highly diffusive low-density media as near and supercritical CO_2. Since the fluorescence intensity is not very reliable or reproducible in SCF experiments performed in high pressure vessels, the fluorescence lifetime is used for the Stern-Volmer quenching experiment.[22-27] Hence, the author also measured the fluorescence lifetime in a high-pressure vessel (with three quartz windows) precisely mounted in the sample chamber of a fluorimeter. The quantitative fluorescence quenching experiments were done by the following procedures: first, an ether solution of **2a** (0.01 mM) and **1** (0-10 mM) was placed in the vessel, the solvent was evaporated under a reduced pressure, the void space of the vessel was purged three times with CO_2 gas, and finally the vessel was charged with $scCO_2$ at a given temperature and pressure. Each sample, containing a fixed amount of **2a** and a varying amount of quencher **1** (0-10 mM) was measured at three different pressures (9, 10, and 18 MPa) to give the results shown in Table1-8.

Table 1-8. Fluorescence Lifetime (τ) of **2a** (0.01 mM) with **1** (0-10 mM) in Near Critical (9 MPa) and Supercritical (10 and 18 MPa) CO_2 Media at 45 °C

media	pressure /MPa	[**1**]/mM	τ/ns[a]
near critical CO_2	9	0	6.7
		0.3	5.5
		0.5	4.9
supercritical CO_2	10	0	6.9
		3	2.5
		5	2.1
		10	1.2
supercritical CO_2	18	0	6.6
		3	3.7
		5	2.7
		10	2.3

[a] Error <0.5 ns.

At all pressures examined, the fluorescence of **2a** was efficiently quenched by **1**, respectively, and the results were analyzed by using the Stern-Volmer equation (eq 1-2)[28] to give the plots shown in Figure 1-7.

$$\tau^0/\tau = 1 + k_Q\tau^0[\mathbf{1}] \qquad (1\text{-}2)$$

where τ and τ^0 refer to the fluorescence lifetimes in the presence and absence of quencher **1**, k_Q the quenching rate constant.

The Stern-Volmer plot gave a good straight line at each pressure (Figure 1-7), from the slope of which the author obtained the Stern-Volmer constant ($k_Q\tau$) in near and supercritical CO_2, as listed in Table 1-9. Interestingly, the Stern-Volmer constants obtained in near and supercritical CO_2 are one order of magnitude larger than those obtained in conventional organic solvents. In order to determine the quenching rate constant k_Q, the author measured the fluorescence lifetime of **2a** (τ^0) in the absence of quencher by using the single-photon-counting technique. As listed in Table 1-9, the lifetimes obtained in diverse media did not greatly differ, ranging from 5.8 to 11.6 ns. Although the lifetime becomes longer in polar aprotic or aromatic solvents, no clear gap exists in the lifetime either between the organic and CO_2 media or between the near critical and supercritical CO_2. From the fact that the fluorescence lifetime of sensitizer is insensitive to the CO_2 pressure and is practically the same in all CO_2 media examined, the author may further suggest that the exciplex intermediate with a charge-transfer character plays the major roles in determining the photochirogenic behavior in near and supercritical CO_2 in view of the much larger pressure dependence observed in product's ee and in exciplex fluorescence behavior.

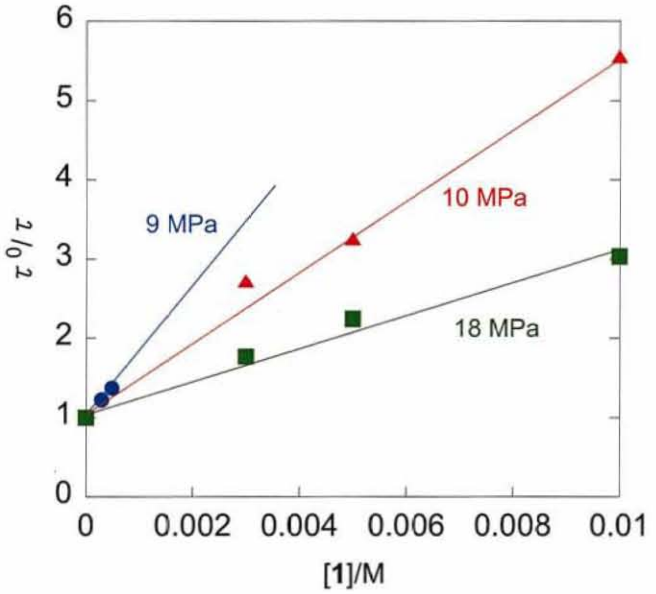

Figure 1-7. Stern-Volmer Plots Obtained for the Fluorescence Quenching of DAF 1,4-Naphthalenedicarboxylate **2a** (0.01 mM) with 1,1-Diphenylpropene **1** (0-10 mM) in Near Critical (9 MPa) and Supercritical (10 and 18 MPa) CO_2 Media.

Table 1-9. Stern-Volmer Constant ($k_Q\tau$), Fluorescence Lifetime (τ), and Quenching Rate Constant (k_Q) Obtained by Fluorescence Quenching of **2a** (0.01 mM) with **1** (0-10 mM) in Near Critical (9 MPa) and Supercritical (10 and 18 MPa) CO_2 Media at 45 °C and in Conventional Solvents at 25 °C

media	temperature /°C	pressure /MPa	k_{diff}[a] /10^{10} M^{-1} s^{-1}	$k_Q\tau$[b]/M^{-1}	τ[c]/ns	k_Q /10^{10} M^{-1} s^{-1}	ref
near critical CO_2	45	9	26	730	6.7	11	*d*
supercritical CO_2	45	10	19	450	6.9	6.5	*d*
		18	9.7	200	6.6	3.0	*d*
methylcyclohexane	25	0.1	0.99	31	5.8	0.54	*e*
diethyl ether	25	0.1	3.0	75	8.6	0.88	*f*
acetonitrile	25	0.1	1.8	89	10.5	0.85	*f*
toluene	25	0.1	1.2	11	11.6	0.094	*e*
methanol	25	0.1	1.2	40	5.8	0.69	*d*

[a] Diffusion rate constant in CO_2 media at 45 °C (reference 29) and in organic solvents at 25 °C (reference 30). [b] Stern-Volmer constant obtained by analyzing the data in Figure 1-7 with eq 1-2. [c] Fluorescence lifetime of **2a** (0.01 mM) determined independently in the absence of **1** by single-photon-counting technique; error <0.5 ns. [d] This work. [e] Reference 1(a). [f] Reference 1(b).

It is also interesting that the unusually large Stern-Volmer constants of up to several hundreds are attributable solely to the very fast fluorescence quenching by substrate **1**, and the quenching rate constant (k_Q) amounts to 3.0×10^{10} M^{-1} s^{-1} in supercritical CO_2 and even to 1.1×10^{11} M^{-1} s^{-1} in near critical CO_2. For fluorescence quenching of 9,10-dimethylanthracene and 9,10-dicyanoanthracene by oxygen, Okamoto and co-workers reported the rate constants of 4×10^{10} and 1×10^{9} M^{-1} s^{-1} in supercritical CO_2 at 10 MPa and 35 °C, respectively.[24] Bunker and co-workers. reported the fluorescence quenching rate constants for anthracene, perylene, 9-cyanoanthracene, and 9,10-diphenylanthracene upon addition of carbon tetrabromide to be $2\text{-}4 \times 10^{10}$, $2\text{-}5 \times 10^{10}$, $1\text{-}2 \times 10^{10}$, and $2\text{-}6 \times 10^{10}$ M^{-1} s^{-1} in near and supercritical CO_2 at 35 °C.[27] These results are compatible with our present data, indicating that the fluorescence quenching is more or less faster in near and supercritical CO_2 media than in organic solvents. In the present case, the quenching rate constants are obviously one to two orders of magnitude faster than those observed in conventional solvents but do not exceed the diffusion limit in CO_2 media[29] (Table 1-9). It may be concluded by therefore that the quenching is not a static but a diffusion-controlled dynamic process even in $scCO_2$.

1-3 Conclusion

Despite the unique features as highly fluctuating, clustering, and "green" media, SCFs have rarely been employed as reaction media particularly in photochirogenesis studies. In this chapter, the scope of photochirogenesis in SCF is expanded to the bimolecular enantiodifferentiating reaction. The photochirogenesis in $scCO_2$ are summarized and rationalized as follows: (1) The product's ee displays a dramatic jump near the critical density. Such a sudden change in ee appears to be common to uni- and bimolecular photochirogeneses in SCF media, and may be used as a convenient tool for controlling the product selectivity not only in photochirogenesis but also in a wide variety of (photo)reactions. (2) The photochirogenesis in $scCO_2$ gives comparable or even higher ee's than that in conventional solvents. This is an encouraging result to further promote the photochirogenesis studies. (3) The clustering of alcohol added as a reagent (and also as an entrainer) dominates both the photophysical properties and the photochemical (stereochemical) consequences of excited sensitizer and exciplex intermediate, and hence the choice of alcohol and its concentration are critical factors for controlling the photochirogenesis. (4) The clustering of polar entrainer becomes stronger in the near critical region, which is the major cause of the lowered ee's in the present case. (5) The fluorescence quenching is dynamic and extremely fast in supercritical CO_2 and even faster in near critical CO_2, although the rate constant never exceeds the diffusion limit.

1-4 Experimental Section

Materials. Carbon dioxide of 99.99 % purity was purchased from Neriki Gas Co. and used without further purification. Spectral grade solvents were used throughout the work. 1,1-Diphenyl-1-alkenes **1** and **5** and chiral sensitizers **2a** and **2b** were synthesized and characterized, as described previously.[1]

Instruments. Fluorescence lifetimes of the sensitizers were determined by the time-correlated single-photon-counting technique, using a Hamamatsu Photonics FL920S instrument equipped with a pulsed H_2 light source. The emission from the sample solution (0.01 mM) was detected through a UV-37 (Toshiba) glass filter. A high-pressure vessel (SUS-316) equipped with three sapphire windows (manufactured by Teramex Co., Kyoto) was used for spectroscopy and photoreaction. Enantiomeric excesses of **4a-c** and **6a** were determined by chiral gas chromatography on a 30-m ASTEC B-PH column for **4a** (operated at 140 °C; retention times 49-50 min), **4b** (operated at 140 °C; retention times 53-54 min) and **5a** (operated at 145 °C; retention times 55-56 min) or a 30-m ASTEC B-DM column for **4c** (operated at 115 °C; retention times 113-114 min). Under these GC conditions, racemic samples prepared separately by using achiral dimethyl 1,4-naphthalenedicarboxylate as sensitizer gave ee's smaller than 0.3% ee upon repeated analyses.

Photolysis. Samples were charged in the high-pressure vessel (16 ml) as follows. First, an ether solution containing given amounts of substrate **1** or **5** and sensitizer **2** was placed in the vessel and the solvent was evaporated under vacuum to leave a residue, to which a given amount of alcohol was added. Then the vessel was closed and carbon dioxide was introduced to the vessel until the desired pressure (7.7-18.3 MPa) was reached at the fixed temperature (45.0 ± 0.1 °C). Unfiltered light from a 500-W ultrahigh-pressure mercury lamp was collimated, passed through a water layer and a UV-32 or UV-31 filter, and then focused in front of the sapphire window with a quartz lens. The phase homogeneity inside the vessel was visually checked through the window. After irradiation for a given period of time at 45.0 °C, the vessel was cooled down to 0 °C and the pressure was released at that temperature. The effluent from the vessel outlet was gently bubbled into ice-cooled hexane or diethyl ether to collect any volatile materials. The residue in the vessel was also extracted with hexane or diethyl ether. Both were combined and subjected to the chiral GC analysis.

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(1) (a) Asaoka, S.; Kitazawa, T.; Wada, T.; Inoue, Y. *J. Am. Chem. Soc.* **1999**, *121*, 8486. (b) Asaoka, S.; Wada, T.; Inoue, Y. *J. Am. Chem. Soc.* **2003**, *125*, 3008.

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Chapter 2

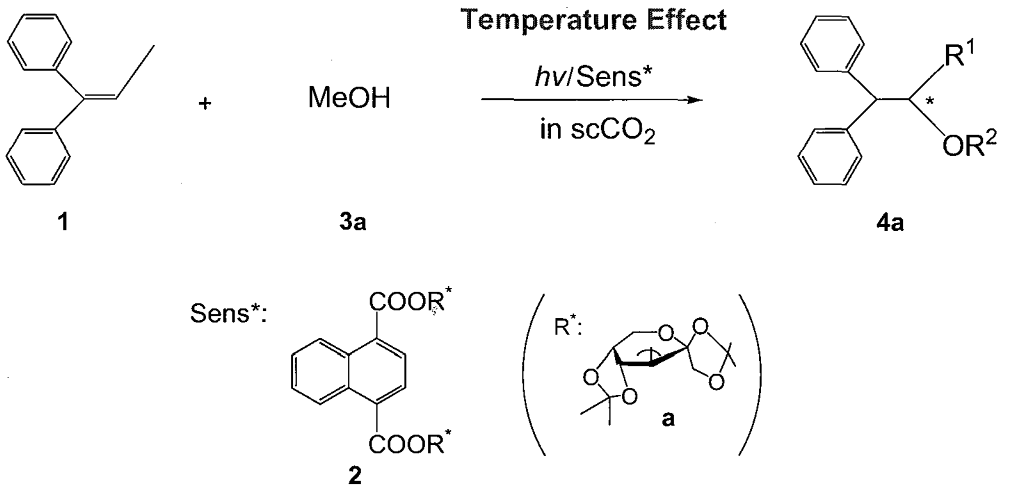
Enantiodifferentiating Photosensitized Polar Additon of Methanol to 1,1-Diphenylpropene in ScCO_2: Temperature, Pressure, and Methanol Concentration Control

2-1. Introduction

In the preceding chapter, it was revealed that the photochirogenesis in scCO_2 was controlled tightly by the clustering effect, which is the specific solvent fluctuation in SCFs. Hence, this clustering effect is also the important entropy-related factor for controlling the asymmetric photoreaction as well the other entropy-related factor (temperature, pressure and solvation etc.).[1] In the examination of pressure effect in scCO_2, it was also revealed that the degree of clustering effect is very different in ncCO_2 and scCO_2, which caused the dramatic ee change in transition region. This shows that the combination of entropy-related factor (clustering effect and pressure in previous chapter) can induce the drastic ee change and even accomplish the best ee in this type reaction compared to the organic solvents.[2,3] From this point of view, it is very important for controlling photochirogenesis in scCO_2 to examine the other combination of entropy-related factor (clustering effect and the other factors).

In this chapter, the author employed the temperature effect of the enantiodifferentiating photoaddition reaction of methanol (**3a**) to 1,1-diphenylpropene (**1**) sensitized by chiral naphthalenedicarboxylates with saccharide (**2a**) under a variety of conditions (Scheme 2-1) and the pressure effect under each temperature.

These examinations are enabled to elucidate which and how entropy-related factors control the photochirogenesis in scCO_2. Furthermore, in this reaction system, the alcohol clustering effect works preferentially compared to the CO_2 molecule clustering effect. This means that changing the degree of methanol clustering effect has also the potential, which control the photochirogenesis in scCO_2. Hence, the author also examined the methanol concentration effect of the enantiodifferentiating photoaddition reaction of methanol (**3a**) to 1,1-diphenylpropene (**1**) sensitized by chiral naphthalenedicarboxylates with saccharide (**2a**) under a variety of conditions at 45 °C. As this chapter goal, the author examined whether more critically control of the photochirogenesis in $scCO_2$ compared to the organic solvents can be accomplished through the multi- dimensional entropy control by comprehensive elucidation of the entropy factors's role in $scCO_2$.



Scheme 2-1. Enantiodifferentiating Photosensitized Polar Addition of Methanol (**3a**) to 1,1-Diphenylpropene (**1**) in $ScCO_2$ at Various Temperatures.

2-2. Results and Discussion

Temperature Effect in $ScCO_2$ Region. Recently, Asaoka and co-workers reported that this bimolecular enantiodifferation was sensitive to the temperature, and the absolute configuration of product was even switched by only changing temperature.[2] From the Eyring-type analysis of ee, the differential entropy change of activation ($\Delta\Delta S^{\ddagger}$) is not always negligible and often plays the key role in determining the product chirality particularly at ambient and higher temperatures. This means that temperature is also crucial factor for controlling this photoreaction. From this point of view, the temperature effect of this photoreaction was examined at $scCO_2$ region (18 MPa) under various temperatures (31, 35, 45, 70 °C) in $scCO_2$.

Table 2-1. Enantiodifferentiating Photosensitized Polar Addition of Methanol to **1** at Various Temperatures at $ScCO_2$ Region (18 MPa) in $ScCO_2$[a].

temperature/°C	conversion/%	yield/%[b]	ee/%[c]
31	54	>6	-25
35	32	>15	-27
45	41	>32	-21
70	82	>13	-22

[a] [**1**] = 2 mM; [**2a**] = 0.3 mM; [methanol] = 0.5 M; irradiated for 1 h. [b] Yield based on the consumption of the starting material. [c] Ee determined by chiral GC.

As shown in Table 2-1, reaction proceeded moderately as well in organic solvents, however, the values of ee were almost same at every temperature in $scCO_2$. This means that the temperature may be not crucial factor for controlling photochirogenesis efficiently at this temperature range unlike in organic solvents. Pressure is a crucial factor for photochirogenesis in $scCO_2$ (the elucidation of chapter 1), and the slight change of pressure and temperature of $scCO_2$ induce the drastic change of solvent property (viscosity, density, and dielectric constant)[4]. From this point of view, this outcome is extraordinary.

Pressure Effect in $ScCO_2$ at Each Temperature. Since Inoue and co-workers reported that the combination of entropy-related factor enable to control the photochirogenesis efficiently,[1] it was examined the pressure effect for asymmetric photoreaction at each temperature in $scCO_2$ (Table 2-2).

Table 2-2. Enantiodifferentiating Photosensitized Polar Addition of Methanol to **1** at Various Temperatures in $ScCO_2$[a].

temperature/ °C	pressure/MPa	conversion/%	yield/%[b]	ee/%[c]
31	7.4	49	>0.2	-23
	7.6	45	>2	-31
	8.0	56	>11	-22
	8.4	64	>7	-24
	8.9	36	>5	-25
	9.9	43	>2	-30
	13.0	33	>2	-31
	18.6	54	>6	-25
35	7.9	49	>2	-14
	8.2	24	>11	-21
	8.3	48	>2	-27

	8.4	49	>7	-25
	8.8	86	>16	-24
	9.2	92	>10	-25
	10.0	39	>8	-25
	11.3	28	>3	-28
	14.0	18	>4	-26
	18.0	32	>15	-27
45	7.7	51	>79	-7
	8.0	25	>20	-7
	8.3	44	>21	-7
	9.0	80	>50	-8
	9.4	55	>49	-10
	10.0	34	>89	-18
	12.0	29	>84	-19
	18.0	41	>32	-21
70	7.6	85	>12	-5
	8.3	100	>4	-6
	8.6	90	>1	-11
	8.9	53	>46	-9
	9.1	77	>19	-8
	10.3	64	>25	-8
	11.8	91	>23	-9
	13.0	26	>5	-14
	14.0	34	>5	-18
	15.0	27	>4	-22
	16.0	41	>9	-24
	18.6	82	>13	-22

[a] [**1**] = 2 mM; [**2**] = 0.3 mM; [methanol] = 0.5 M; irradiated for 1 h. [b] Yield based on the consumption of the starting material. [c] Ee determined by chiral GC.

As shown in Figure 2-1-(a), at 31 °C, the ee values of **4** obtained at different pressures (7.4-18.6 MPa) are scattered over a relatively wide range (22-31% ee) particularly in the low pressure region (<10 MPa). This somewhat unexpected behavior would be inherent to the reaction near the critical point, where even a small deviation in temperature or pressure may lead to a significant change in medium property[4] and hence in ee. Unfortunately, more precise control is not feasible at least with this SCF apparatus.

At temperatures higher than 35 °C, the pressure-dependence profiles are more coherent. As can be seen from Fig. 2-1-(b)-(d), the ee's obtained at 35, 45 or 70 °C consistently exhibit a sudden leap around the pressure that gives transition region at each temperature, for which the abrupt change in medium properties should be responsible.[4] Nevertheless the all examination was conducted upper the critical point, the ee behavior to pressure change is very different at each temperature though the examining pressure range is same at every temperature. This may be attributed to the transition nature of the plot in this pressure range at each temperature, or to the dynamic nature of this critical region, as demonstrated physicochemically by the density fluctuation.[5] This outcome showed that the photochirogenesis in $scCO_2$ is controlled by the pressure and temperature as multi- dimensional entropy control.

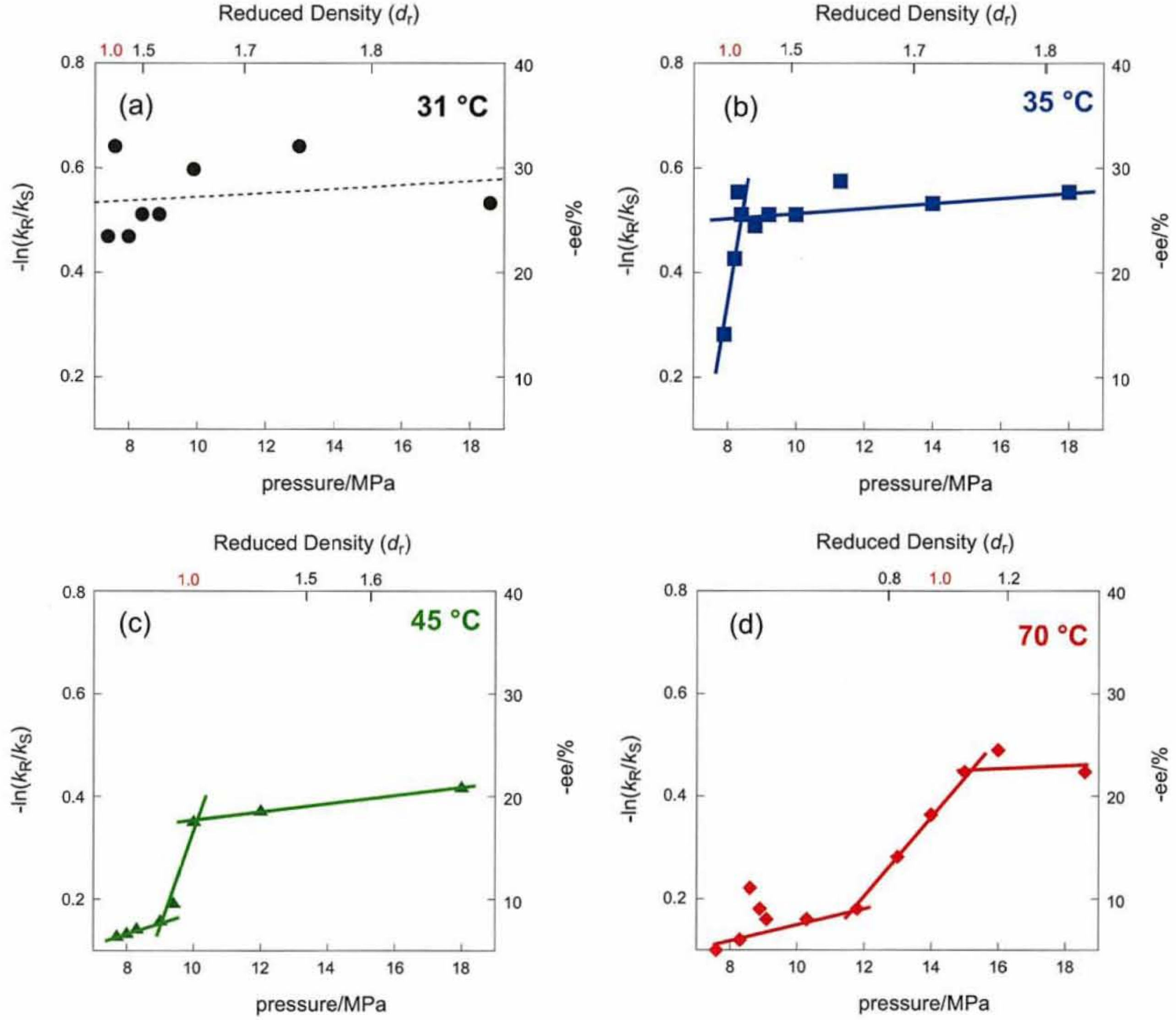


Figure 2-1. Pressure Dependence of the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photoaddition of **3a** to **1** Sensitized by **2a** in $ScCO_2$ at (a) 31 °C, (b) 35 °C, (c) 45 °C, and (d) 70 °C.

Controlled by Density in ScCO$_2$. As shown in Figure 2-1, the ee's obtained at 35, 45 or 70 °C consistently exhibit a sudden leap around the pressure that gives transition region, in particularly the unit reduced density ($d_r = 1$), at each temperature. Furthermore, Brennecke and co-worker reported that the clustering effect is associated with the change of CO$_2$ molecule density.[4(a)] Since the solvent properties, which are density (dielectric constant), are very sensitive to the change of pressure and temperature, it is more reasonable that the photochirogenesis in scCO$_2$ is controlled by the change of density. Hence, the pressure dependence at each temperature was re-plotted as one figure (Figure 2-2), and was compared the density change of CO$_2$ molecule (Figure 2-3).[6]

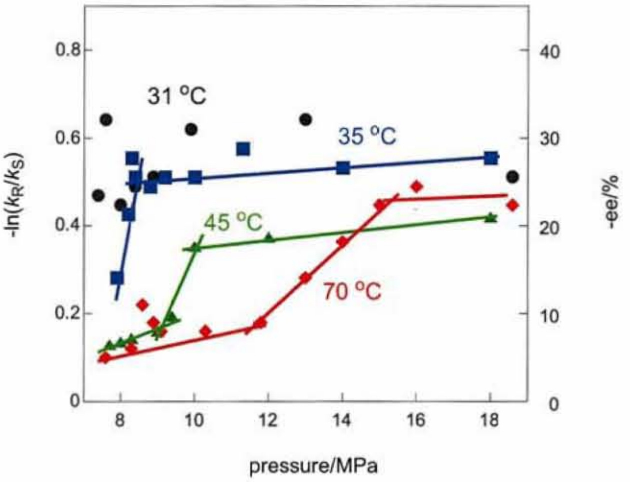


Figure 2-2. Pressure Dependence of the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photoaddition of **3a** to **1** Sensitized by **2a** in ScCO$_2$ at Every Temperature.

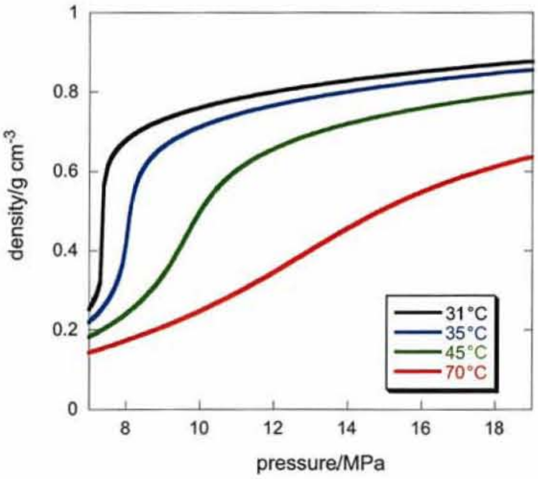


Figure 2-3. Pressure Dependence of the Density of ScCO$_2$ at Every Temperature.

As shown in Figure 2-2, the pressure range and the slope of a sudden leap of ee was very different apparently. Furthermore, this pressure dependence at each temperature was very similar to the density change of CO_2 molecule. It was also reported that the density of CO_2 change dramatically accompanying the very narrow change of pressure and temperature as the specific media property of $scCO_2$.[4] This may be rationalized that the density of $scCO_2$, which is associated with the clustering effect, controls the photochirogenesis in $scCO_2$. Since the dielectric constant of $scCO_2$ is nicely correlated with the density[6] and the density data at different temperatures and pressures are readily available.[7] Hence, the product's ee was re-plotted as a function of the density.

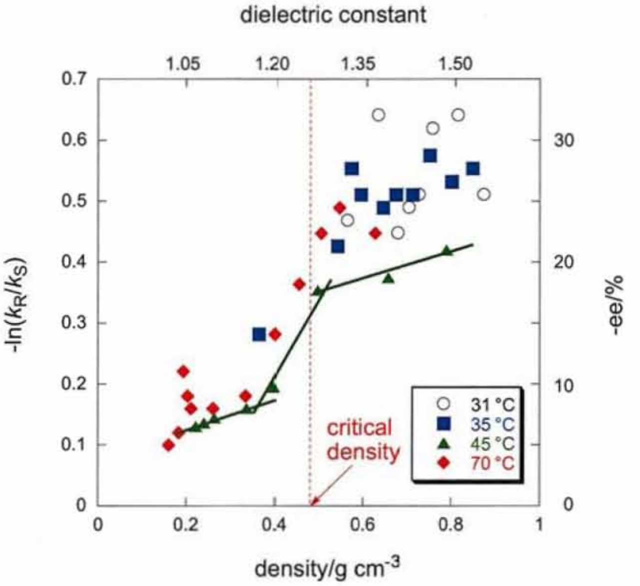


Figure 2-4. Density and/or Dielectric Dependence of the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photoaddition of **3a** to **1** Sensitized by **2a** in $ScCO_2$ at Every Temperature.

As can be seen from Figure 2-4, on the surface, the product's ee is better correlated with the density rather than the pressure, and more importantly all the ee data obtained at different temperatures reveal a single trend. This also may be reasonable that the photochirogenesis in $scCO_2$ is controlled by the density and/or dielectric constant, which are controlled by the pressure and temperature as multi-dimensional entropy control. Nevertheless, the assembled plot still exhibits a small leap near the critical density (0.481 g cm^{-3}).[7] In this relation, Asaoka and co-workers previously reported that the precise control of solvent polarity around the exciplex intermediate is essential for obtaining a good ee in this polar photoaddition.[2] Thus, polar solvents accelerate the dissociation of exciplex to a solvent-separated or free radical ion pair to give a good chemical yield but only a poor ee, whereas the degree of charge transfer in exciplex is not large enough to accept the alcohol attack in nonpolar solvents. After some trials, diethyl ether was chosen as the best solvent for this enantiodifferentiating photoaddition.[2] Consequently, it is reasonable that the density and/or dielectric constant of $scCO_2$ significantly affects the product's ee in the present case, however, the degree of clustering effect between $ncCO_2$ and $scCO_2$ is different, and $ncCO_2$ and $scCO_2$ have the different media property. A more intriguing aspect of this photoaddition is the preferential solvation of methanol to exciplex, which increases the microenvironmental polarity around the exciplex intermediate, facilitating charge transfer, but the low bulk polarity of diethyl ether does not allow dissociation to a radical ion pair, securing the chiral sensitizer-substrate interaction in the exciplex. A similar mechanism, i.e. methanol clustering to exciplex, should also operate in the CO_2 media between $ncCO_2$ and $scCO_2$.

Effect of Methanol Concentration in $ScCO_2$. In previous examination, it was elucidated that alcohols as reagent, clustering controls willingly compared to CO_2 molecule clustering. Furthermore, the media property is very different between $ncCO_2$ and $scCO_2$ owing to the difference of clustering effect. As expected from the radical ionic nature of the intermediate involved in this reaction, a change in the solvent polarity significantly affected the product's ee. Herein, to assess the effect of methanol clustering on ee, methanol concentration effect and pressure effect at each concentration of enantiodifferentiating photosensitized polar addition of methanol to 1,1-diphenylpropene **1** was conducted in $scCO_2$ in the presence of methanol at varying concentrations (0.1-1.0 M) at 45 °C (Table 2-3). To elucidate in detail, the product's ee was re-plotted as a function of the concentration of methanol (Figure 2-5).

Table 2-3. Methanol Concentration Effect of Enantiodifferation in ScCO$_2$ at 45 °C^a

[MeOH]/M	pressure/MPa	density (d_r)	ee/%^{b}
0.1	8.0	0.52	-13.5
	8.2	0.55	-11.8
	8.6	0.62	-11.8
	8.9	0.69	-11.2
	9.3	0.82	-12.3
	10.0	1.07	-17.5
	10.3	1.15	-19.0
	11.2	1.32	-25.7
	11.7	1.38	-27.0
	17.6	1.68	-25.9
0.2	7.7	0.47	-7.6
	8.2	0.55	-7.4
	8.3	0.56	-8.9
	8.5	0.60	-9.2
	9.1	0.75	-10.7
0.3	8.3	0.56	-6.1
	8.6	0.62	-7.6
	8.7	0.65	-7.9
	9.1	0.75	-8.4
	9.3	0.82	-10.9
	9.4	0.85	-9.3
	9.8	0.99	-9.5
	9.9	1.03	-12.1
	10.9	1.27	-24.2
	11.7	1.38	-24.1
	17.0	1.66	-23.1
0.4	10.1	1.10	-10.9
	10.2	1.13	-18.1
	11.5	1.36	-24.2
	17.0	1.66	-21.8

0.5	7.7	0.47	-6.5
	8.0	0.52	-6.8
	8.3	0.56	-7.2
	9.0	0.72	-8.0
	9.4	0.85	-9.7
	10.0	1.07	-17.5
	10.9	1.27	-20.8
	12.0	1.41	-18.5
	18.0	1.69	-20.7
1.0	8.2	0.55	-6.2
	17.3	1.67	-19.1

[a] [**1**] = 2 mM; [**2**] = 0.3 mM; [methanol] = 0.5 M; irradiated for 1 h. [b] Ee determined by chiral GC.

As shown in Figure 2-5, in diethyl ether, the ee continuously increased with decreasing methanol concentration from 1.0 M to 0.2 M, which is very reasonable because the sensitizer-substrate interactions in the exciplex are expected to be more intimate and enantiodifferentiating as the solvent polarity decreases. However, the ee decreased with decreasing methanol concentration from 0.2 M to 0.05 M. This may be reasonable by assuming that the selective solvation of alcohol to the exciplex, leading to a lower product's ee, in diethyl ether if the alcohol concentration is sufficiently lowered (<0.2 M).[2]

In the supercritical region (18 MPa), the ee does not show any rapid change, but moderately decreased with increasing methanol concentration from 0.3 M to 1.0 M. Interestingly, the changing profile is analogous to that obtained in ether (Fig. 2-5), implying that the clustering of methanol in $scCO_2$ apparently resembles to the preferential solvation in ether.[2] However, the ee increased additionally with decreasing methanol concentration, which behavior differ in case of diethyl ether. This may be rationalized that the methanol clustering rises up the microenvironmental polarity, which induce the dissociation of exciplex in case of organic solvents. However, in $scCO_2$, the environment of exciplex and/or methanol clustering layer is gas-like. This environment is not enables to dissociate the exciplex by the methanol clustering. In other words, selective methanol clustering is very efficient for rising up the ee, which is unlike with the selective solvation in organic solvents. This increasing ee is due to the inherent clustering effect in $scCO_2$.

In the near critical region (8 MPa), the ee was kept constant from 0.3 M to 1.0 M. It is likely that the addition of methanol of up to 0.3 M enhances the microenvironmental polarity around the exciplex (most probably through strong clustering)[4] to reduce the ee, while further addition does not further increase the polarity sensed by the exciplex. However, ee was rapidly increased from 6% to 14% by decreasing the methanol concentration from 0.3 to 0.1 M. This enhancement is also due to the specific selective clustering effect. Hence, it was elucidated that methanol clustering effect is enable to operate for rising up the selectivity both $ncCO_2$ and $scCO_2$, however, that enhancement is accentuated in $ncCO_2$ for strong clustering effect.

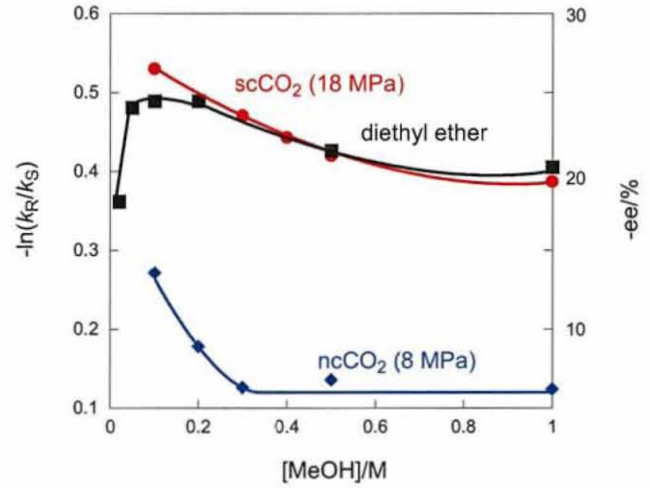


Figure 2-5. Effects of Methanol Concentration on the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photosensitized Polar Addition of Methanol to **1** in Near Critical (9 MPa) and Supercritical (18 MPa) CO_2 at 45 °C, as well as in Diethyl Ether at 25 °C.

Fluorescence Spectral Behavior and Fluorescence Lifetime of Chiral Sensitizers in $scCO_2$. As demonstrated in previous and this chapters, the abrupt change of product's ee was observed in transition region near the critical density at each temperature. Thus, the nature of intervening excited species and also the detailed enantiodifferentiation mechanism can be appreciably different in $ncCO_2$ versus $scCO_2$. As stated previously, it is well known that fluorescence spectrum is a good measure way of the local polarity around solute molecule.[4,8-15] Furthermore, fluorescence lifetime measurement also assesses justly the degree of methanol clustering effect.[15-21] Hence, it was conducted the fluorescence measurement and fluorescence lifetime measurement to elucidate the nature of methanol clustering effect quantitatively (Table 2-4).

Table 2-4. Fluorescence Maxima (λ_{max}) and Lifetimes (τ_{max}) of Saccharide Sensitizer **2** in the Presence/Absence of 0.5 M Methanol in ScCO$_2$ at Various Temperatures[a]

Temperature /°C	Pressure/MPa	λ_{max}^{o} ([MeOH] = 0)	λ_{max} ([MeOH] = 0.5 M)	$\Delta\lambda_{max} = \lambda_{max} - \lambda_{max}^{o}$	τ^{o} ([MeOH] = 0)	τ ([MeOH] = 0.5 M)	τ/τ^{o}
35	7.5	394	398	4	6.8	3.6	0.53
	8.0	395	396	1	7.1	4.3	0.61
	18.0	397	398	1	6.6	4.0	0.61
45	9.0	394	398	4	6.7	3.8	0.57
	10.0	394	396	2	6.9	4.4	0.64
	18.0	396	397	1	6.6	4.3	0.65
70	11.0	393	399	6	6.2	2.9	0.47
	14.0	393	396	3	6.5	3.1	0.48
	18.0	394	396	2	6.6	3.6	0.55

[a] [2] = 0.01 mM; excitation at 340 nm.

All case of the fluorescence intensity was enhanced by raising the pressure simply due to the increased solubility as well in case of 35 °C (Figure 2-6). Interestingly, the bathochromic shift of fluorescence peak upon addition of 0.5 M methanol was more pronounced in near critical CO$_2$ region ($\Delta\lambda_{max}$ = 4-6 nm) than in supercritical CO$_2$ region($\Delta\lambda_{max}$ = 1-3 nm) at all the temperatures examined (Table 2-4). This is compatible with the idea that the methanol clustering to excited sensitizer is stronger in ncCO$_2$ region compared in scCO$_2$ region. In case of lifetime measurement, in the absence of methanol, the lifetime was insensitive to CO$_2$ pressure, exhibiting almost the same value in nc- and scCO$_2$ media. However, the addition of 0.5 M methanol significantly shortened the lifetime in general, and the reduction is appreciably more pronounced in the near critical region, as judged from the τ itself as well as the τ/τ^{o} value. This is also in good agreement with the stronger clustering of methanol to saccharide sensitizer in near critical CO$_2$ media.

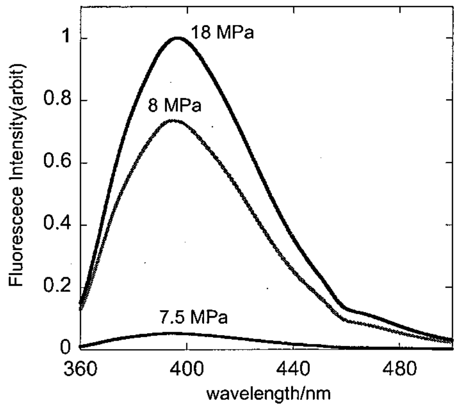


Figure 2-6. Fluorescence Spectrum of **2a** Only at 35 °C

2-3. Conclusions

In this chapter, the temperature effect, which is important entropy-related factor for manipulating photochirogenesis in organic solvent, and pressure effect at each temperature of asymmetric photoreaction in $scCO_2$ were conducted for the first time, which led to the realization of detail controlling photo-enantiodifferentiation with the clustering effect as new entropy-related factor, as described below.

(1) Although the photosensitizations of bimolecular reaction in organic solvent were manipulated by temperature, pressure, and solvation as entropy-related factors, in case of $scCO_2$, the inherent clustering effect, which is controlled by the combination of pressure and temperature, is the main factor for critically manipulating as a new entropy-related factor. Moreover, the degree of clustering effect differs between in $ncCO_2$ media and $scCO_2$ media. The over-enhanced microenvironmental polarity due to the more strong clustering effect in $ncCO_2$ region attributed the extra-lowered ee. Therefore, this difference of clustering effect induced the dramatic ee variant in transition region at each temperature.

(2) Although it was reported that the clustering effect is associated with the density variant of CO_2 density, the reaction outcome as a function of density did not show the correlation. Therefore, the photochirogenesis in $scCO_2$ was controlled by the density and/or clustering effect at some level compared temperature or pressure only. However, $ncCO_2$ media and $scCO_2$ media have completely dissimilar media property because the degree of clustering effect is different, though both media are SCFs.

(3) In this bimolecular reaction in $scCO_2$, methanol clustering manipulates preferentially. Methanol cluster enhanced the microenvironmental polarity around exciplex particularly in $ncCO_2$. Although the

over-enhanced microenvironmental polarity for selective salvation causes the lower ee in organic solvent, selective methanol clustering can discourage for dissociating the exciplex to solvent-separated ion pair. This clustering layer, which operates both $ncCO_2$ media and $scCO_2$ media, for governing dissociation enabled to enhance the enantioselectivity in $scCO_2$.

2-4. Experimental Section

Materials. Carbon dioxide of 99.99 % purity was purchased from Neriki Gas Co. and used without further purification. Spectral grade solvents were used throughout the work. 1,1-Diphenyl-1-alkenes **1** and **5** and chiral sensitizers **2a** were synthesized and characterized, as described previously.[8,9]

Instruments. Fluorescence lifetimes of the sensitizers were determined by the time-correlated single-photon-counting technique, using a Hamamatsu Photonics FL920S instrument equipped with a pulsed H_2 light source. The emission from the sample solution (0.01 mM) was detected through a UV-37 (Toshiba) glass filter. A high-pressure vessel (SUS-316) equipped with three sapphire windows (manufactured by Teramex Co., Kyoto) was used for spectroscopy and photoreaction. Enantiomeric excesses of **4a** was determined by chiral gas chromatography on a 30-m ASTEC B-PH column for **4a** (operated at 140 °C; retention times 49-50 min). Under these GC conditions, racemic samples prepared separately by using achiral dimethyl 1,4-naphthalenedicarboxylate as sensitizer gave ee's smaller than 0.3% ee upon repeated analyses.

Photolysis. Samples were charged in the high-pressure vessel (16 ml) as follows. First, an ether solution containing given amounts of substrate **1** and sensitizer **2a** was placed in the vessel and the solvent was evaporated under vacuum to leave a residue, to which a given amount of alcohol was added. Then the vessel was closed and carbon dioxide was introduced to the vessel until the desired pressure (7.7-18.3 MPa) was reached at the fixed temperature (31.0, 35.0, 45.0 and 70.0 ± 0.1 °C). Unfiltered light from a 500-W ultrahigh-pressure mercury lamp was collimated, passed through a water layer and a UV-32 filter, and then focused in front of the sapphire window with a quartz lens. The phase homogeneity inside the vessel was visually checked through the window. After irradiation for a given period of time at each temperature, the vessel was cooled down to 0 °C and the pressure was released at that temperature. The effluent from the vessel outlet was gently bubbled into ice-cooled hexane or diethyl ether to collect any volatile materials. The residue in the vessel was also extracted with diethyl ether. Both were combined and subjected to the chiral GC analysis.

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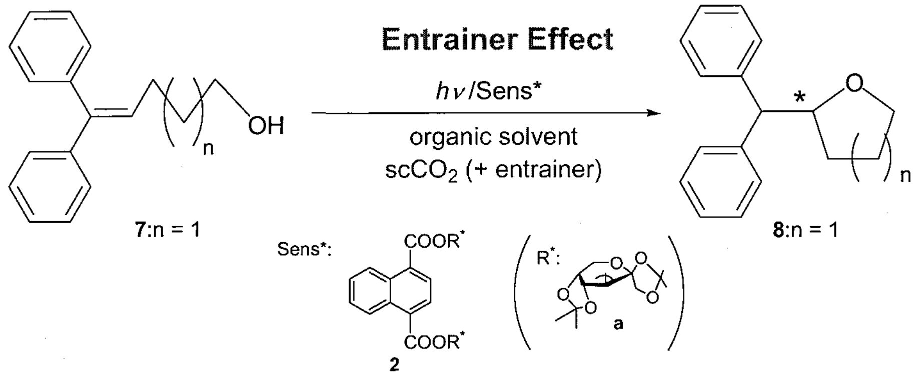
Chapter 3

Enantiodifferentiating Photosensitized Intramolecular Cyclization of ω-Hydroxy-1,1-diphenyl-1-alkenes in $ScCO_2$: Pressure and Entrainer Control

3-1. Introduction

In the preceding chapters, it was revealed that $scCO_2$ possesses unique physicochemical properties that enables one to perform the enantiodifferentiating polar photoaddition in a better efficiency than conventional organic solvents. Furthermore, the clustering effect, which is specific to SCF,[1] functions as a new entropy-related factor for manipulating the photochirogenic process. These advantages of using nc- and $scCO_2$ as reaction media will lead us to the "real" green chemistry by achieving better enantiodifferentiation in environmentally benign media. However, there still remain several mechanistic questions about the roles of clustering in the enantiodifferentiation process of the photochemical polar addition of alcohol to aromatic alkenes, in contrast to the same photoreaction conducted in conventional organic solvents.[2,3] This is partly because the alcohol added to SCF functions not only as an entrainer (or co-solvent) by strongly clustering to solutes but also as a reagent that attacks the radical cationic substrate in an exciplex intermediate. Thus, the roles of added alcohols are quite complicated and therefore controversial in the intermolecular photoaddition of alcohol described in the foregoing chapters. Other problems in the intramolecular photoaddition system include the critical control of microenvironmental polarity around the exciplex and the trade-off relationship between reactivity and enantioselectivity. Most of these issues will be solved by introducing a hydroxyl group into the aromatic alkene substrate.

In this chapter to elucidate the effect of "pure" CO_2-clustering on the photochirogenesis in nc- and $scCO_2$, ω-hydroxyl-1,1-diphenyl-1-alkenes (7) were selected as substrates and subjected to the enantiodifferentiating photosensitized intramolecular cyclization (Scheme 3-1) under the conditions similar to those for the intermolecular photoadditions described in the preceding chapters.



Scheme 3-1. Enantiodifferentiating Photosensitized Cyclization of ω-hydroxyl-1,1-diphenyl-1-alkenes (7) in Organic Solvents at Various Temperatures and in ScCO$_2$ at 45 °C.

Intramolecular photocyclization of ω-hydroxyl-1,1-diphenyl-1-alkenes sensitized by achiral sensitizers was originally reported by Mizuno et al. and Ishii et al.,[4] although no chiral sensitizer was used. The "intramolecularization" of the attacking alcohol moiety simplifies the system and allows us to examine the pure clustering effect of CO$_2$ upon the enantiodifferentiation in the absence of added alcohol that functions as an entrainer and clustering agent. Entrainers are known in general to enhance the solubility,[5] accelerate reaction rate,[6] and/or affect the product selectivity[6] in scCO$_2$. For example, Andrew et al. reported that the addition of entrainer leads to a higher yield of the rearrangement product in photo-Fries rearrangement of naphthyl acetate in scCO$_2$.[7] However, as shown in the previous chapters, methanol added as an entrainer decreases the ee of photoproduct particularly in ncCO$_2$. In this context, it is interesting and important to examine the pure entrainer effects on the intramolecular photochirogenesis reaction.

3-2. Results and Discussion

Intramolecular Photocyclization in Organic Solvents. First of all, this enantiodifferentiating intramolecular photocyclization was performed in various conventional organic solvents at varying temperatures to elucidate the clustering and entrainer effects on the reaction and enantiodifferentiation mechanisms in detail (Table 3-1).

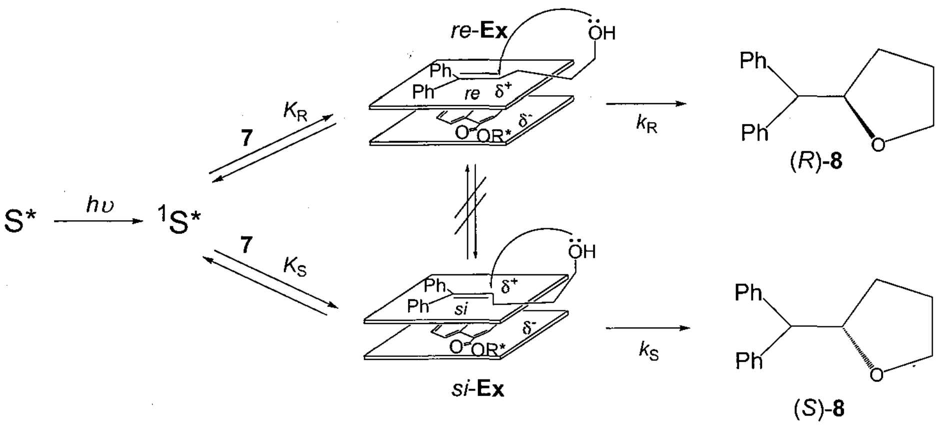
In this reaction, substrate **7** gave the corresponding cyclized product **8** as the major product, as reported previously.[9]

Table 3-1. Enantiodifferentiating Photosensitized Cyclization of **7** in Organic Solvents at Various Temperatures[a]

solvent	temperature/°C	conversion/%[b]	yield/%[c]	ee/%[d]
MCH	20	*e*	*e*	20
	0	*e*	*e*	20
	-20	*e*	*e*	14
toluene	40	46	27	27
	25	24	25	28
	0	14	17	36
	-40	12	14	34
diethyl ether	25	68	12	22
	0	30	13	33
	-20	63	6	35
	-30	5	8	30
	-40	34	4	19
acetonitrile	25	18	14	5
	0	30	12	1
	-20	33	13	0
	-30	34	11	0

[a] [**7**] = 20 mM; [**2**] = 3 mM; irradiated for 2 h. [b]Conversion determined by GC. (See Experimental Section) [c] Yield based on conversion. [d] Ee determined by HPLC. (See Experimental Section) [e] Not determined.

As shown in Table 3-1, the product's ee is very sensitive to solvent polarity. In a polar solvent such as acetonitrile, the product's ee is close to zero at all temperatures examined. Since this result is exactly the same as that observed in the bimolecular photoaddition reaction reported previously,[2] it is reasonable to conclude that this intramolecular version of the photoaddition of alcohol also proceeds through a polarized exciplex intermediate. The enhanced electron transfer from substrate to excited sensitizer in polar solvent leads to the formation of solvent-separated ion pair of chiral sensitizer and substrate. This ion pair ruins the ee of photoproduct. In previous bimolecular report,[2] the combination of saccharide derivative sensitizer and diethyl ether solvent optimizes the trade-off between chemical and optical yield because the bulk polarity of diethyl ether and the microenvironmental polarity around exciplex formed by the polar saccharide moiety were the best combination for facilitating the electron transfer yet keeping the exciplex in contact. The same mechanism operates in the present unimolecular case to give moderate 35% ee again in diethyl ether at a low temperature. It is interesting to note that toluene also gave a similar ee of 36 %. This is probably because the specific π-π interaction between solvent and naphthalene sensitizer facilitates the degree of charge transfer and stabilizes the resulting exciplex despite the relatively low polarity of toluene. In support of this idea, the fluorescence measurement of sensitizer or exciplex in toluene showed unexpectedly large bathochromic shifts compared with the other nonpolar solvents.[2] Although the moderate ee values were accomplished at temperatures lower than the ambient temperature in all solvents employed, the ee value became worse by further decreasing the temperature. Consequently, the enantiodifferentiation mechanism of this intramolecular photocyclization is deduced to involve two distinctly different steps, which are the equilibrium between the diastereomeric exciplexes, i.e. *re*- and *si*-Ex, and the relative rate of intramolecular cyclization from the two exciplexes, i.e. k_R and k_S, as shown in Scheme 3-2.



Scheme 3-2. Reaction Mechanism of Enantiodifferentiating Photosensitized Cyclization of ω-hydroxyl-1,1-diphenyl-1-alkenes (7).

In Scheme 3-2, the product's ee is controlled in general by thermodynamic and kinetic terms. Thus, the *R*/*S* ratio of product may be expressed as a product of the relative population of *re*- and *si*-Ex and the relative rate constant of the subsequent attack of the hydroxyl group, as shown in eq 3-1.

$$\frac{[R]}{[S]} = \left(\frac{K_R}{K_S}\right)\left(\frac{k_R}{k_S}\right) \qquad (3\text{-}1)$$

If the temperature is high enough, the equilibrium should be established and the subsequent intramolecular attack should also be fast. Under such circumstances, the two diastereomeric exciplexes are fully equilibrated with each other and their relative thermodynamic stability determines the product ratio of (*R*)- and (*S*)-**8**, since the subsequent intramolecular attack of the hydroxyl group is very fast and the rate constants are comparable for *re*- and *si*-Ex, i.e. $k_R = k_S$. At lower temperatures, the attack becomes slower and more discriminating. The observed decrease in ee at lower temperatures indicates that the less-stabilized exciplex reacts faster than the stable one to diminish the enantiomer ratio achieved by the equilibrium.

Effects of Mixed Solvent. To examine the influence of specific solvation around sensitizer or exciplex, the photocyclization was performed in representative polar and nonpolar solvents, containing 0.6 M diethyl ether, at various temperatures; the results are shown in Table 3-2.

Table 3-2. Enantiodifferentiating Photosensitized Cyclization of **7** in Organic Solvent Mixtures at Various Temperatures[a]

solvent	temperature/°C	conversion/%[b]	yield/%[c]	ee/%[d]
acetonitrile	0	30	12	1
	-30	34	11	0
	-40			0[e]
acetonitrile + diethyl ether (0.6 M)	0	23	12	0
	-30	39	9	0
	-40	23	11	0
ether	20			24[e]
	0	30	13	33
	-20	63	6	35
MCH	20	*f*	*f*	20
	0	*f*	*f*	20
	-20	*f*	*f*	14
MCH + diethyl ether (0.6 M)	20	*f*	*f*	27
	0	*f*	*f*	30
	-20	*f*	*f*	20

[a] [**7**] = 20 mM; [**2**] = 3 mM; irradiated for 2 h. [b] Conversion determined by GC (see Experimental Section.) [c] Yield based on conversion. [d] Ee determined by HPLC (see Experimental Section). [e] Estimated by extrapolation. [f] Not determined.

As can be seen from Table 3-2, the addition of 0.6 M ether to acetonitrile does not appear to affect the product's ee, consistently affording the racemic products at all temperatures examined. The conversions and yields are also almost the same as those obtained in pure acetonitrile. Obviously, the specific solvation of ether does not appear to occur in polar acetonitrile. In sharp contrast, the addition of 0.6 M ether to MCH greatly improved the ee. This is because a small amount of diethyl ether selectively solvates to polar exciplex to accelerate the electron transfer, yet keeping the radical ionic sensitizer-substrate pair in close contact due to the low bulk polarity of MCH. However, the use of pure ether as a solvent did not improve the ee, as the bulk polarity is higher than that of MCH. We may conclude therefore that the preferential solvation of polar solvent in nonpolar solvent works to some extent in enhancing the product's ee but the degree of enhancement is not very large.

Photocyclization in $scCO_2$. In the photoaddition of alcohol described in the previous chapters, the product's ee was significantly enhanced by using $scCO_2$ as a reaction medium. Since similar enhancement of ee was expected to occur in the intramolecular attack of the hydroxyl group by performing the photoreaction in $scCO_2$, the photocyclization of 7 was performed in $scCO_2$ at 45 °C and the results obtained were compared with those in conventional solvents.

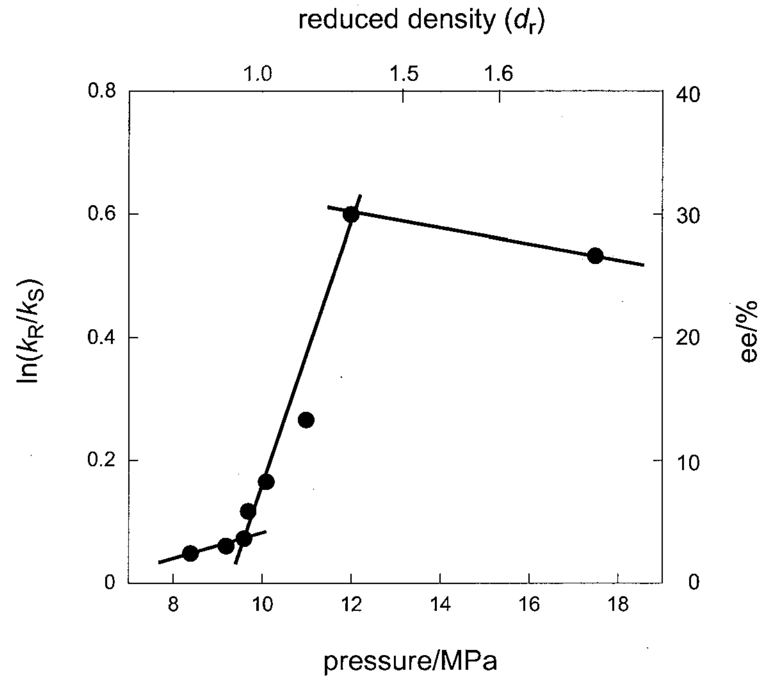


Figure 3-1. Pressure Dependence of the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photocyclization of 7 Sensitized by **2a** in $ScCO_2$ at 45 °C.

As can be seen from Figure 3-1, the ee values obtained in $ncCO_2$ were very low or nearly zero. In a low density and polarity media such as $ncCO_2$, the hydroxyl group of substrate 7 is not extended out but stays around the exciplex intermediate. The presence of hydroxyl group should enhance the microenvironmental polarity around the exciplex and allow its penetration between the radical ion pair to make it "solvent-separated," which in turn reduce the enantioselectivity of the product. Furthermore, a sudden jump of ee was also observed around the transition region in close analogy with the intermolecular photoaddition. However, the pressure range of the transition shift to higher pressure region by ca. 2 MPa, compared with the intermolecular photoaddition. Kolář et al. reported that a small amount of high molecular-weight alkanes changes the critical point dramatically.[8] Bulgarevich and co-workers reported that a small amount of alcohols (from methanol to 1-hexanol) can readily change the solvent parameters, such as π^* and β values.[9] Considering these reports, it is possible that the addition of aromatic alkenol **7** may change the properties of scCO$_2$.

It was expected that the product's ee is inherently higher in this intramolecular photocyclization, since more stabilized diastereomeric exciplex was preferentially formed by the clustering of substrate itself. The attack of the hydroxyl group also proceeded to the preferential prochiral substrate phase. Although the maximum ee obtained in scCO$_2$ is moderate 29% at 12 MPa (Table 3-3), this value is lower than that obtained in diethyl ether and toluene. It is thus concluded that, in pure CO$_2$ media, this intramolecular photocyclization does not afford particularly high ee's that exceed the values obtained in organic solvents.

Table 3-3. Enantiodifferentiating Photosensitized Cyclization of **7** in ScCO$_2$ at 45 °C[a]

pressure/MPa	density(d_r)	ee/%[b]
8.4	0.58	2.4
9.2	0.78	3.0
9.6	0.92	3.6
9.7	0.96	5.8
10.1	1.10	8.2
11.0	1.29	13.2
12.0	1.41	29.1
17.5	1.67	26.0

[a] [**7**] = 2 mM; [**2**] = 0.3 mM; irradiated for 2 h. [b] Ee determined by HPLC. (See Experimental Section)

Effects of Entrainer on Photochirogenesis. To assess the effect of entrainer on this unimolecular photochirogenic reaction, the same photoreaction was examined in scCO$_2$ containing a small amount (0.3 M) of acetonitrile (Figure 3-2).

As mentioned above, the product was consistently racemic in pure acetonitrile under any conditions, because acetonitrile facilitates the dissociation of exciplex to solvent-separated radical ion pair due to its high polarity. Interestingly, the ee was significantly increased by the addition of acetonitrile as entrainer in both nc- and scCO$_2$ media, as shown in Figure 3-2. This selectivity enhancement is rationalized by the preferential clustering of acetonitrile to the exciplex in the CO$_2$ media of low density and polarity. The acetonitrile clustering enhances the microenvironmental polarity around the exciplex, facilitating further charge transfer yet preventing the dissociation due to the gas-like environment around it. The enhanced microenvironmental polarity stabilizes the originally more polarized, and hence more stabilized, diastereomeric exciplex, enhancing its population and susceptivity to the nucleophilic attack by the hydroxyl group. This strategy to utilize the entrainer effect that enables the synergistic thermodynamic stabilization and kinetic acceleration should operate in general in this type of photochirogenic reactions performed in SCF media. In conventional organic solvents, it is much more difficult to find the most favorable conditions to counterbalance the two effects, since higher concentrations of polar solvent added to nonpolar solvent easily accelerate the dissociation, as demonstrated previously.[2]

The parallel shift of the pressure dependence profiles in the presence and absence of acetonitrile (Figure 3-2) indicates that the basic features of nc- and sc CO_2 media are not changed by the addition of entrainer but only the environment around the diastereomeric exciplex is manipulated by the entrainer.

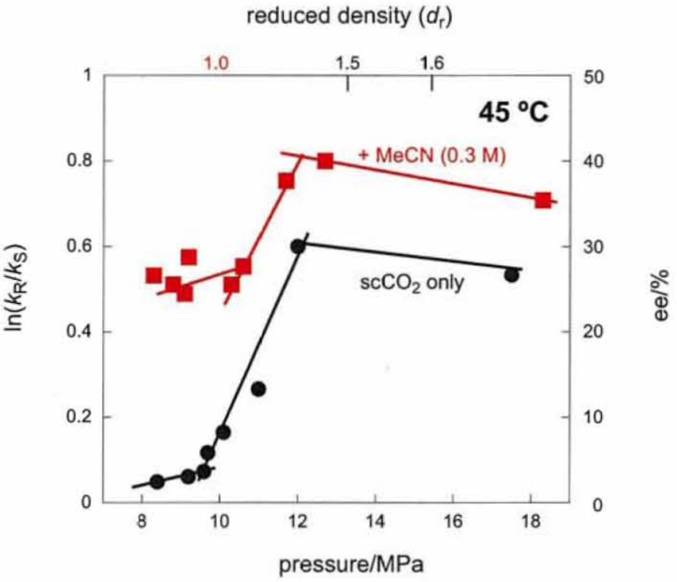


Figure 3-2. Pressure Dependence of the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photocyclization of **7** Sensitized by **2a** in Nc- and $ScCO_2$ at 45 °C in the Presence and Absence of 0.3 M Acetonitrile Added as an Entrainer.

The effect of entrainer concentration on the product's ee was further examined by doubling the acetonitrile concentration. The ee's obtained in the presence of 0.6 M acetonitrile are also plotted against the CO_2 pressure in Figure 3-3. Interestingly, the addition of 0.6 M acetonitrile further enhanced the product's ee in particular in the $ncCO_2$ region, and the $scCO_2$ region as well, to give 40-50% ee. The tremendous ee enhancement from nearly zero to 40% ee in the $ncCO_2$ region makes the pressure dependence profile almost flat in the pressure range examined. However, this does not mean that the $scCO_2$ region moved to a lower pressure, since the addition of entrainer is believed to move the unit critical density to a higher pressure,[10] but rather indicates that the exciplex intermediate is fully clustered by acetonitrile molecules and hence thermodynamically stabilized and kinetically accelerated to give similar ee's, irrespective of the surrounding media, nc- or $scCO_2$. It should be emphasized that, unlike the intermolecular photoaddition case, the entrainer clustering is quite useful in solubilizing the substrate and more importantly in significantly enhancing the enantioselectivity of photochirogenesis in SCF.

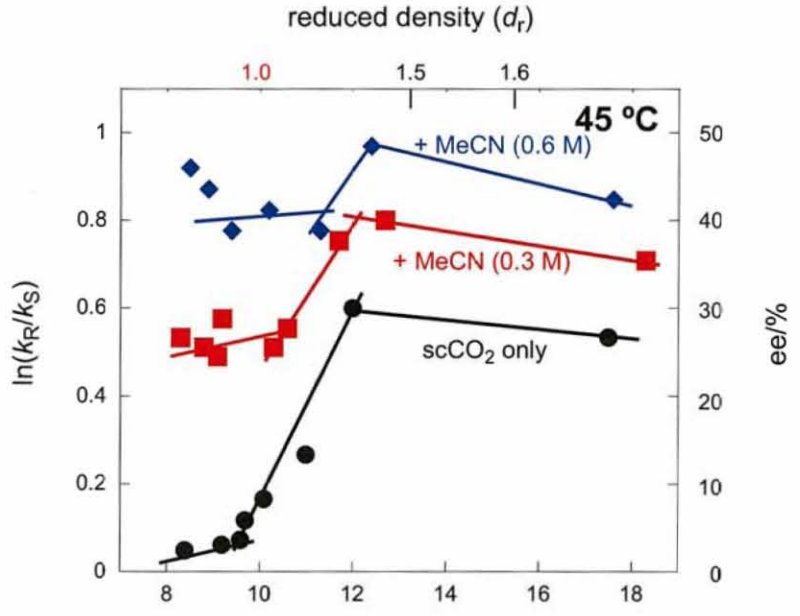


Figure 3-3. Pressure Dependence of the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photocyclization of **7** Sensitized by **2a** in $ScCO_2$ and in $ScCO_2$ with 0.3 M Acetonitrile and 0.6 M Acetonitrile as Entrainer at 45 °C.

The effect of different entrainer was investigated by using diethyl ether and the results of the photocyclization in nc- and $scCO_2$ in the presence of 0.6 M ether are plotted as a function of pressure in Figure 3-4. The overall behavior of ee is very similar to that observed for acetonitrile entrainer, but the sudden leap near the unit critical density still remains and the ee enhancement appears to be more effective in the presence of 0.6 M ether between in $ncCO_2$ and in $scCO_2$. Probably, the weak-polar clustering of ether around the exciplex would be not enable to accelerate forming the more stabilized diastereomeric exciplex and give somewhat lower ee's in $ncCO_2$ comparing in case of acetonitrile. It is crucial and encouraging that both polar acetonitrile and less polar diethyl ether can significantly enhance the ee not only in $ncCO_2$ but also in $scCO_2$ media and the highest ee's obtained in the presence of entrainer are much higher than those obtained in pure $scCO_2$ or organic solvents. It is possible that entrainer clustering can improve the reaction selectivity in general due to the specific entrainer-solute interactions in nc- and $scCO_2$.

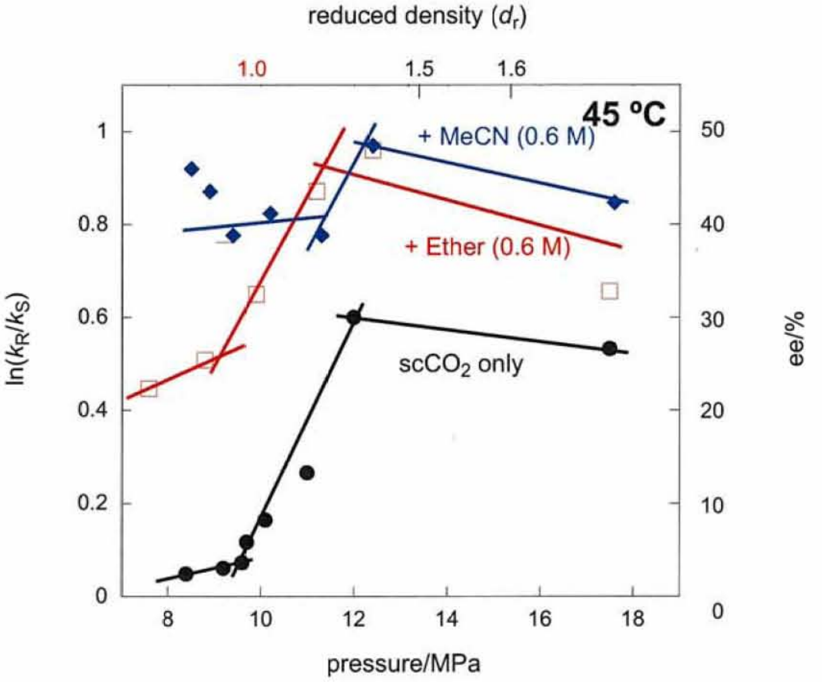


Figure 3-4. Pressure Dependence of the Relative Rate Constant (k_R/k_S), or the Product's Ee, in the Enantiodifferentiating Photocyclization of **7** Sensitized by **2a** in $ScCO_2$ and in $ScCO_2$ with 0.6 M Acetonitrile and Diethyl Ether as Entrainer at 45 °C.

3-3. Conclusions

In this chapter, a new type of asymmetric photosensitization, which does not necessitate the addition of alcohol as reagent, was investigated in order to elucidate the roles of pure CO_2 clustering to the photochirogenesis in $scCO_2$. In this reaction, the product's ee is determined thermodynamically by the relative stability of intevening diastereomeric exciplexes and kinetically by the relative rate of subsequent intramolecular attack of the hydroxyl group to the electron-deficient carbon of alkene substrate. At ambient and higher temperatures, the ee was determined predominantly by the relative stability of the exciplex intermediates because the attack is very rapid. On the other hand, at lower temperatures, the attacking rate of the less stable diastereomeric exciplex becomes faster than that of the stable exciplex to cancel to some extent the initial diastereodifferentiation achieved thermodynamically upon exciplex formation. In pure CO_2, although the difference in CO_2 clustering effect was observed between nc- and $scCO_2$ media, this clustering effect does not function as an efficient entropy-controlling factor to enhance the enantioselectivity.

However, when small organic compound is added to CO_2 media as entrainer, preferential clustering of entrainer takes place to accomplish the enhancement of the enantioselectivity, which cannot be realized by the selective solvation in organic solvent. This enantioselectivity enhancement is achieved by entrainer clustering that simultaneously accelerates charge transfer of the exciplex yet preventing the dissociation of the radical ionic exciplex in the cluster most probably due to the gas-like environment of SCF around the exciplex. Since the intramolecular attack is considered to be very fast in nc- and $scCO_2$ at 45 °C, the product's ee is likely to be determined thermodynamically by the relative stability of diastereomeric exciplex pair.

Strong clustering of polar entrainer, such as diethyl ether and acetonitrile, can significantly enhance the product's ee in both nc- and $scCO_2$ media by further stabilizing the originally more stable diastereomeric exciplex. This preferential entrainer clustering effect may be more widely applicable to other photochirogenic reactions in SCF.

3-4. Experimental Section

Materials. Carbon dioxide of 99.99 % purity was purchased from Neriki Gas Co. and used without further purification. Spectral grade solvents were used throughout the work. 5,5-diphenyl-4-penten-1-ol **7** was synthesized and characterized, as previous reported.[11]

Instruments. A high-pressure vessel (SUS-316) equipped with three sapphire windows (manufactured by Teramex Co., Kyoto) was used for spectroscopy and photoreaction. UNISOKU temperature controller was used for controlling temperature in organic solvent reaction with quartz cells (1 cm x 1 cm x 4 cm). Analytical HPLC of a product's ee was performed on a chiral column (DAICEL IB, 5μm, 4.6 × 250 mm) using a JASCO plus series; the mobile phase was a 98:1:1 (v/v) mixture of *n*-hexane/isopropanol/1,2-dichloroethane under isocratic conditions and the run-time was 25-26 min at a flow rate of 0.3 mL/min. UV detectors were fixed at 220 nm and the eluent and the HPLC column were at 5 °C. The conversion, yield of **7** were determined by capillary gas chromatography on Shimadzu CBP-20 column (30 m × 0.25 mm ϕ); initial column temperature: 180 °C; injector and detector temperature: 250 °C. 8 min after the injection of sample, the column temperature was raised to 220 °C at a rate of 20 °C/min, and kept at that temperature for 40 min. Product's beak was observed at 18 min. All GC peaks were integrated with a Shimazu C-R6A integrator connected to the GC instrument.

Photolysis. In organic solvent, various organic solutions (3 mL) in quartz cells (1 cm x 1 cm x 4 cm), containing **7** (20 mM) and sensitizer (3 mM), were irradiated for 2 h under an Ar atmosphere at each temperature with UNISOKU temperature controller by using a 500-W ultrahigh-pressure mercury lamp fitted with a UV-31 glass filter. Cyclopentadecane was added as an internal standard. Conversion and yield was analyzed on GC and ee was analyzed on HPLC. In case of $scCO_2$, samples were charged in the high-pressure vessel (16 ml) as follows. First, an ether solution containing given amounts of substrate **7** (2 mM) and sensitizer **2a** (0.3 mM) was placed in the vessel and the solvent was evaporated under vacuum to leave a residue. Entrainer was added after evaporation. Then the vessel was closed and carbon dioxide was introduced to the vessel until the desired pressure was reached at 45.0 ± 0.1 °C). Unfiltered light from a 500-W ultrahigh-pressure mercury lamp was collimated, passed through a water layer and a UV-31 filter, and then focused in front of the sapphire window with a quartz lens. The phase homogeneity inside the vessel was visually checked through the window. After irradiation for a given period of time at each temperature, the vessel was cooled down to 0 °C and the pressure was released at that temperature. The effluent from the vessel outlet was gently bubbled into ice-cooled diethyl ether to collect any volatile materials. The residue in the vessel was also extracted with diethyl ether. Both were combined and subjected to the chiral HPLC and the achiral GC analysis.

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General Conclusions

Supercritical carbon dioxide ($scCO_2$) is well documented as a unique medium alternative to the conventional organic solvents not only from the environment-conscious point of view, but also from the viewpoint of unique solvent properties, including clustering effect. Nevertheless, no asymmetric photoreaction in SCFs was reported until very recently. In the present study to explore the feasibility of photochirogenesis in $scCO_2$, the following enantioselective photoreactions were examined in detail. In particular, the effect of clustering, which is specific to SCF and involves temporal and spatial fluctuation of medium density and polarity, was examined for the first time in bimolecular enantiodifferentiating photoreactions as a new entropy-related factor to controlling asymmetric photoreactions. As a representative bimolecular asymmetric photoreaction that was well investigated in organic solvents, the photochemical polar addition of various alcohols to some aromatic alkenes was investigated in detail (Chapters 1 and 2). In Chapter 1, the effects of applied pressure and different substituents (substrate, alcohol, and sensitizer) were examined, while in Chapter 2 the effects of temperature and methanol concentration were investigated. In Chapter 3, the unimolecular photosensitized intramolecular cyclization of aromatic alkenol was used for elucidating the pure clustering effects of CO_2 or entrainer (not as reagent) on the photochemical enantiodifferentiating process.

In Chapter 1, the pressure and substituent effects on the photosensitized polar addition of various alcohols to some aromatic alkenes were investigated in $scCO_2$ at 45 °C. It was revealed that the degree and strength of clustering are significantly different between nc- and $scCO_2$ media. This difference in clustering causes the drastic change in ee observed in the transition region between nc- and $scCO_2$ states, irrespective of the substrate, alcohol, and sensitizer. In the $ncCO_2$ region, the enantioselectivity becomes lower due to the high microenvironmental polarity caused by strong clustering of alcohol. However, in $scCO_2$, efficient enantiodifferentiation is accomplished to give the photoproduct in much better ee's, which are comparable to those obtained in organic solvents. These observations indicate that the clustering effect can be used as a new entropy-related factor for controlling the enantioselectivity of photochirogenesis in $scCO_2$.

In Chapter 2, the temperature effect on the photosensitized polar addition of methanol to 1,1-diphenylpropene was investigated for the first time in $scCO_2$ at 31, 35, 45, and 70 °C. In the $scCO_2$ region, the product's ee was almost the same at each temperature. However, as the temperature is raised, the pressure dependence becomes less steep and the pressure range that gives the rapid ee change shifts to higher pressure. Thus, the near-critical and supercritical regions are clearly discriminated and are connected by the transition region. It is concluded that the photochirogenesis can be multi-dimensionally manipulated by the combination of pressure and temperature as entropy-related factors. Moreover, although it was reported that the clustering effect is associated with the change in CO_2 density, the stereochemical outcomes as a function of the medium density did not show a good correlation with the CO_2 density. Thus, the photochirogenesis in $scCO_2$ is controlled not only by the density but also by the clustering particularly in $ncCO_2$. Furthermore, since methanol clustering efficiently operates in this bimolecular photoreaction in $scCO_2$, the addition of methanol enhances the microenvironmental polarity around the exciplex intermediate. Although the addition of an excess amount of methanol leads to a poor ee due to the formation of a solvent-separated radical ion pair, selective methanol clustering does not appear to accelerate dissociation of the exciplex because of the gaseous environment just outside the clustering layer. This clustering layer, inhibiting the dissociation to a solvent-separated or free radial ion, enables to keep or enhance the enantioselectivity in $scCO_2$.

In Chapter 3 to examine the effect of pure CO_2 clustering or entrainer (not as reagent) clustering on photochirogenesis, photosensitized intramolecular cyclization of aromatic alkenol was investigated. Although the degree of CO_2 clustering was also different between nc- and $scCO_2$, the CO_2 clustering did not enhance the selectivity obtained in organic solvent at the same temperature. However, the addition of a small amount of organic solvent as entrainer dramatically improved the enantioselectivity. CO_2 and entrainer clustering inhibit the exciplex dissociation and facilitate the preferential formation of more stabilized exciplex. This enantioselectivity enhancement is more evident particularly in $ncCO_2$ medium since the preferential clustering effect of CO_2 and entrainer is stronger in $ncCO_2$ rather than $scCO_2$ media.

In conclusion, although only the sudden leap of ee (in the transition region) was observed in the previous unimolecular asymmetric photoreaction, this thesis was unequivocally revealed that the clustering effect of CO_2 itself or entrainer functions as a new entropy-controlling factor for manipulating the photochirogenic reactions in $scCO_2$. Moreover, it was also revealed that the clustering effect (in particularly adding polar entrainer not as reagent) controls the photochirogenesis critically and efficiently to give enhanced ee. The author believes that the present study has paved the way to accomplish the environmentally benign green (photo)chemistry with superior selectivity.

Acknowledgement

First of all, I would like to express my gratitude for Professor Yoshihisa Inoue, who always gave me exact advice, helpful suggestions, and taught me the basics and elegance of chemistry. I also thank him for providing me with special opportunity to study as a visiting scholar at State University of New York, University at Buffalo with Professor Frank V. Bright for 3 months. I owe my special thanks to him, as well.

I am indebted to Professor Takehiko Wada, currently Professor at Tohoku University, who always helped me with valuable advice and helpful suggestions.

I am also grateful to Associate Professor Tadashi Mori, and Assistant Professor Yuko Yamashoji, who retired in March 2006, and Dr. Cheng Yang for their helpful advice and daily encouragement.

I express my special thanks to all members of the Inoue group for their friendship and warm assistance; they have made my research life comfortable and productive.

I am indebted to the member of "Team-Ueno", especially Dr. Hirohisa Todo, for their friendship and showing me the good behavior to chemistry.

I wish to express my sincere thanks to my family: my parents and brother, Kozaburo, Kazue and Takeshi for their continuous favor, support, encouragement and understanding. Without their support and understanding, this research thesis has never completed.

Finally, I wish to thank again to all people for their support and encouragement to me.

Financial support of this work by the JSPS research fellowship for young scientists (No. 08910) is gratefully acknowledged.