First Asymmetric Photosensitization in Supercritical Fluid. Exceptionally High Pressure/Density Dependence of Optical Yield in Photosensitized Enantiodifferentiating Isomerization of Cyclooctene

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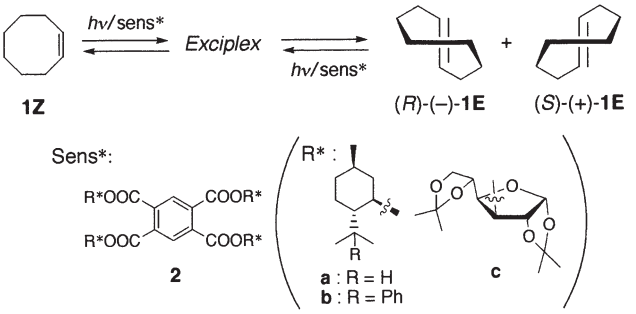
The photosensitized enantiodifferentiating isomerization of (*Z*)-cyclooctene (**1Z**) in supercritical carbon dioxide has been performed for the first time. The critical control of the enantiomeric excess (ee) of chiral product, (*E*)-cyclooctene (**1E**), and even the switching of the product's chirality were achieved through a small change of pressure particularly in the low-density region near the critical density. Quantitative evaluation of these ee changes was achieved by estimating differential activation volumes between the diastereomeric transition states of the reaction.

Asymmetric photochemistry provides us with a direct access to various chiral compounds with unique/constrained structures through the electronically excited states, which is distinctly different from the conventional thermal and enzymatic counterparts.[1–3] In a series of our studies of the enantiodifferentiating photosensitization of cycloalkenes,[4–11] we have revealed that the entropy-related factors, such as temperature, pressure, and solvation, play essential roles in determining the chiral sense and enantiomeric excesses (ee's) of photoproducts. As a consequence of the vital contribution of the entropy factors, even antipodal products can be obtained by changing one of these variants, and the combined use of these factors leads to high ee's in both uni- and bimolecular asymmetric photoreactions.

This principle of chirality variation with entropy can be verified in any phase from gas to solid, although all possibilities have not been examined experimentally. In practice, no attempt has been reported in lower density or viscosity phases such as gases and supercritical fluids (SCFs).

In this context, SCFs are of particular interest, because the use of SCFs as reaction media offers the rare opportunity to control reaction rate and selectivity[12,13] through the dramatic changes of the solvent property in relatively narrow ranges of pressure and/or temperature.[14–16] Despite this attractive features of SCFs, no asymmetric photochemical reaction in SCFs have been reported. In the present study, we conducted the enantiodifferentiating *Z-E* photoisomerization of cyclooctene sensitized by optically active benzenetetracarboxylates (Scheme 1) in supercritical carbon dioxide ($scCO_2$), which is readily accessible ($T_c = 31\,°C$, $P_c = 7.38\,MPa$) and behaves as a solvent of fairly low polarity with variable density and viscosity.[17] The low polarity environment is essential for securing intimate interactions in the exciplex intermediate. We now report the pronounced effects of $scCO_2$ on the chiral sense and ee of the product, resulting in the unprecedented inversion of the product chirality induced by pressure change.



Scheme 1.

The enantiodifferentiating photoisomerization of **1Z** sensitized by enantiopure benzenetetracarboxylates (**2a–c**)[11,18] was run in $scCO_2$ at varying pressure in a temperature-controlled ($45.0 \pm 0.1\,°C$) high-pressure vessel (SUS-316) with sapphire windows. Unfiltered light from a 500-W super high-pressure mercury lamp was collimated, passed through water layer and a Vycor filter, and then focused in front of the sapphire window by a quartz lens. The homogeneity of the phase was visually checked through the window. After 1 h irradiation, the pressure was released at 0 °C and the effluent was softly bubbled into ice-cooled pentane. The residue in the vessel was also extracted with pentane. The gas chromatographic (GC) analysis of the combined extract demonstrated that the major course of the photoreaction was the *Z-E* isomerization, giving chiral **1E**, in all runs. **1E** obtained was selectively extracted from the combined pentane solution with aqueous silver nitrate,[5] and was subjected to a chiral GC analysis[19] to determine its ee value.

The CO_2-pressure effects on the ee value obtained are depicted in Figure 1, where the natural logarithm of the relative rate constant for the formation of (*S*)-(+)- and (*R*)-(−)-**1E**, i.e. $\ln(k_S/k_R)$ or $\ln[(100 + \%ee)/(100 - \%ee)]$, is plotted as a function of pressure.

Interestingly, the pressure dependence of the ee was not uniform over the employed pressure range from 7.8 to 23 MPa, featuring a sudden change near the critical density ($\rho_C = 0.468\,g/cm^3$; $P = 9.8\,MPa$ at 45 °C) in all cases examined, while unidirectional pressure dependence was observed for the same photoreaction in the conventional organic solvents.[7] It should be emphasized that the pressure dependence of product ee is exceptionally high only in a very narrow pressure range (8 and 11 MPa) near the critical density of $scCO_2$. As can be seen from Figure 1, $\ln(k_S/k_R)$ was significantly enhanced in the low-pressure region near the critical density upon sensitization with terpenoid ester **2a** or **2b** to give more (*R*)- or (*S*)-**1E**, respectively. In contrast, the use of saccharide ester **2c** as a chiral sensitizer led

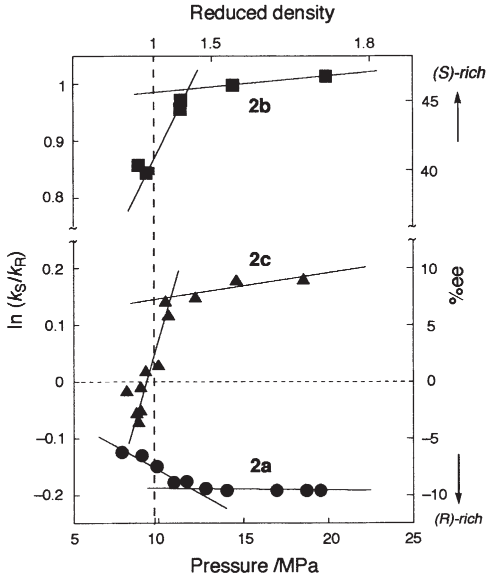


Figure 1. Pressure dependence of the relative rate constant (k_S/k_R), or the product ee, in the enantiodifferentiating photoisomerization of **1Z** sensitized by **2a** (●), **2b** (■) and **2c** (▲) in scCO$_2$ at 45 °C.

to a switching of the product chirality from *R* to *S* near the reduced density of 1. In each case, the ee approaches an apparent plateau at higher pressures to give the ultimate ee.

To analyze the pressure effect in scCO$_2$ more quantitatively, the differential activation volume ($\Delta\Delta V^{\ddagger}{}_{\text{S-R}} = \Delta V^{\ddagger}{}_{\text{S}} - \Delta V^{\ddagger}{}_{\text{R}}$) for the formation of (*S*)- and (*R*)-**1E** was evaluated from the ee changes shown in Figure 1. Based on the transition state theory, the pressure effect on k_S/k_R at a given temperature (T) is given by eq 1.[7]

$$[\partial \ln(k_S/k_R)/\partial P]_T = -\Delta\Delta V^{\ddagger}{}_{\text{S-R}}/RT \tag{1}$$

Integration of eq 1, assuming a constant activation volume over the entire pressure range employed, gives eq 2:

$$\ln(k_S/k_R) = -(\Delta\Delta V^{\ddagger}{}_{\text{S-R}}/RT)P + C \tag{2}$$

where C is the integration constant equal to $\ln(k_S/k_R)_{P=0}$.

From the slopes of the plots in Figure 1, distinctly different $\Delta\Delta V^{\ddagger}{}_{\text{S-R}}$ values were obtained for **2a–c** in the near-critical and higher pressure regions; the results are listed in Table 1, along with those obtained in pentane. The absolute $\Delta\Delta V^{\ddagger}{}_{\text{S-R}}$ values for the near-critical region are far greater than those obtained for the same photoisomerizations performed in pentane (-5.6 to $+3.5\,\text{cm}^3/\text{mol}$).[7] These striking differences in $\Delta\Delta V^{\ddagger}$ clearly indicate that the transition-state structure and/or enantiodifferentiation mechanism involved in near-critical CO$_2$ and conventional organic solvent are completely different from each other, although well-compressed scCO$_2$ at pressures >15 MPa appears to behave like a liquid solvent.

Table 1. Differential activation volumes ($\Delta\Delta V^{\ddagger}{}_{\text{S-R}}/\text{cm}^3\,\text{mol}^{-1}$) for the enantiodifferentiating photoisomerization of **1Z** sensitized by **2a–c** in scCO$_2$ and in pentane

	in scCO$_2$		in pentane
Sensitizer	$P < 11$ MPa	$P > 15$ MPa	$P = 0.1$–400 MPa
2a	45	1.0	−3.71[a]
2b	−160	−7.7	−2.08
2c	−274	−12.1	−1.22

[a] Reference 7.

In the near-critical density region, the local density of CO$_2$ around the solute molecules is much higher than the bulk density,[20–22] as a result of so-called "solvent clustering." Under the condition of density fluctuation, it is deduced that the entropy gain and/or required energy for transferring CO$_2$ molecules from the clusterized exciplex to the much more disordered bulk during the enantiodifferentiating process are large, affording the very large $\Delta\Delta V^{\ddagger}$ values in the present system. At the higher pressures, the difference between the local density and the bulk density is not considerable, and the entropy of the CO$_2$ molecules around the solutes is close to that of the bulk solvent. Therefore, lower sensitivity of ee at higher pressure region is well compatible with the results of the high-pressure study in conventional organic solvents,[7] where a hydrostatic pressure of up to several hundreds of MPa is required to achieve an appreciable change in ee. The effect of the sensitizer structure on the $\Delta\Delta V^{\ddagger}$ might be also explained by the difference of the microenvironmental structures and/or the reaction mechanism for each reaction.

In this first asymmetric photosensitization in SCF we elucidated the critical control of product ee and even the switching of product chirality can be attained in scCO$_2$ with an appropriate sensitizer through a small change of pressure particularly in the low density region near the critical density. Furthermore, the entropy is much more effective on the chirality control in scCO$_2$ near the critical density rather than in liquid phases or highly compressed scCO$_2$.

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