CHIRAL PHOTOCHEMISTRY IN SUB- AND SUPERCRITICAL CARBON DIOXIDE. SUDDEN JUMP OF OPTICAL YIELD IN ASYMMETRIC *Z-E* PHOTOISOMERIZATION OF CYCLOOCTENE

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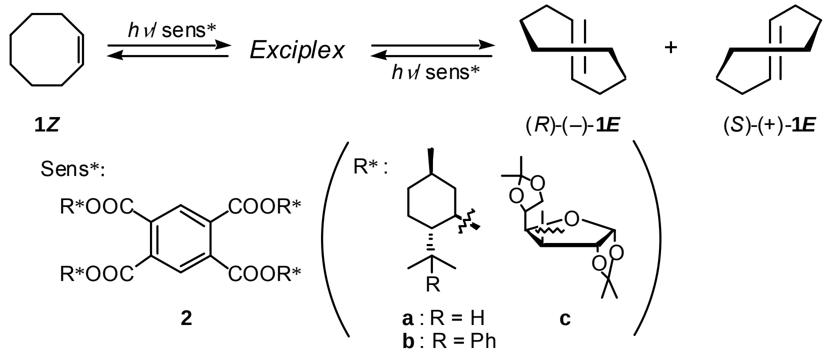
Introduction: Photochirogenesis, or photochemical asymmetric synthesis, provides us with a direct access to a wide variety of chiral compounds with unique and/or constrained structures through the electronically excited states, which is distinctly different from the conventional thermal and enzymatic counterparts.[1-3] However, the low enantiomeric excesses (ee's) reported so far would have discouraged the detailed investigations of mechanism and factors governing the excited-state chiral interactions. In a series of 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 ee of photoproduct. 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 enantiodifferentiating photoreactions.

In this context, supercritical fluids (SCFs) are of particular interest, since the use of SCFs as reaction media offers the rare opportunity to control the rate and selectivity of reaction[12,13] through the dramatic changes of solvent properties in relatively narrow ranges of pressure and/or temperature.[14-16] In the present study, we conducted the enantiodifferentiating *Z-E* photoisomerization of cyclooctene sensitized by optically active benzenetetra-carboxylates (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] We now wish to report the pronounced effects of reduced density of scCO_2 on the chiral sense and ee of product, resulting in the unprecedented inversion of the product chirality induced by density change.

Scheme 1. Enantiodifferentiating Photoisomerization of **1Z** in Suprecritical Carbon Dioxide Sensitized by Optically Active Benzenetetracarboxylates (**2a-c**)



Methodology: The enantiodifferentiating photoisomerization of **1Z** sensitized by enantiopure benzenetetracarboxylates (**2a-c**) was run in scCO_2 at varying pressure in a temperature-controlled high-pressure vessel with sapphire windows. Unfiltered light from a 500-W super high-pressure mercury lamp was collimated, passed through a water layer and a Vycor filter, and then focused in front of the sapphire window by a quartz lens. The pressure was adjusted by charging CO_2 into the vessel under the isothermal condition (45.0 ± 0.1 °C). In all runs, the major course of the photoreaction was the *Z*-*E* isomerization, giving chiral **1E** of varying ee's, which were determined by chiral GC on a Supelco β-Dex 225 column.

Results and Discussion: 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 (□$_C$ = 0.468 g/cm^3; P = 9.8 MPa at 45 °C) in all cases examined. As can be seen from Figure 1, logarithm of the relative rate constant for the formation of (*S*)- and (*R*)-**1E**, i.e. ln (k_S/k_R), was significantly enhanced in the low pressure region near □$_C$ (i.e. reduced density = 1) 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 to a switching of the product chirality from *R* to *S* at the reduced density of 1. In each case, the ee approaches an apparent plateau at higher pressures to give the ultimate ee.

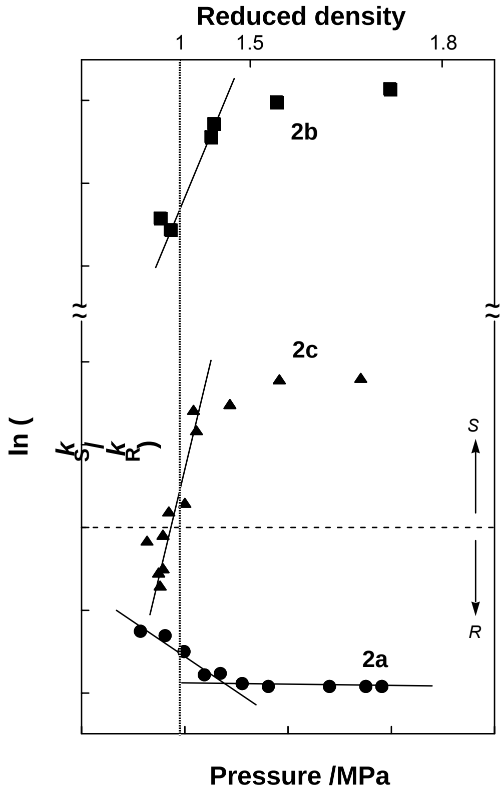


Figure 1. Pressure dependence of the relative rate constant, k_S/k_R or (100 + %ee)/(100 – %ee), in the enantiodifferentiating photoisomerization of **1Z** sensitized by **2a** (●), **2b** (■) and **2c** (▲) in scCO$_2$ at 45 °C.

The critical changes in k_S/k_R or ee particularly at the low pressure region may be related to the high compressibility of the medium CO$_2$ in the near-critical region, as the ee is relatively insensitive to pressure above 15 MPa, where scCO$_2$ is much less compressible than in the near-critical region. The low sensitivity of ee at the high pressure region is well compatible with the results of the high-pressure study reported for the same photoreaction in conventional organic solvent,[7] where a hydrostatic pressure of up to several hundreds of MPa is required to achieve an appreciable change in ee. 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$_2$.

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

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

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

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

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 $\Delta\Delta V^{\ddagger}_{S-R}$ values were obtained for **2a**,-**2c** in the near-critical and higher pressure regions; the results are listed in Table 1, along with those obtained in pentane. The absolute $\Delta\Delta V^{\ddagger}_{S-R}$ values for the near-critical region are far greater than those (–5.6 to +3.5 cm^3/mol)[7] obtained for the same photoisomerizations performed in pentane. These striking differences in $\Delta\Delta V^{\ddagger}$ clearly indicate that the exciplex 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 conventional liquid.

Table 1. Differential Activation Volumes ($\Delta\Delta V^{\ddagger}_{S-R}$/$cm^3$ mol^{-1}) for the Enantiodifferentiating Photoisomerization of **1Z** Sensitized by **2a-c** in Supercritical Carbon Dioxide ($scCO_2$) and in Pentane

sensitizer	$scCO_2$		pentane
	$P < 11$ 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 general, pressure effects on reaction rate are attributed to the changes in free volume rather than intrinsic volume. In the near- critical density region, where isothermal compressibility is high, the local density around solute molecules is much higher than the bulk density of CO_2.[18-20] This phenomenon, termed “local density augmentation” or “clustering,” is thought to be responsible at least in part for the dramatic changes in product selectivity (ee) and extremely large $\Delta\Delta V^{\ddagger}_{S-R}$ values observed in the present system.

It is crucial to assess the cluster size[21] in evaluating the effect of solvation structure on the product selectivity and its pressure dependence. According to the fluctuation theory of Debeneditti,[21] the cluster size, ξ, at the infinite dilution can be calculated by eq 3:

$$\xi = \rho k_B T \kappa_T - V^{\infty} \rho \tag{3}$$

where ρ denotes the density of $scCO_2$, k_B the Boltzmann constant, and V^{∞} the partial molar volume of solute at the infinite dilution. The relevant CO_2 densities were calculated from the Lee-Keslar equation.[22] Using the activation volume $\Delta V^{\ddagger}$ instead of V^{∞} after Ikushima *et al.*,[23] the differential cluster size of the transition states to (*S*)- and (*R*)-**1E** in the present enantiodifferentiating photoisomerization is given by eq 4.

$$\Delta\xi_{S-R} = -\rho\, \Delta\Delta V^{\ddagger}_{S-R} \tag{4}$$

Figure 2 illustrates the pressure dependence of the differential cluster size $\Delta\xi_{S-R}$ value, for the enantiodifferentiating photosensitized isomerization of **1Z**. It is noted that only in the near-critical region the cluster size varies by one to three between the two enantiomeric transition states giving (*S*)- and (*R*)-**1E**, while no difference in cluster size is observed at higher pressures even in scCO$_2$. The different cluster sizes at the transition state must be responsible for the huge $\Delta\Delta V^{\ddagger}_{S-R}$ values observed near the critical density region observed for all sensitizers examined.

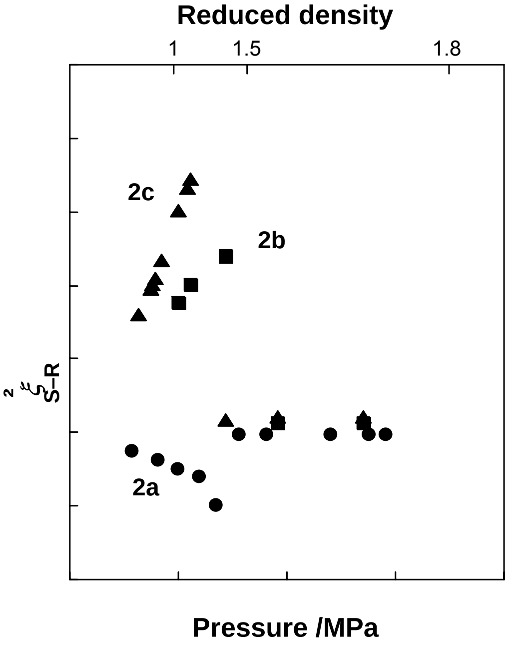


Figure 2. Differential cluster sizes $\Delta\xi_{S-R}$, or $-\Delta\Delta V^{\ddagger}_{S-R}\rho$ values, obtained for the enantiodifferentiating photoisomerization of **1Z** sensitized by **2a** (●), **2b** (■) and **2c** (▲) in scCO$_2$ as a function of pressure at 45 °C.

Conclusions: In this first asymmetric photosensitization in SCF we found the highly pressure-dependent ee's and the unprecedented inversion of the sense of product chirality by changing the medium density of SCF. Thus, the critical control of product ee and even the switching of product chirality can be attained in scCO$_2$ through a small change of pressure particularly in the low density region near the critical density, where the entropy factor play the major role. The large free volume and high compressibility of SCF and the dynamic change of cluster size and structure are jointly responsible for such unique behavior in the asymmetric photosensitization performed in SCF.

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