Critical Control by Temperature and Pressure of Enantiodifferentiating Anti-Markovnikov Photoaddition of Methanol to Diphenylpropene in Near Critical and Supercritical Carbon Dioxide

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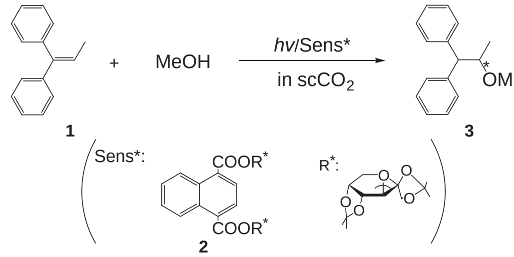
The enantiomeric excess of photoadduct obtained in the title reaction was critically manipulated not only by pressure (*P*) but also by temperature (*T*), exhibiting substantially different *P*-dependence profiles at different *T*, yet sharing a sudden leap near the critical density at each *T*, for which the difference in clustering property of methanol in near and supercritical CO_2 is thought to be responsible.

Recently, chiral photochemistry, or photochirogenesis, attracts much attention as an attractive alternative to the conventional catalytic asymmetric syntheses.[1] Of several strategies employed in photochirogenesis, enantiodifferentiating photosensitization is mechanistically intriguing and synthetically engaging in view of the chiral-source efficiency.[1b,2,3] For several photochirogenic reactions, we have shown that the enantiomeric excess (ee) of photoproduct is highly sensitive to temperature,[4] pressure,[5] and solvation,[6] which indicates that these entropy-related factors critically manipulate freedoms of the intervening exciplex of chiral sensitizer with substrate.

From the entropic point of view, dynamically fluctuating supercritical fluids (SCFs) are of our special interest. In particular, supercritical carbon dioxide ($scCO_2$) is desirable not only as a "green" reaction medium but also as an SCF attainable under mild conditions (the critical point at 31 °C and 7.38 MPa). It was shown that regio- and stereochemical fates of (photo)chemical reactions[7,8] can be manipulated by changing medium property (density, dielectric constant, etc.) through alteration of pressure and/or temperature in a narrow range.[9–11] 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 SCF, on photochirogenic reactions by examining the product's ee. Indeed, we performed the photosensitized enantiodifferentiating isomerization of (*Z*)-cyclooctene[12] and polar addition of alcohols to aromatic alkenes in $scCO_2$ at 45 °C.[13,14] In both cases, the product's ee showed discontinuous pressure-dependence behavior around the pressure that gives the critical density (9.9 MPa at 45 °C).[15] Such an abrupt ee change at a specific pressure had never been reported for the same photoreactions conducted in conventional organic solvents,[16] and was tentatively ascribed to the difference in cluster structure in near and supercritical CO_2 without further examining the temperature effect, the most important entropy-related factor.

In this first study to investigate the temperature effect on the pressure-dependence profile and to elucidate the origin of the discontinuous pressure dependence of product's ee, we performed the enantiodifferentiating photoaddition of methanol to 1,1-diphenylpropene (**1**) sensitized by chiral 1,4-naphthalenedicarboxylate (**2**) and examined the fluorescence spectra and lifetimes under some SCF conditions (Scheme 1).



Scheme 1. Photosensitized enantiodifferentiating polar addition of methanol to 1,1-diphenylpropene (**1**).

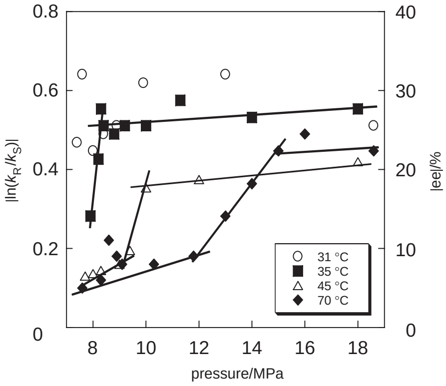


Figure 1. The logarithm of relative rate constant (k_R/k_S), and the product's ee of **3**, as a function of pressure in the enantiodifferentiating photosensitized polar addition of methanol to **1** in $scCO_2$ at 31, 35, 45, and 70 °C.

As shown in Figure 1 (see also Figures S1–S4),[17] the pressure-dependence profile turned out to be a critical function of reaction temperature. At 31 °C (the critical temperature), the ee's of **3** 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 unprecedented behavior would be inherent to the reaction near the critical point, where even a small deviation in temperature or pressure may lead to significant changes in medium properties and hence in ee.

At temperatures ≥35 °C, the pressure-dependence profiles are more coherent (Figure 1). In sharp contrast to the moderate pressure dependence observed in $scCO_2$ (as was the case in organic solvents),[5] the product's ee exhibited a sudden leap near the specific pressure that gives the unit reduced density ($d_r = 1$) at each temperature (i.e., 8.1, 9.9, and 14.2 MPa at 35, 45, and 70 °C, respectively),[15] for which the abrupt change in medium properties should be responsible.[12,13] Hence, it is more

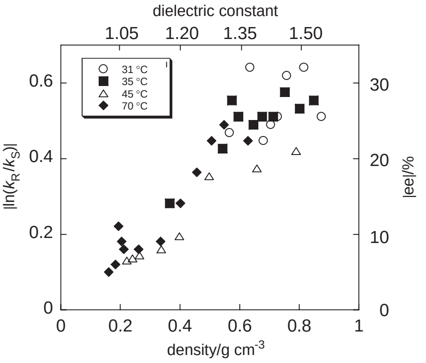


Figure 2. Density effect on the relative rate constant (k_R/k_S), or the product's ee, in $scCO_2$ at various pressures and temperatures.

Table 1. Fluorescence maxima and lifetimes of saccharide sensitizer **2** in the presence (λ and τ) and absence (λ° and τ°) of 0.5 M methanol in $scCO_2$ at various temperatures (T) and pressures (P)

T/°C	P/MPa	λ°/nm	λ/nm	$\Delta\lambda$/nm	τ°/ns	τ/ns	τ/τ°
35	7.5	394	398	4	6.8	3.6	0.53
	18.0	397	398	1	6.6	4.0	0.61
45	9.0	394	398	4	6.7	3.8	0.57
	18.0	396	397	1	6.6	4.3	0.65
70	11.0	393	399	6	6.2	2.9	0.47
	18.0	394	396	2	6.6	3.6	0.55

reasonable to correlate the obtained ee with the medium density or dielectric constant. Since the dielectric constant of $scCO_2$ is known to nicely correlated with the density,[18] we plotted the product's ee as a function of the density.

As shown in Figure 2, the product's ee is better correlated with density (and dielectric constant) rather than pressure, and more importantly all the ee data obtained at different temperatures follow a single trend. Nevertheless, the assembled plot still exhibits a small leap near the pressure that gives the unit reduced density. In this relation, we previously reported that the precise control of solvent polarity around the exciplex is essential for obtaining a good ee in this polar photoaddition.[16] Thus, polar solvents accelerate dissociation of the intervening exciplex to a solvent-separated or free radical ion pair to give good chemical yield but only poor ee, whereas the degree of charge transfer in the exciplex is not large enough to be attacked by alcohol in nonpolar solvents.[14,16] After some trials, diethyl ether was chosen as the optimal solvent for this enantiodifferentiating photoaddition.[16] Consequently, it is reasonable that the density of $scCO_2$ significantly affects the product's ee in the present case.

To elucidate the nature of methanol clustering in near and supercritical CO_2, we performed the fluorescence spectral examinations of sensitizer **2** in the presence and absence of methanol in $scCO_2$ at 35, 45, and 70 °C. The fluorescence intensity was enhanced by raising the pressure simply due to the increased solubility (see Figures S6–S11).[17] Interestingly, the bathochromic shift of fluorescence peak upon addition of 0.5 M methanol was more pronounced in near critical CO_2 ($\Delta\lambda = 4$–6 nm) than in supercritical CO_2 ($\Delta\lambda = 1$–2 nm) at the temperatures examined (Table 1).

We also measured the fluorescence lifetime of **2** under comparable conditions. As shown in Table 1, in the absence of methanol, the lifetime was insensitive to the CO_2 pressure. However, the addition of 0.5 M methanol significantly shortened the lifetime in all cases, degree of which is appreciably more pronounced in the near critical region, as judged from the τ itself as well as the τ/τ° value. These spectroscopic data are in good agreement with the stronger clustering of methanol to sensitizer in near critical CO_2.

In this variable temperature study, we have revealed that the product's ee is better correlated with the density of CO_2, and that the microenvironmental polarity around the exciplex is significantly enhanced in the near critical region through the strong clustering of methanol. These insights into the nature of exciplex in SCF not only contribute to our understanding of the factors and mechanisms manipulating the photoenantiodifferentiation but also promote the use of SCFs in chiral photochemistry and related area of chemistry.

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