

Enantiodifferentiating Photoaddition of Alcohols to 1,1-Diphenylpropene in Supercritical Carbon Dioxide: Sudden Jump of Optical Yield at the Critical Density

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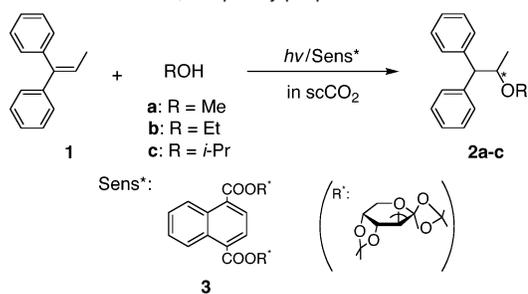
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Recent studies on photochirogenesis have greatly promoted our understanding of the mechanisms and factors that control the stereochemical outcome of enantio- and diastereodifferentiating processes in the excited state.^{1,2} In particular, enantiodifferentiating photosensitization, as a method of efficient chirality transfer alternative to the conventional thermal catalytic and enzymatic strategies, has attracted much attention and interest.^{2–4} Not only the enantiomeric excess (ee) but also the absolute configuration of the photoproduct is critically affected, or even inverted, by entropy-related factors such as temperature (*T*),⁵ pressure (*P*),⁶ and solvation.⁷ This enables us to obtain antipodal products by simply manipulating one of these factors, further controlling the ee of each enantiomer by raising or lowering *T*. In both cases the entropy factor plays the vital role in the enantiodifferentiating step occurring in the exciplex.^{3–7}

Supercritical fluids (SCFs), particularly carbon dioxide (scCO₂), have been employed as environmentally benign replacements for more traditional solvents in green chemistry, because of their nontoxicity, abundance, low cost, and other favorable features. From the entropic point of view, SCFs are of particular interest, since the use of SCFs as reaction media provides us with a rare opportunity to control the reaction rate and selectivity⁸ through the significant changes of solvent properties (viscosity, density, dielectric constant, etc.) in narrow ranges of *P* and *T*.^{10–12} Despite these attractive features, no asymmetric photoreaction in SCF had been reported until very recently. In our recent study on the photosensitized enantiodifferentiating *Z–E* isomerization of cyclooctene performed in scCO₂, we demonstrated that the ee of the produced (*E*)-isomer is highly pressure dependent in the subcritical region, but becomes much less dependent in the supercritical region, affording an obvious transition slightly above the critical density, which was tentatively rationalized in terms of the different degrees of CO₂ clustering in the exciplex intermediate.¹³

In this study to expand the scope of photochirogenesis in SCF to bimolecular reaction systems and also to elucidate the origin of the discontinuous pressure dependence of ee in scCO₂, we chose the enantiodifferentiating polar photoaddition of alcohol to 1,1-diphenylpropene (**1**) sensitized by chiral naphthalenecarboxylates (**3**) (Scheme 1), which is mechanistically well understood, highly sensitive to microenvironmental polarity, and well-suited for fluorescence spectral examinations.^{14,15} All of these features are indispensable for elucidating the role of clustering in photochirogenesis in SCF.

Scheme 1. Photosensitized Enantiodifferentiating Polar Addition of Various Alcohols to 1,1-Diphenylpropene in scCO₂.



Photolyses of a mixture of substrate **1**, alcohol (*R* = Me, Et, *i*-Pr), and sensitizer **3** (*R** = 1,2:4,5-di-*O*-isopropylidene- α -D-fructopyranosyl) dissolved in scCO₂ were run at *P* = 7.7–18 MPa in a temperature-controlled (45 °C) pressure vessel (SUS-316) equipped with sapphire windows for irradiation and spectral measurements (Teramecs Co., Kyoto). Radiation from a 500-W ultrahigh-pressure Hg arc (Ushio USH-500SC) was collimated, passed through a water layer and a UV-32 filter, and then focused in front of the sapphire window. The homogeneity of scCO₂ inside the vessel was checked visually. After irradiation, the pressure was released at 0 °C, and gas from the reaction vessel was gently bubbled into ice-cooled hexane to collect any volatile materials. The residue in the vessel was extracted with hexane. Chiral GC analyses (ASTEC B-PH column operated at 120–140 °C for **2a** and **2b** or B-DM column operated at 120 °C for **2c**) of the extracts gave moderate-to-excellent chemical yields and varying ee's for adducts **2a–c** (see Supporting Information).

The pressure-dependence profiles of product ee are illustrated for **2a–c** in Figure 1, where the absolute value of the natural logarithm of the relative rate constant for the formation of (*R*)- and (*S*)-**2**, i.e., $|\ln(k_R/k_S)|$ or $|\ln[(100 + \% ee)/(100 - \% ee)]|$, is plotted as a function of *P*, as the absolute configurations of **2b** and **2c** have not been determined.

As shown in Figure 1, there is a clear correlation between the bulkiness of the alcohol and the product ee, giving the best ee for 2-propanol over the *P* range employed. A much more intriguing feature unique to this bimolecular enantiodifferentiating photo-reaction is the sudden jump of ee at around the critical density ($d_C = 0.468 \text{ g cm}^{-3}$ at 9.9 MPa and 45 °C), which is common to all the alcohols employed. A similar jump slightly above d_C was observed in the enantiodifferentiating photoisomerization of cyclooctene in scCO₂, although further examinations in the subcritical region were not possible for solubility reasons.¹³ It is noted in the present case that the pressure dependence of ee is continuous at

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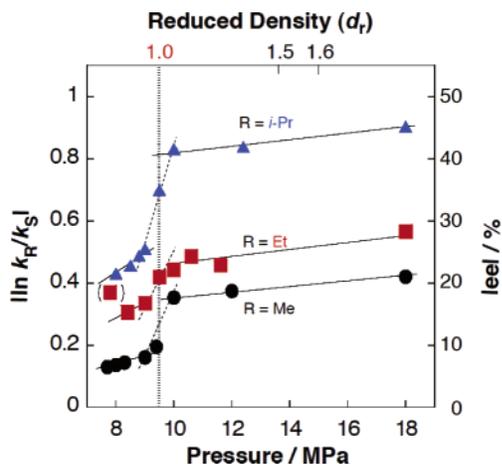


Figure 1. Pressure dependence of the relative rate constant (k_R/k_S), or the product ee, in the enantiodifferentiating photoaddition of methanol (R = Me), ethanol (R = Et), and 2-propanol (R = *i*-Pr) to **1** sensitized by **3** in scCO_2 at 45 °C.

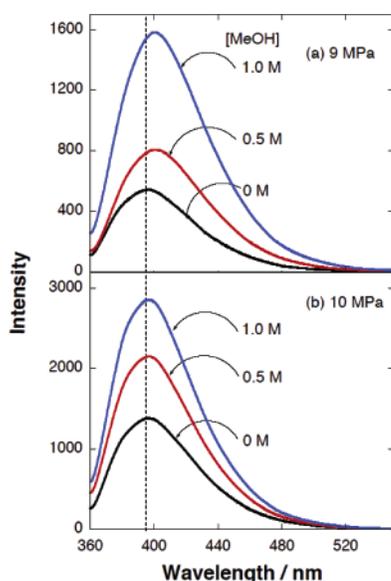


Figure 2. Fluorescence spectra of **3** excited at 340 nm in the presence and absence of methanol (0–1 M) in scCO_2 (45 °C) in (a) subcritical ($P = 9$ MPa) and (b) supercritical ($P = 10$ MPa) regions.

least in the subcritical ($P < 9$ MPa) and supercritical ($P > 10$ MPa) regions, but a big jump of ee was observed around d_C , giving a “step” profile in each case.

To elucidate the origin of this unusual pressure dependence of ee, we performed fluorescence spectral examinations of **3** in scCO_2 in the presence and absence of methanol at two crucial pressures (9 and 10 MPa) near d_C . As illustrated in Figure 2, the fluorescence spectrum of **3** in scCO_2 , the peak of which is essentially the same as that measured in MCH,¹⁴ showed no change in wavelength or in bandwidth at the two pressures in the absence of methanol. In contrast, both the appreciable bathochromic shift of 5 nm and the band broadening from 61 to 65 nm (fwhm) were induced by lowering P from 10 to 9 MPa in the presence of 0.5–1.0 M methanol. Such a peak shift and broadening are reasonably accounted for in terms of the extra stabilization and differing electronic/structural populations caused by enhanced clustering of the methanol to the saccharide sensitizer in the excited state, particularly in the subcritical (9 MPa), rather than supercritical (10 MPa), region. To analyze the pressure effect more quantitatively, we calculated the differential activation volume ($\Delta\Delta V_{R-S}^\ddagger = \Delta V_{R-S}^\ddagger$

Table 1. Differential Activation Volumes ($|\Delta\Delta V_{R-S}^\ddagger/\text{cm}^3 \text{mol}^{-1}$) for Each Pressure Region upon Enantiodifferentiating Photoaddition of Various Alcohols to **1** Sensitized by **3** in scCO_2

| R | $ \Delta\Delta V_{R-S}^\ddagger/\text{cm}^3 \text{mol}^{-1}$ | | |
|--------------|--|----------|-----------|
| | 7.7–9 MPa | 9–10 MPa | 10–18 MPa |
| Me | 60 | (530) | 22 |
| Et | 130 | (260) | 27 |
| <i>i</i> -Pr | 180 | (800) | 25 |

– ΔV_S^\ddagger) from the pressure dependence of ee by using eq 1:^{9,13}

$$\ln(k_R/k_S) = -(\Delta\Delta V_{R-S}^\ddagger/RT)P + C \quad (1)$$

As shown in Table 1, the $|\Delta\Delta V_{R-S}^\ddagger|$ values obtained for the supercritical, and particularly the subcritical regions, are much larger than those ($1\text{--}2 \text{ cm}^3 \text{mol}^{-1}$) obtained with the same photoreaction in conventional solvents,¹⁶ indicating the more selective solvation to one of the diastereomeric exciplexes particularly in the subcritical region. The tentative $|\Delta\Delta V_{R-S}^\ddagger|$ values calculated from the slopes around d_C are anomalously large, which may be attributed to the transition nature of the plot in this pressure range, or to the dynamic nature of this critical region, as demonstrated physicochemically by the density fluctuation.¹⁷

In this first bimolecular chiral photosensitization in scCO_2 , we showed that the product ee is enhanced by increasing alcohol size and pressure, thus affording a best ee of 43% for the photoaddition of 2-propanol in scCO_2 at 18 MPa. However, the pressure dependence of ee is discontinuous at the critical density, accompanying a big jump caused most probably by enhanced clustering of the alcohol. This unprecedented behavior, its scope, and potential applications are targets of further spectroscopic, mechanistic, and synthetic investigations.

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Supporting Information Available: Data for Figures 1 and 2. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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