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Discontinuous pressure effect upon enantiodifferentiating photosensitized isomerization of cyclooctene

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A hydrostatic pressure of up to 750 MPa induced discontinuous changes in the enantiomeric excess of the (*E*)-isomer obtained in the enantiodifferentiating photoisomerization of (*Z*)-cyclooctene and (*Z*,*Z*)-cycloocta-1,5-diene, sensitized by chiral benzene-1,2,4,5-tetracarboxylates; indicating a switching of the enantiodifferentiation mechanism, which is attributable to dramatic conformational changes of chiral alkoxycarbonyl auxiliaries at a specific pressure.

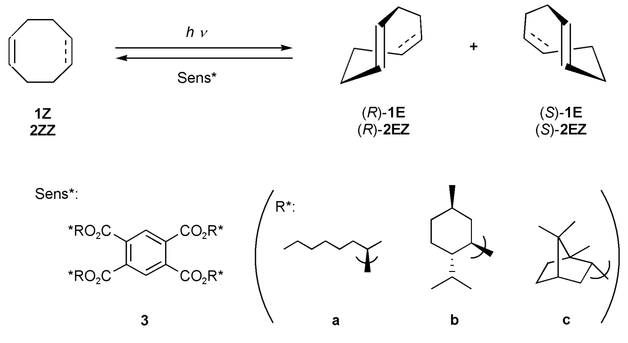
Asymmetric photosensitization is an attractive alternative to conventional asymmetric synthesis using chiral catalysts or enzymes.[1–3] In a series of studies on the enantiodifferentiating photosensitized isomerizations of several cycloalkenes,[4–12] we demonstrated that good-to-high enantiomeric excesses (ee's) of up to 77%, and interestingly an inversion of the product chirality, or the relative rate of (*S*)- and (*R*)-product formation (k_S/k_R), can be obtained by solely changing the temperature[4–12] and solvent.[9,12] Such unprecedented switching phenomena have been accounted for in terms of the entropy factors operating in the enantiodifferentiating process within the intervening exciplex.[13]

Although the pressure effect upon (asymmetric) photochemistry has not been extensively explored, particularly at high pressures,[14] we have demonstrated that similar switching of product chirality can be induced by applying pressure.[8] Thus, the enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**) afforded antipodal products at ambient and high pressures. The results appeared to be well described by the linear relationship between pressure (*P*) and $\ln(k_S/k_R)$:

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

where $\Delta\Delta V^{\ddagger}_{S\text{-}R}$ represents the differential activation volume, R the gas constant and C the $\Delta\Delta V^{\ddagger}_{S\text{-}R}$ value at $P = 0$.[8] However, further attempts to examine the effect of even higher pressures, in an attempt to enhance the product's ee, were not possible owing to instrument limitations.

In the present study we employed a newly developed high-pressure vessel, and examined the enantiodifferentiating photoisomerizations of **1Z** and a new substrate, (*Z*,*Z*)-cycloocta-1,5-diene (**2ZZ**), at much higher pressures for further elucidation of the pressure effect upon asymmetric photosensitization.



Scheme 1 Enantiodifferentiating photoisomerization of **1Z** and **2ZZ** sensitized by chiral sensitizer **3a–c**.

A pentane solution (11 cm^3) of **1Z** or **2ZZ** (5 mmol dm^{-3}), containing 1 mmol dm^{-3} of (−)-1-methylheptyl, (−)-menthyl or (−)-bornyl benzene-1,2,4,5-tetracarboxylate (**3a–c**) as chiral sensitizer (Scheme 1), was irradiated at $\lambda > 250$ nm under an applied pressure of up to 750 MPa in a vessel equipped with a sapphire window for UV irradiation (Hikari Koatsu Co., Hiroshima, Japan), by using a 250 W ultra-high pressure mercury lamp (Ushio UI-501C) fitted with a Vycor filter and a cylindrical quartz vessel filled with water. The irradiated solution was retrieved from the vessel and subjected to capillary GC analyses over a PEG-20M column (20 m × 0.25 mmΦ) for determination of the *E/Z* ratio and over a chiral column (Supelco β-DEX 225; 30 m × 0.25 mmΦ) for ee determination (error < 0.5% ee) after selective extraction of the produced (*E*)-isomer, **1E** or **2EZ**, with aqueous silver nitrate solution as described previously.[8] The results are summarized in Table 1 and Fig. 1.

Unexpectedly, the product ee did not display a straightforward pressure dependence. As can be seen from Fig. 1 the $\ln(k_S/k_R)$ value obtained for each sensitizer/substrate combination is

Table 1 Enantiodifferentiating photosensitization of **1Z** and **2ZZ** sensitized by chiral benzene-1,2,4,5-tetracarboxylates **3a–c** at various pressures in pentane at 25 °C

Substrate	Sens*	*P*/MPa	% Conv	% Yield	*E/Z* ratio	% ee	ref.
1Z	**3a**	0.1	31	15	0.22	−3.8	*a*
		100	37	22	0.35	0.0	*a*
		200	43	26	0.46	+2.1	*a*
		300	*b*	9.7	0.048	+4.3	*c*
		400	*b*	5.5	0.034	+4.4	*c*
		485	*b*	4.8	0.055	+4.4	*c*
	3b	0.1	38	13	0.21	−11.2	*a*
		100	45	18	0.32	−3.6	*a*
		200	41	21	0.36	+5.7	*a*
		300	*b*	24	0.020	+12.4	*a*
		400	*b*	23	0.050	+17.9	*a*
		400	15.3	12.4	0.146	+19.2	*c*
		450	12.3	9.0	0.105	+19.9	*c*
		500	*b*	*b*	*b*	+18.9	*c*
		525	*b*	6.7	0.055	+21.0	*c*
		650	*b*	7.0	0.052	+23.1	*c*
	3c	0.1	39	19	0.31	+14.2	*a*
		100	41	20	0.34	+14.3	*a*
		200	46	23	0.43	+13.0	*a*
		300	*b*	7.1	0.065	+10.3	*c*
		400	*b*	6.6	0.045	+7.1	*c*
		500	*b*	3.2	0.021	+5.4	*c*
		650	*b*	7.0	0.035	+5.2	*c*
		750	*b*	4.4	0.034	+4.8	*c*
2ZZ	**3a**	0.1	16.4	3.6	0.044	−4.4	*c*
		100	17.1	3.9	0.047	−0.7	*c*
		200	15.9	5.0	0.059	+2.3	*c*
		300	16.7	3.5	0.043	+4.2	*c*

[a] Reference 8. [b] Value not determined. [c] This work.

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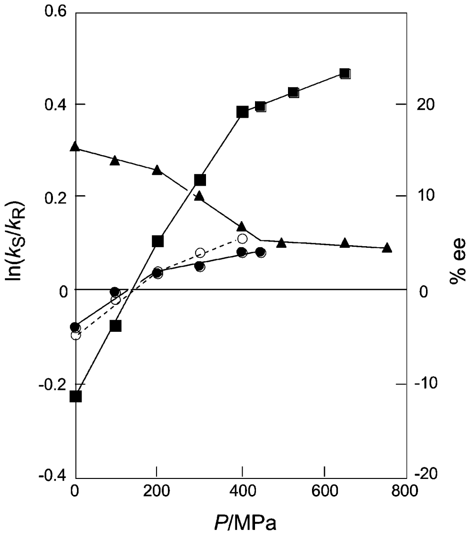

Fig. 1 Pressure dependence of the ee of **1E** (solid line) or **2EZ** (broken line) obtained upon enantiodifferentiating photoisomerization of **1Z** or **2ZZ** sensitized by **3a** (●,○), **3b** (■) and **3c** (▲).

not a simple linear function of P over the entire pressure range employed, but instead, in each case, affords a bent plot approximated by two or three straight lines. These results clearly indicate that the $\Delta\Delta V^{\ddagger}$ value (eqn. 1) and therefore the sensitizing species and enantiodifferentiation mechanism differ in each pressure range, even though the same chiral sensitizer is used. In view of the discontinuity of the ln(k_S/k_R)-*versus*-P plot, the pressure-induced change in viscosity or diffusion rate constant, each of which is a continuous variable, does not appear to be responsible for this unusual behavior.

In this context, it should be noted that the bending positions observed in Fig. 1 are common to all the chiral sensitizers and substrates employed, occurring at 200 and *ca.* 400 MPa. Hence, the structural variations in the chiral auxiliaries or the substrate structure cannot account for the discontinuous changes of product ee. It is, however, the benzenetetracarboxylate moiety, shared by all of the sensitizers, which appears most responsible. In this light, it is found that the ester moiety of the alkyl benzoate starts to fold into a more compact structure at the transition pressures, as revealed by observing a discontinuous change in the C = O stretching vibration by means of high-pressure Raman spectroscopy.[15] It is likely that, in the present system, a similar conformational change occurs in the ester moieties of each chiral benzenetetracarboxylate sensitizer, at least in the ground state, by applying the pressure beyond a certain limit. Subsequent photoexcitation of the resulting more compact conformer, or analogous conformational changes in the excited state, can lead to a distinctly different exciplex conformation and therefore induce the discontinuous changes observed in the ee at higher pressures.

Inspection of the electronic spectra of **3a** under pressure showed only a slight bathochromic peak shift and absorbance enhancement, which are too small to confidently discuss the spectroscopic discontinuity. Circular dichroism (CD) spectroscopy, however, would be more sensitive to such conformational changes, but the sapphire window used does not allow CD spectral examination due to birefringence; probably, a diamond window would be more suitable for such measurements.

The unprecedented discontinuous pressure dependence of the ee found in the present study can be useful as an additional tool for controlling the product chirality and ee, wherever such conformational switching is induced by pressure. Further studies to elucidate the detailed mechanism, as well as CD spectral examination at high pressure, are currently in progress.

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