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Pressure control of diastereodifferentiating [2 + 2] photocycloaddition of (*E*)-stilbene to chiral fumarate upon direct and charge-transfer excitation†

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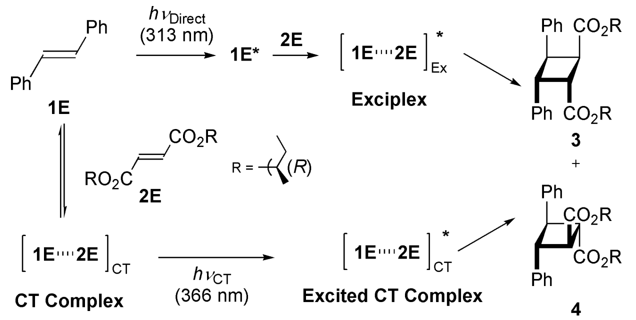
The geometry (donor–acceptor distance) and association constant of the ground-state CT complex were considerably affected by applied pressure, thus enhancing the reaction rate and the adduct yield particularly upon CT excitation, but the diastereoselectivity did not show any substantial change at elevated pressures in both excitation modes.

The effect of hydrostatic pressure on a charge-transfer (CT) complex in the ground electronic state has extensively been studied in condensed media[1] and also in the solid state.[2] The pressure-induced spectral changes are attributed to the increased orbital overlap caused by a decrease in donor–acceptor distance. It is reasonable therefore that the applied pressure affects the rate and selectivity of thermal reactions, such as Diels–Alder reaction.[3,4] Photochemical reactions are also known to be significantly affected by pressure.[3–5]

Photocycloaddition of (*E*)-stilbene (**1E**) to dimethyl fumarate gives two stereoisomeric cyclobutanes, μ- and δ-truxinates, in good combined yield, along with the Paternó–Büchi adduct, *i.e.* oxetane.[6] Among the cyclobutanes, the μ-isomer is favored due to the extensive π,π-interactions between the phenyl and ester moieties.[7] Irradiation at the CT band affords the same products in a similar ratio.[6] Diastereodifferentiating photocycloaddition of **1E** to di-L-bornyl and methyl L-bornyl fumarates has also been investigated but only through the direct irradiation.[8] Recently, we have revealed that the conventional exciplex and the excited CT complex are distinctly different in structure and reactivity. This was done by closely examining the photochemical and photophysical behavior of diastereodifferentiating photocycloaddition of **1E** to bis((*R*)-1-methylpropyl) fumarate (**2E**) upon direct and CT excitation (Scheme 1).[9] Thus, the selective excitations of **1E** at 313 nm and of CT complex at 366 nm led to different product ratios and diastereomeric excesses (de's) particularly at low temperatures. This result prompted us to investigate the effects of pressure on this bimolecular photoreaction, since the diastereomeric pairs of CT complex and/or exciplex are expected to be different in volume.

We now report the results of our study on the diastereoselective photocycloaddition of **1E** to **2E**, yielding stereoisomeric μ- and δ-truxinates (**3** and **4**), at varying pressure and temperature. In this first comparative study to investigate the pressure effects on the photobehavior of ground- and excited-state complexes, we intended to unequivocally discriminate and critically control the photobehavior of these two species by changing the hydrostatic pressure.



Scheme 1 Charge-transfer *versus* direct excitation leading to [2 + 2] photocycloaddition of (*E*)-stilbene **1E** to chiral fumarate **2E**.

The formation of ground-state CT complex between **1E** and **2E** was quantitatively examined at P = 0.1, 200 and 400 MPa in toluene at 25 °C. Upon stepwise addition of **2E** to a toluene solution of **1E**, a new absorption, assignable to a CT complex, emerged at wavelengths 350–400 nm. The association constant (K_{CT}) was determined at each pressure by the Benesi–Hildebrand analysis of the absorbance changes at 355 nm, and the results are listed in Table 1, along with some parameters of the CT band. The CT complex formation is dramatically enhanced by applying pressure to give rapidly increasing K_{CT} values, apparently doubling every 200 MPa at least in the pressure range employed. An appreciable bathochromic shift of the absorption edge of the CT band and an increase of the molar extinction coefficient were also observed, as was the case with the typical donor–acceptor systems.[1] A pressure dependence analysis of K_{CT} affords a reaction volume (ΔV_{CT}) of -4.1 cm^3 mol^{-1} for the present CT complex, which is in the same range as those reported for conventional CT complexes, indicating the comparable compressibility.[10]

A toluene solution of **1E** (0.1 M) and **2E** (1 M) was irradiated under argon at 0.1, 200, and 400 MPa in a high-pressure vessel equipped with a quartz window. The irradiation was performed at 313 nm (an effective radiation for direct excitation) or at 366 nm (for selective excitation of CT complex), by using a 250 W high-pressure Hg lamp (Ushio UI-501C) fitted with a Toshiba UV-34 or UV-37 glass filter, respectively. The photolyzate was qualitatively analyzed by GC employing cyclopentadecane as the internal standard, and the results obtained are summarized in Table 2. The major photoreaction observed was the geometrical isomerization of **1E** to the (*Z*)-isomer (**1Z**). Therefore, we have examined the photolyzates at conversions lower than *ca.* 30% in order to eliminate the possible contamination by the secondary photoreactions of these products.

Somewhat unexpectedly, the reaction rate, as judged from the conversion, was only moderately accelerated by pressure. In contrast, the combined yield of cyclobutenes **3** and **4**, based on the consumed **1**, was dramatically enhanced from *ca.* 30% or 50% at 0.1 MPa to >70% at 400 MPa upon direct and CT excitation,

Table 1 Association constant (K_{CT}) and relevant parameters of the CT complex of **1E** with **2E** at different pressures in toluene at 25 °C[a]

P/MPa	K_{CT}/M^{-1}	$\lambda_{\mathrm{edge}}{}^{b}$/nm	[CT]^{c}/M	A_{CT}/ $A_{\mathrm{direct}}{}^{d}$	$\varepsilon_{366}{}^{e}$/M^{-1} cm^{-1}
0.1	1.5	397	0.012	5	1.6
200	3.1	398	0.020	19	3.2
400	6.7	405	0.031	38	4.4

[a] $[\mathbf{1E}]_0 = [\mathbf{2E}]_0 = 0.1$ M. [b] Absorption edge of the CT band, defined as the wavelength at which the absorbance becomes 0.003. [c] Calculated concentration of the CT complex under the condition employed. [d] Absorbance ratio of CT complex *versus* **1E** at 366 nm. [e] Molar extinction coefficient of the CT complex at 366 nm.

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† Electronic supplementary information (ESI) available: pressure effect on the product ratio **4**/**3**. See http://www.rsc.org/suppdata/cc/b4/b404555f/

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Table 2 Pressure and temperature effects on diastereodifferentiating photocycloaddition of (*E*)-stilbene **1E** to bis((*R*)-1-methylpropyl) fumarate **2E** upon direct and charge-transfer excitation.[a]

Excitation mode	*P*/MPa	*T*/°C	Irradiation time/h	Conversion[b] (%)	Yield[c] (%)	*E*/*Z* ratio[d]	**4**/**3** ratio	% de[e] **3**	% de[e] **4**
Direct	0.1	25	3	18	27	16	1.2	69	6
			5	26	33	9	1.2	69	2
	200	25	2.5	9	64	17	1.5	65	7
		0	4	7	52	9	1.3	41	[f]
	400	25	1	6	72	33	1.7	81	[f]
			1.5	15	74	15	1.5	64	5
			3	24	78	10	1.4	48	[f]
CT	0.1	25	24	9	49	19	1.3	87	3
	200	25	5	8	45	32	1.7	86	6
			21	31	53	10	1.4	65	[f]
		0	24	10	54	8	1.3	65	[f]
	400	25	3	6	68	46	1.6	86	[f]
			4	8	55	51	1.7	87	9[e]
			19	24	79	11	1.4	65	[f]

[a] Irradiated either at 313 nm (direct excitation) or 366 nm (CT excitation). $[\mathbf{1E}]_0 = 0.1$ M, $[\mathbf{2E}]_0 = 1.0$ M. [b] Consumption of total stilbene (**1E** + **1Z**); photoisomerization of **1E** to **1Z** not taken into account. [c] GC yield of **3** and **4** based on the conversion of **1**. [d] **1E**/**1Z** ratio of the remaining stilbenes. [e] The major diastereomers of **3** and **4** eluted first on a Varian CP-Sil 8CB capillary column. [f] Not determined.

respectively. It is known that the photolysis of stilbene and fumarate leads not only to the cyclobutanes but also to the oxetane formation,[6] reducing the cyclobutane yield. It is likely that the cyclobutane formation experiences a more compact transition state (with a smaller activation volume) than the oxetane formation, irrespective of the excitation mode.

Although the **4**/**3** ratio is a function of conversion, the ratio at the lowest conversion (6–18%) increases appreciably with increasing pressure at 25 °C. From the slope of the plot of the logarithmic **4**/**3** ratio against pressure (see Supporting Information†), we may roughly estimate the differential activation volumes (or at least the sign) for the formation of **3** and **4** ($\Delta\Delta V^{\ddagger}_{\mathbf{4-3}}$) for each excitation mode, as shown in Table 3. The negative $\Delta\Delta V^{\ddagger}_{\mathbf{4-3}}$ values, though difficult to seriously discuss the difference, indicate that the transition state to **4** is slightly compact than that to **3**. This seems reasonable, since the precursor exciplex or CT complex to **4**, lacking the severe steric hindrance between the donor–acceptor pair, is thought to be readily compressed by applying pressure.

The photoisomerization to **1Z** appears to be retarded at high pressures upon direct excitation, as reported previously.[11] This may be attributable to the larger volume of the perpendicular singlet of **1**. Upon CT excitation, a more evident deceleration is seen, for which the larger steric hindrance in the CT complex should be responsible.

Despite the obvious pressure effects on the reactivity, yield, **4**/**3** ratio, and *E*/*Z* ratio, the de's of **3** and **4** at the initial stages did not show any appreciable pressure effect both upon direct and CT excitation. Although the ground-state geometries are altered by pressure, the differential activation volume for the formation of a diastereomeric pair of **3** and **3′** is negligible ($|\Delta\Delta V^{\ddagger}_{\mathbf{3-3'}}| < 0.1$ cm^3 mol^{-1}). Such a small difference in activation volume for a diastereomeric pair may arise from the similarity in structure between the precursor exciplex or CT complex. The temperature effect upon de, examined at 200 MPa, is clearer especially in the direct excitation, giving lower de's at 0 °C in both excitation modes (at comparable conversions), as was the case under normal pressure.[9]

Table 3 Differential activation volumes ($\Delta\Delta V^{\ddagger}$) for the photocycloaddition of **1E** to **2E**

Excitation mode	$\Delta\Delta V^{\ddagger}_{\mathbf{4-3}}$[a]/ cm^3 mol^{-1}	$\Delta\Delta V^{\ddagger}_{\mathbf{3-3'}}$[b]/ cm^3 mol^{-1}
Direct	−0.8 ± 0.3	< ±0.1
Charge transfer	−0.6 ± 0.2	< ±0.1

[a] Differential activation volumes for the formation of δ- and μ-truxinates **4** and **3**. [b] Differential activation volumes for the formation of major diastereomer of μ-truxinates **3** and its minor diastereomer.

In this study, the pressure effect can be used as a convenient tool for accelerating the photocycloaddition and enhancing the yield of cyclobutanes **3** and **4** without accompanying any significant loss of diastereoselectivity. It is noted also that the difference in photobehavior upon direct and CT excitation becomes less evident at higher pressures, which may indicate that the exciplex and the excited CT complex resemble to each other in structure and reactivity under pressure. Further studies on the pressure effects upon the ground- and excited-state complexes and the mechanistic details are currently in progress.

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