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Switching of Product's Chirality in Diastereodifferentiating [2+2] Photocycloaddition of (*E*)- versus (*Z*)-Stilbene to Chiral Fumarate upon Direct and Charge-Transfer-Band Excitation

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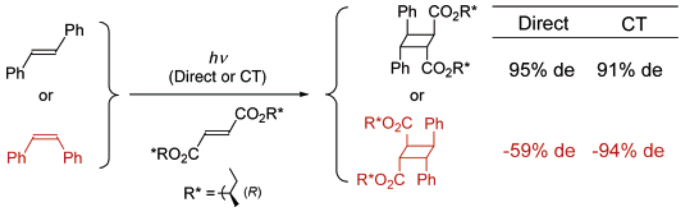
ABSTRACT



Diastereodifferentiating [2+2] photocycloadditions of (*E*)- and (*Z*)-stilbenes to bis((*R*)-1-methylpropyl) fumarate were performed through the direct excitation of stilbenes and the selective excitation of the charge-transfer (CT) complex at various temperatures. The geometrical isomers of stilbene afforded the opposite diastereomers of μ-truxinate in both excitation modes, with a dramatic decrease in the product's diastereoselectivity upon prolonged irradiations.

Controlling molecular chirality in photochemical reactions is one of the most intriguing topics in current organic chemistry because of the inherently challenging nature of the excited-state reactions which involve weak interactions and short-lived excited species.[1−4] To overcome such drawbacks, researchers have devised a variety of methodologies that utilize multiple interactions in ground and/or excited states, such as exciplex formation,[5] hydrogen bonding,[6,7] hydrophobic, electrostatic,[8] and charge-transfer (CT) interactions,[9−11] all of which have been shown to function as crucial factors for controlling the chiral sense and optical yield of the photoproduct.

CT interactions, as one of the weak interactions working in the ground state, have been extensively investigated, particularly with respect to the chromogenic nature of the

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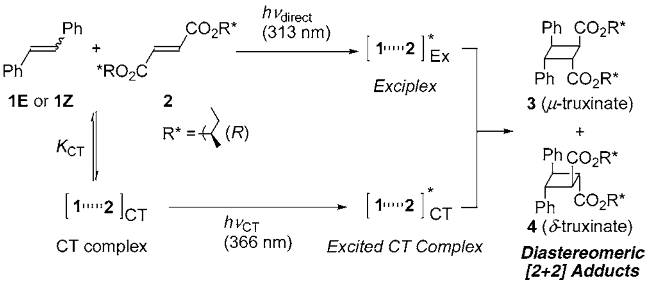
new absorption in the visible region.[12−14] In our recent study on the diastereodifferentiating [2+2] photocycloaddition of (*E*)-stilbene to a chiral fumarate, we have revealed for the first time that the selective excitation of the CT complex (CT excitation) affords [2+2] photoadducts in diastereoselectivities different from those obtained upon direct excitation of stilbene (Scheme 1). These results indicate that the selective CT excitation can be a tool for controlling the product chirality in photochirogenesis.

Scheme 1. [2+2] Photocycloaddition of (*E*)- and (*Z*)-Stilbene (**1E** and **1Z**) to Bis((*R*)-methylpropyl) Fumarate (**2**)



In the present study, to elucidate the factors and mechanism that lead to the different reactivities and diastereoselectivities upon CT vs direct excitation, we have employed isomeric (*Z*)-stilbene as a substrate and investigated the effects of alkene geometry on the product ratio and diastereoselectivity of the [2+2] photoadducts.

A toluene solution of **1E** (0.1 M) and **2** (1.0 M) was irradiated either at 313 nm (direct excitation) or at 366 nm (CT excitation) at 25 °C under a N_2 atmosphere for a given period of time, and the photolyzate was analyzed by GC. It turned out that the diastereoselectivity of photoadduct **3** (μ-truxinate, **3a** and **3b** are the second- and first-eluted diastereomers of μ-truxinate upon GC analysis, respectively) significantly decreases with increasing irradiation time (Figure 1). As can be seen from Figure 1, the diastereomeric excess (de) of **3** is a linear function of the conversion particularly at the early stages of the photoreaction in both direct and CT excitations, which enables us to obtain the *inherent de* values by extrapolating the plot to zero conversion. A similar trend was found upon photocycloaddition of isomeric **1Z** to **2**, forming **3b** as the major product. Hence, we performed the photoreactions[10] with varying irradiation periods and determined the *inherent de* value at each temperature by using the de data at relatively low conversions to obtain a good linear regression line; only these extrapolated values will be referred to throughout the following discussion.

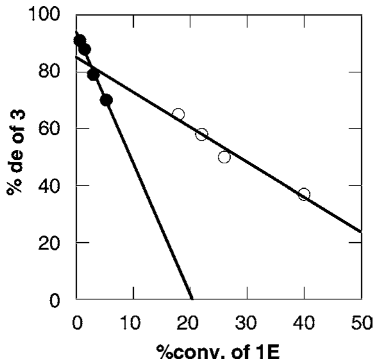


Figure 1. Dependence of de of **3** on the conversion of **1E** upon direct (○) and CT (●) excitations in toluene at 25 °C ([**1E**] = 0.1 M, [**2**] = 1.0 M).

First, we examined the photoreactions of **1E** with **2** employing the extrapolated values. It should be noted that the extrapolated de values of **3** obtained upon CT excitation are consistently high throughout the temperature range employed, whereas those for direct excitation are sensitive to temperature, giving lower de values at reduced temperatures: 97% de at 50 °C and 34% de at −50 °C. In contrast, the de values of **4** (δ-truxinate) are generally low and show practically no temperature dependence upon either direct or CT excitation, as one would anticipate from the less-congested all-trans structure of **4** or its precursor complex.

Interestingly, the product ratio **4**/**3** constantly increased with decreasing temperature in both excitation modes, with the ratio obtained upon CT excitation slightly greater than that of direct excitation, which is more discernible at low temperatures (Table S1 in Supporting Information). For more quantitative information, the logarithm of the **4**/**3** ratio was plotted against the reciprocal temperature. Similarly, the logarithm of the relative formation rate of diastereomeric **3a** and **3b** (see the caption of Figure 2), $\ln(k_{3a}/k_{3b})$ or ln[(100 + %de)/(100 − %de)], was plotted and analyzed by the differential Eyring equation.[4,15] The differential activation enthalpy ($\Delta\Delta H^{\ddagger}$) and entropy ($\Delta\Delta S^{\ddagger}$) for the formation of **4** vs **3** and for the diastereomeric pair of **3a** vs **3b** were calculated, respectively, from the slopes and intercepts of the regression lines shown in Figure 2, although the plot for the diastereomeric **3** obtained upon CT excitation is consistently high (90−97%) and hence significantly scattered (Figure 2, Ib (open square)). The good linear relationship obtained over the entire temperature range indicates that a single diastereodifferentiating mechanism operates in each excitation mode.[10]

Stilbene is known to undergo efficient reversible geometrical photoisomerization in relatively high quantum yields; $\Phi_{E-Z} = 0.52$, $\Phi_{Z-E} = 0.35$ in pentane.[16] It is also reported that photoreaction of **1Z** with dimethyl fumarate gives [2+2] photoadducts, i.e., dimethyl μ- and δ-truxinates, although the quantum yields are much lower.[17] Hence, it is

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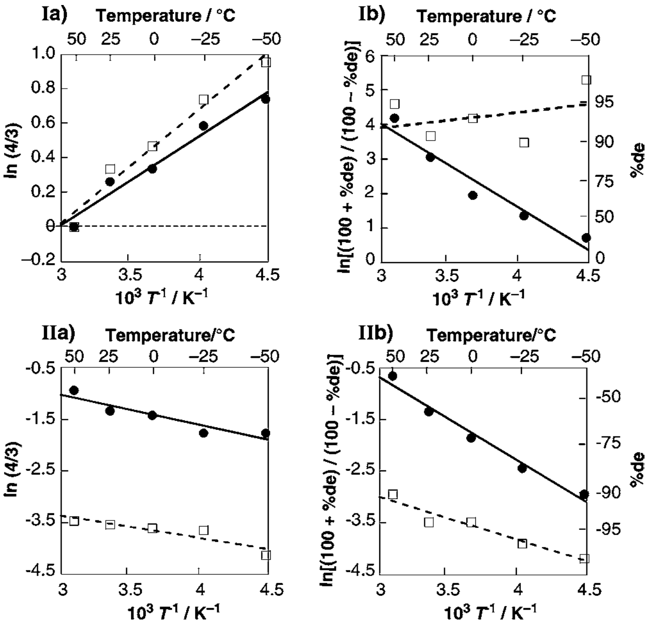

Figure 2. Differential Eyring plots for diastereodifferentiating [2+2] photocycloaddition of **1E** to **2** (graphs Ia,b) and of **1Z** to **2** (IIa,b) in toluene: (a) product ratio **4**/**3** upon direct (●, solid line) and CT (☐, dotted line) excitation; (b) de of **3** upon direct (●, solid line) and CT (☐, dotted line) excitation. The negative and positive signs of the product's de are not directly related to the sign of optical rotation but mean the predominant formation of the first- (**3b**) and second-eluted (**3a**) diastereomers, respectively, upon GC analysis on a Varian CP−Sil 8CB column.

reasonable to assume that **1Z**, produced through the photoisomerization of **1E**, is involved in the photocycloaddition and affects the isomer ratio and the de values even from the early stage of irradiation. To test this supposition, we employed **1Z** as the substrate and performed the photocycloaddition with **2** at various temperatures.

The product ratios and the de values, obtained in the photoreaction of **1Z** with **2**, were also conversion dependent and decreased by extending the irradiation time upon both direct and CT excitations. Therefore, the *inherent* product ratios **4**/**3** and de values of **3** were again determined by extrapolation to zero conversion. To our surprise, the use of **1Z** (instead of **1E**) not only led to the formation of more congested isomer **3** but also gave the opposite diastereomer of **3**, irrespective of the excitation mode. Thus, **1E** affords the first-eluted photoadduct **3b** in 91 and 95% de, whereas **1Z** gave the second-eluted **3a** in −59 and −94% de upon direct and CT excitation, respectively. This observation unambiguously reveals that the photoisomerization of **1E** to **1Z** and the subsequent photocycloaddition to **2** are jointly responsible for the rapid decrease in de observed upon prolonged irradiations in the reaction of **1E** and **2**.

Again, in the photoreaction of **1Z** with **2**, the de of **3** from direct excitation showed significant temperature dependence, with that from CT excitation displaying a smaller temperature dependence. The low **4**/**3** ratios obtained upon CT excitation may indicate that the excited CT complex favors a π-stacked conformation that preferentially affords **3**. The differential Eyring plots of the **4**/**3** ratio and the de of **3** (Figure 2) afforded good straight lines, indicating that a single diastereodifferentiating mechanism is operating in each excitation mode, as was the case with **1E**. The obtained $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values are collected in Table 1.

Table 1. Differential Activation Parameters for the Product Ratio **4**/**3** and the de of **3** in Diastereodifferentiating Photocycloaddition of **1E** or **1Z** to **2** in Toluene (T = 298 K)[a]

selectivity	donor	excitation mode	$\Delta\Delta H^{\ddagger b}$/ kJ mol^{-1}	$\Delta\Delta S^{\ddagger b}$/ J mol^{-1} K^{-1}	$T\Delta\Delta S^{\ddagger b}$/ kJ mol^{-1}
isomer (**4**/**3**)	**1E**	direct	−4.5	−14	−4.2
		CT	−5.8	−18	−5.4
	1Z	direct	4.8	6.0	1.7
		CT	3.6	−17	−5.1
diastereomer (**3a**/**3b**)	**1E**	direct	20 (20^c)	94 (79^c)	28 (24^c)
		CT	∼ −4	∼20	∼6
	1Z	direct	13	34	10
		CT	6.9	−4.2	−1.3

[a] **3a** and **3b** are the second- and first-eluted diastereomer of **3** on GC, respectively. [b] For isomer ratio: $\Delta\Delta H^{\ddagger} = \Delta H^{\ddagger}_4 - \Delta H^{\ddagger}_3$; $\Delta\Delta S^{\ddagger} = \Delta S^{\ddagger}_4 - \Delta S^{\ddagger}_3$. For diastereomer ratio: $\Delta\Delta H^{\ddagger} = \Delta H^{\ddagger}_{3a} - \Delta H^{\ddagger}_{3b}$; $\Delta\Delta S^{\ddagger} = \Delta S^{\ddagger}_{3a} - \Delta S^{\ddagger}_{3b}$. [c] Values obtained without extrapolation in the previous work (ref 10).

The differential activation parameters obtained for the photoreaction of **1E** (Table 1) reveal that the comparable formation of **3** and **4** upon both direct and CT excitations (Figure 2, Ia) at ambient temperature originates from a counterbalance of the enthalpic gain and the entropic loss (see the $\Delta\Delta H^{\ddagger}$ and $T\Delta\Delta S^{\ddagger}$ values in Table 1), whereas the decreasing contribution of the entropic loss at lower temperatures moderately enhances the formation of **4** (because of the small $\Delta\Delta H^{\ddagger}$ values of ca. −5 kJ mol^{-1}).

In contrast, the high preference for **3** upon both direct and CT excitations of **1Z** is enthalpic in origin, but its magnitude is entropically controlled. As can be seen from Table 1, the positive $\Delta\Delta H^{\ddagger}$, favoring formation of **3**, is almost comparable in magnitude for both excitation modes but is slightly canceled by the small positive $\Delta\Delta S^{\ddagger}$ upon direct excitation or assisted by the negative $\Delta\Delta S^{\ddagger}$ upon CT excitation. These completely different $\Delta\Delta H^{\ddagger}$ and $T\Delta\Delta S^{\ddagger}$ values indicate that the photocycloaddition mechanism is distinctly different for **1E** and **1Z**, particularly upon CT excitation. The differential activation parameters determined for the diastereoselectivity (**3a**/**3b**) also differ significantly, depending on the excitation mode (direct or CT excitation) as well as the stilbene's geometry (**1E** or **1Z**). These results unequivocally indicate that the structure and reactivity that determine the chemo- and stereoselectivity of cycloadducts critically differ depending on the excitation mode and the geometry of the reactant stilbene.

A plausible reaction mechanism is proposed in Scheme 2. The critical difference observed in the reactivity of **1E**

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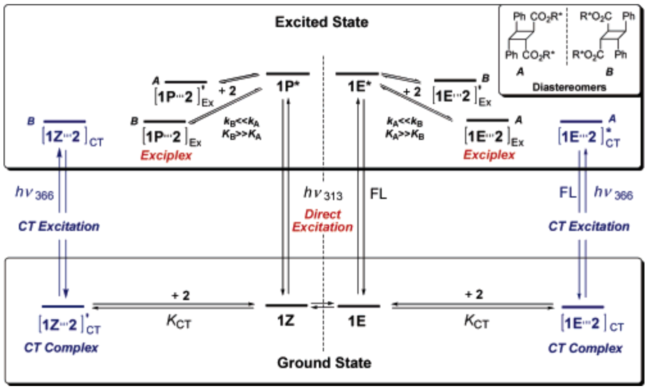
Scheme 2. Reaction Mechanisms Proposed for the Diastereodifferentiating Formation of **3** in the Photocycloaddition of **1E** or **1Z** and **2** upon Direct and CT Excitation



and **1Z** may be reasonably accounted for in terms of the isomerization of stilbene in the excited state. Stilbene has two local energy minima in the excited state; one has an *E*-like structure (**1E***), and the other has a perpendicular structure (**1P***), in which two phenyls are twisted by ca. 90°. No *Z*-like energy minimum exists because of the rapid rotational relaxation to **1P*** from the Franck−Condon excited state of **1Z**. It is likely therefore that the reactive (excited) species involved in the photoreactions of **1E** and **1Z**, i.e., **1E*** and **1P*** (the latter is already chiral), are, respectively, responsible for the cycloaddition to **2**. This should be the case not only with the direct excitation but also with the CT excitation because in most cases the ground-state CT complex retains the original structure of each component, and the excited-state potential curve for stilbene could not be very different from that of free stilbene.

In this study, we first reexamined the diastereodifferentiating [2+2] cycloadditions of (*E*)-stilbene to bis((*R*)-methylpropyl) fumarate upon direct and CT excitations and the results were compared with those obtained with (*Z*)-stilbene. Although the conversion-dependent decrease of the de was revealed to arise from the concomitant photochemical isomerization of stilbene during the course of the irradiation, the conventional exciplex and the excited CT complex were demonstrated to be distinctly different in structure and reactivity by closely examining the product ratio and de obtained at the very initial stages of the reactions. The product's de obtained upon direct excitation critically depends on the reaction temperature, whereas the de from CT excitation exhibits a much smaller temperature dependence. This is attributed to the different degree of steric interactions and freedoms in the intervening species generated in the different excitation modes. It is also crucial that the major diastereomer obtained is switched in both excitation modes by using the geometrical isomer, which enables us to obtain both diastereomers in high optical yields not by using the antipodal chiral auxiliaries but by using the geometrical isomers. Further investigations on direct vs CT excitations are currently in progress with this and related systems.

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Supporting Information Available: Experimental details and complete tables of the product ratios and de values obtained in the diastereodifferentiating [2+2] photocycloaddition of (*E*)- and (*Z*)-stilbenes to bis((*R*)-1-methylpropyl) fumarate. This material is available free of charge via the Internet at http://pubs.acs.org.

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