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Solvent and Temperature Effects on Diastereodifferentiating Paternó−Büchi Reaction of Chiral Alkyl Cyanobenzoates with Diphenylethene upon Direct versus Charge-Transfer Excitation

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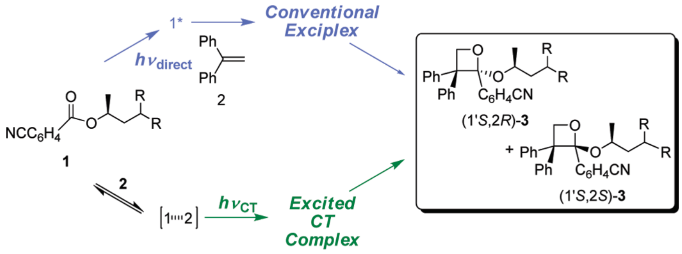

In the Paternó−Büchi reaction of chiral *p*-cyanobenzoates (**1**) with 1,1-diphenylethene (**2**), we revealed that the excited charge-transfer (CT) complex formed upon selective excitation at the CT band is distinctly different in structure and reactivity from the conventional exciplex generated through the direct excitation of acceptor **1** which subsequently associates with donor **2**. Thus, the favored diastereoface upon photocycloaddition, as well as the temperature- and solvent-dependent behavior of the product's diastereoselectivity, were highly contrasting, often opposite, to each other upon direct versus CT excitation. From the activation parameters obtained by the Eyring analyses of the diastereoselectivity, we are able to infer that the conventional exciplex is relatively flexible and susceptible to the environmental variants, whereas the CT complex is better $\pi-\pi$ stacked and more rigid in the ground state and also in the excited state, leading to the significantly smaller differential activation enthalpies and entropies. More interestingly, the signs of the differential activation parameters determined for direct and CT excitation are consistently opposite to each other and the isokinetic temperatures calculated therefrom differ significantly, unambiguously revealing the distinctly different nature in structure and reactivity of these two excited-state complex species. Thus, the combined use of irradiation wavelength, temperature, and solvent provides us with a convenient, powerful tool not only for elucidating the mechanistic details of photoreaction but also for critically controlling the stereochemical outcomes of photochirogenic reaction.

Introduction

The Paternó−Büchi reaction,[1] i.e., [2 + 2] photocycloaddition of a ketone to an alkene leading to oxetane formation, has attracted much attention from the mechanistic and synthetic viewpoints,[2] as the photochemical route to oxetane is more advantageous in several aspects than conventional thermal ones.[3] Mechanistic studies on Paternó−Büchi reaction were carried out in considerable detail to reveal the vital role of temperature in determining the product selectivity.[4] The knowledge accumulated through these studies provides the crucial clues to effectively control the distribution and stereochemistry of oxetane products. More recently, asymmetric Paternó−Büchi reactions of chirally modified substrates were also studied

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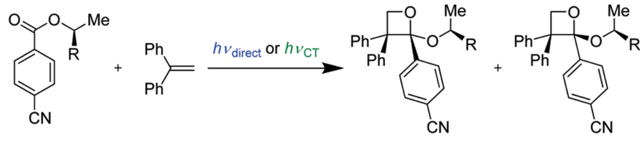
extensively to find that a wide variety of chiral oxetanes were produced in generally high diastereoselectivities.[5] A considerable amount of effort has been devoted to the manipulation of regio- and diastereoselectivities in asymmetric Paternó−Büchi reactions,[6] and in particular, the use of allylic strain and hydrogen-bonding interaction were demonstrated to be highly effective in controlling the stereochemical consequence of the diastereodiffeentiating [2 + 2] photoreaction.[7] However, the precise control of the face selectivity of Paternó−Büchi reaction is still a challenging task. The excited-state dynamics of a donor−acceptor system can be manipulated by changing the excitation wavelength, but the focus is rather on the photophysical aspects in the literature,[8] and the importance of excitation wavelength on Paternó−Büchi reaction has not been fully recognized or examined in detail.[9]

We have recently investigated the temperature dependence behavior of the diastereodifferentiating [2 + 2] photocycloaddition of chiral alkyl benzoates (**1**) to 1,1-diphenylethene (**2**) (Scheme 1).[10] The stereochemical outcome was critically affected by the mode of excitation, and the direct excitation of acceptor **1** and the selective excitation at the charge-transfer (CT) band gave the same oxetane but in entirely different diastereoselectivities, indicating the existence of two distinct excited-state complex species that are not equilibrated each other. The CT-band excitation of he ground-state complex has been a target of intensive studies,[11] but the observed difference in photochemical outcome upon direct versus CT excitation was rather small or controversial, except for the clear excitation-wavelength dependence observed in the diastereodifferentiating [2 + 2] photocycloaddition of stilbene to chiral fumarate.[12]

SCHEME 1. Diastereodifferentiating [2 + 2] Photocycloaddition of Chiral Alkyl Benzoates 1 to 1,1-Diphenylethene 2 upon Direct and Charge-Transfer Band Excitation



(S)-**1a**: R = Et
(S)-**1b**: R = *i*-Bu
2
(1′*S*,2*R*)-**3**
(1′*S*,2*S*)-**3**

In this study, we closely investigated the solvent and temperature effects on the diastereodifferentiating photocycloaddition of chiral alkyl cyanobenzoates **1** to diphenylethene **2** to elucidate the nature and the difference of two excited-state complex species generated upon direct and CT excitation. Interestingly, the CT, rather than direct, excitation led to lower diastereoselectivities in general, which is in keen contrast to the photocycloaddition of stilbene to chiral fumarate, where the CT excitation consistently affords better diastereoselectivities. Although the photoreaction of stilbene with fumarate is not very clean (accompanying the *E*−*Z* isomerization and dimerizaiton of stilbene), the reaction of **1** with **2** exclusively affords oxetane **3**, allowing more detailed examinations of the product selectivities. The differential activation parameters obtained by the Eyring analysis of the diastereoselectivities of **3** obtained under a variety of conditions provide us with rich insights into the photocycloaddition mechanism and the nature of excited-state intermediates, which will be discussed below.

Results and Discussion

Ground-State Interaction of Cyanobenzoate 1a with Diphenylethene 2. It was reported that despite no clear indication of the ground-state interaction between electron-deficient aromatic esters, such as dimethyl tere- and isophthalate, and several olefinic donors in the UV spectra, these donor−acceptor pairs smoothly underwent the Paternó−Büchi reaction to give the corresponding oxetanes upon photoexcitation.[13] Because such interactions are elusive in general, it is likely that the failure to detect the ground-state interaction was due to the insufficient formation of the CT complex under the experimental conditions employed. Indeed, we were able to observe weak but appreciable UV spectral changes only by mixing donor **2** and acceptor **1a** at relatively high concentrations (~0.2 M). The new absorption band, visible at the red edge of the original spectrum, can be ascribed to the formation of donor−acceptor or charge-transfer complex. Association constants (K_{CT}) were determined in a variety of solvents by using the modified Benesi−Hildebrand method; the original Benesi−Hildebrand treatment[14] was avoided in the present case, as the method is not suitable for accurately determining a

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TABLE 1. Association Constants (K_{CT}) of Charge-Transfer Complex of 1a with 2 in Some Solvents[a]

solvent	dipole moment (μ)/debye	dielectric constant/ε	λ_{edge}/nm[b]	K_{CT}/M^{-1}
methylcyclohexane	0	2.02	337	0.04 (0.03)[c]
toluene	0.37	2.38	343	0.8
tetrahydrofuran	1.68	7.39	328	0.02
acetonitrile	3.94	37.5	338	0.2

[a] Determined by the modified Benesi−Hildebrand method for solutions of [**1a**] = [**2**] = 0.2−0.07 M at 25 °C. For data in methylcyclohexane, see ref. 10. [b] Edge of the absorption spectrum of CT complex (defined as the wavelength at which the absorbance becomes 0.005), which was obtained by subtracting the spectral sum of **1a** and **2** from the observed spectrum. [c] At 50 °C.

low K value. Thus, we recorded the UV spectral changes upon simultaneous reduction of the donor and acceptor concentrations from 0.2 M to 0.07 or 0.08 M, keeping the 1:1 stoichiometry. The deviation of the observed spectrum from the spectral sum of each component at a given concentration indicates the net absorption of the CT complex, which appeared at 300−340 nm (Figure S1, Supporting Information). The absorbance change in the CT band region was plotted against the product of the donor and acceptor concentrations,[15] followed by the curve fitting procedure, to afford the association constants listed in Table 1. The detailed discussion on the evaluation of such low K_{CT} values for weak CT complexes may be found in the literature.[16]

The association constant for the **1a**/**2** pair is comparable to or slightly lower than the typical values reported for the conventional CT complexes formed between aromatic donors and tetracyanoethene or chloranil.[17] The relatively low K_{CT} value found for **1a**/**2** pair may be attributed at least in part to the steric hindrance of the acceptor's ester moiety. The K_{CT} values are known to be significantly affected by the steric inhibition between donor and acceptor, in addition to the electrostatic and stacking interactions.[18] The K_{CT} value became considerably larger in polar acetonitrile than in less polar methylcyclohexane or tetrahydrofuran, indicating that the charge delocalization within the complex plays some role to stabilize the complex. The much larger K_{CT} value in toluene may be attributed to the effective stabilization of the complex through the π-stacking interaction with toluene molecules. The complexation thermodynamic parameters could not be determined, as the difference in K_{CT} determined at 25 and 50 °C (in methylcyclohexane) was so small to give a reliable van't Hoff plot. Due to the low K_{CT} values in all the solvents, relatively high donor/acceptor concentrations were used to keep a satisfactory amount of the complex in the solution. However, by irradiating the CT band at 330 nm through a band-path filter (with a xenon light source), the selective excitation of the CT complex was possible (vide infra).

The ground-state interaction was further examined by circular dichroism (CD) spectroscopy,[19] as cyanobenzoate **1a** has a chiral handle. The electronic CD is frequently used as a tool for analyzing the conformational behavior of chiral molecules in solution.[20] Thus, the CD spectral changes of a methylcyclohexane solution of **1a** upon addition of **2** were examined. Although no appreciable induced CD associated with the complexation developed at 25 °C under the same conditions employed for the photoreaction, a fairly weak but appreciable negative Cotton effect was observed for the CT band at around 320−330 nm decreasing the temperature down to −25 °C (Figure S2, Supporting Information). Note that cyanobenzoate **1a** and the related (*S*,*S*)-bis(2-methylpropyl) terephthalate were not fluorescent at 25 °C in the presence and absence of donor **2**; nevertheless, achiral methyl terephthalate was subjected to the fluorescence study.[13]

Diastereodifferentiating [2 + 2] Photocycloaddition of 1a to 2 upon Direct versus CT Excitation. Photoirradiation of a concentrated solution of **1a** and **2** (0.2 and 1.0 M, respectively) afforded diastereomeric oxetane **3a** in moderate to good combined yields in all of the solvents examined (Table 2). The photoreaction was essentially very clean, and only small amounts of minor byproduct were detected by HPLC analysis; therefore, the low material balance and modest chemical yield would be ascribed at least in part to the less accurate evaluation of consumed **1a** in particular at low conversions. The diastereomeric excess (de) of photoadduct **3a** was determined by HPLC with satisfactory accuracy (error ±3%), and the effects of irradiation wavelength, temperature, and solvent on the de of **3a** obtained upon photoirradiation of a mixture of **1a** and **2** were systematically examined.

(a) Effect of Irradiation Wavelength. The effect of irradiation wavelength on the product's de was examined with a toluene solution of **1a** and **2** at low conversions.[10] The de of **3a** was kept almost constant upon irradiation at 254−290 nm but gradually decreased by shifting the irradiation wavelength to 310−320 nm, and eventually the epimeric product was obtained upon excitation at 330 nm. When irradiated at 340 nm, the starting material was recovered even after prolonged irradiations. We initially investigated the wavelength effect on the diastereoselectivity of **3a** at 254 nm (from a low-pressure mercury lamp) and at 313 nm (from a high-pressure mercury lamp fitted with a Pyrex filter), and the temperature-dependent de values obtained at each wavelength were subjected to the Eyring analysis by plotting the relative rate constant forming diastereomeric **3a** as a function of reciprocal temperature. The de values obtained upon excitation at 254 nm gave a good linear Eyring plot over the entire temperature region employed. However, the de data obtained at 313 nm led to a curved plot (Figure S3, Supporting Information), revealing operation of two distinct diastereodifferentiation mechanisms that are switched at the middle of the temperature range employed (ca. 15 °C). The Eyring plot for the de's obtained at 330 nm became normal again, giving a single straight line of oppositely signed slope without showing any curvature over the entire temperature range. Hence, the spectral overlap between **1a** and the CT complex is likely to be responsible for the curved Eyring plot and the mixed diastereodifferentiation mechanism observed at 313 nm. We therefore chose the excitation wavelengths of 290 and 330 nm

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TABLE 2. Diastereodifferentiating [2 + 2] Photocycloaddition of (*S*)-1-Methylpropyl *p*-Cyanobenzoate 1a to 1,1-Diphenylethene 2 upon Direct and Charge-Transfer Band Excitation in a Variety of Solvents[a]

solvent	excitation mode[b]	irrad time/h	temp/ °C	% conv[c]	% yield[d]	% de[e]
methylcyclohexane	direct	3	50	31	12	77
			25	31	12	64
			0	33	11	63
			−25	32	11	43
			−50	32	9	34
	CT	10	50	20	5	3
			25	23	4	4
			0	31	4	3
			−25	26	4	24
			−50	26	6	26
toluene	direct	3	50	18	12	74
			25	25	13	65
			0	18	9	68
			−25	26	10	54
			−50	24	10	37
	CT	6	50	[f]	4	−11
			25	[f]	4	−4
			0	[f]	5	4
			−25	[f]	4	6
			−50	[f]	5	21
tetrahydrofuran	direct	3	50	12	9	57
			25	18	7	54
			−50	8	4	32
	CT	5	50	13	4	−12
			25	17	5	−8
			−50	24	4	12
acetonitrile	direct	3	50	20	4	−13
			25	25	4	−12
			−20	22	5	−11
			−40	23	6	−11
	CT	7	50	23	11	−3
			25	27	15	−8
			−20	26	15	−10
			−40	26	14	−11
2% acetonitrile in methylcyclohexane	direct	3	50	14	3	1
			25	22	3	−2
			−20	22	4	−4
			−40	22	4	−2
	CT	8	50	10	4	16
			25	6	3	13
			−20	21	3	0
			−40	20	4	3

[a] [**1a**] = 0.2 M, [**2**] = 1.0 M. For data in methylcyclohexane, see ref. 10. [b] Irradiation was performed at 290 nm (direct excitation) or at 330 nm (CT excitation) using an appropriate band-path filter fitted to the light source LAX-101 (100 W xenon lamp). [c] Consumption of **1a** determined by HPLC. [d] HPLC yield of **3a**. [e] The absolute configurations of diastereomeric **3a** were established by X-ray crystallography (ref 10), and the positive and negative de values indicate the predominant formation of (1′*S*,2*R*)- and (1′*S*,2*S*)-**3a**, respectively. [f] Not determined.

for direct and selective CT excitation, respectively, throughout the study. Although the possible contribution of hidden CT bands at shorter wavelengths is difficult to strictly exclude, the same de values obtained at 254 and 290 nm indicate the insignificant contribution of the excited CT complex in the direct excitation.

(b) Effect of Triplet Quencher on the Diastereoselectivity. While typical Paternó−Büchi reactions of ketones with olefins undergo via triplet biradical intermediates,[21] the photoaddition of cyanobenzoate **1** with diphenylethene **2**, in both direct and CT excitation, is thought to proceed in the singlet manifold, as judged from the triplet quenching experiments shown below. This view also agrees with the results of previous studies on the photocycloaddition reactions of electron-deficient aromatic esters with olefinic donors.[13] Thus, the Paternó−Büchi reaction of **1a** and **2** upon direct and CT excitation was examined in the presence of (*E*)-1,3-pentadiene (0.2−0.4 M), whose triplet energy, $E_T = 248$ kJ mol^{-1}, is reasonably lower than that of methyl *p*-cyanobenzoate, $E_T = 301$ kJ mol^{-1}.[22] The addition of diene lowered the conversion but enhanced the de in both excitation modes (Table S1, Supporting Information). On the contrary, the yield and de of **3a** obtained upon direct and CT excitation were almost unaffected (within the experimental error) in the presence of molecular oxygen added as a triplet quencher,[23] suggesting that the triplet species are not the major species in the present photoreaction.[10] As the Eyring treatment of the de data always afford good linear plots (vide infra), a single diastereodifferentiation mechanism should be operative under the reaction conditions employed. We may conclude, therefore, that 1,3-pentadiene behaves not only as a triplet quencher but also acts as a chemical quencher. It seems that the singlet manifold of the cyanobenzoate is also quenched by this diene presumably via energy or electron transfer process. Accordingly, the intervention of triplet species in the overall mechanism and its effect on de in the reaction of **1** with **2** are insignificant under our experimental conditions.

(c) Temperature and Solvent Effects on the Photoreaction. For better comparison of the direct versus CT excitation and also the diastereodifferentiation mechanisms operative in both excitation modes, we performed the photoreaction of **1a** and **2** at various temperatures ranging from +50 to −50 °C to obtain the results shown in Table 2. Attempts to further lower the reaction temperature down to −70 °C in toluene resulted in extremely low conversion and yield (**3a** in < 2%) after 6 h irradiation at 330 nm, for which the insufficient solubility of **1** or **2** seems to be responsible as the sample solution was not completely transparent at this temperature. As can be seen from Table 2, the direct, rather than CT, excitation affords much higher de's particularly in nonpolar solvents, and the temperature-dependence profiles of de are just opposite in the direct and CT excitation.

The solvent effects on the photoreaction of **1a** with **2** were also studied in methylcyclohexane, toluene, tetrahydrofuran, and acetonitrile (Table 2). By increasing the solvent polarity, the yield of oxetane **3a** was reduced in the direct excitation but improved in the CT excitation. The conversion and the yield of **3a** obtained were remarkably insensitive to the reaction temperature as far as the same excitation mode and solvent were used. In methylcyclohexane, (1′*S*,2*R*)-**3a** was obtained as the major product irrespective of the excitation mode and the reaction temperature, while the epimer, (1′*S*,2*S*)-**3a**, was favored particularly upon CT excitation in polar solvents [the absolute configurations of diastereomers of **3a** were already established by X-ray crystallography,[10] and the negative de value in Table 2 indicates the predominant formation of (1′*S*,2*S*)-**3a**]. Thus, the (1′*S*,2*S*)-isomer was formed as the major product in the CT excitation at the

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[21] (a) Freilich, S. C.; Peters, K. S. *J. Am. Chem. Soc.* **1981**, *103*, 6257–6259. (b) Freilich, S. C.; Peters, K. S. *J. Am. Chem. Soc.* **1985**, *107*, 3819–3822. (c) Yang, N. C.; Loeschen, R. L.; Mitchell, D. *J. Am. Chem. Soc.* **1967**, *89*, 5465–5466.

[22] Kellogg, R. E.; Simpson, W. T. *J. Am. Chem. Soc.* **1965**, *87*, 4230–4234.

[23] (a) Gorman, A. A.; Rodgers, M. A. J. *J. Am. Chem. Soc.* **1986**, *108*, 5074–5078. (b) Sajimon, M. C.; Ramaiah, D.; Thomas, K. G.; George, M. V. *J. Org. Chem.* **2001**, *66*, 3182–3187.

TABLE 3. Activation Parameters Determined by the Eyring Treatment of the Diastereomeric Excess (de) of 3a (or 3b) Obtained in Diastereodifferentiating Photocycloaddition of 1a (or 1b) to 2 in Various Solvents[a]

excitation mode	solvent	$\Delta\Delta H^\ddagger$/kJ mol^{-1}	$\Delta\Delta S^\ddagger$/J mol^{-1} K^{-1}	$T\Delta\Delta S^{\ddagger a}$/kJ mol^{-1}	T_0/°C[b]
direct	methylcyclohexane	+6.4	+39	+12	−109
		(+1.6	+21	+6.3	−197)[c]
	toluene	+6.3	+35	+11	−93
	tetrahydrofurane	+3.9	+23	+6.8	−104
	acetonitrile	−0.2	−2.7	−0.8	−199
	2% acetonitrile in methylcyclohexane	+0.4	+1.2	+0.3	+60
CT	methylcyclohexane	−3.3	−10	−3.1	+57
		(−3.8	−9	−2.7	+149)[c]
	toluene	−3.6	−13	−3.8	+4
	tetrahydrofurane	−2.8	−11	−3.2	−19
	acetonitrile	+1.0	+2.4	+0.7	+144
	2% acetonitrile in methylcyclohexane	+2.1	+9.1	+2.7	−42

[a] T = 298 K. For data in methylcyclohexane, see ref. 10. [b] Equipodal temperature. [c] For the reactions of **1b** with **2** to give **3b**.

higher temperatures in toluene and tetrahydrofuran, while the (1′*S*,2*R*)-isomer was predominant at any (examined) temperature in the direct excitation. Interestingly, in acetonitrile, the (1′*S*,2*S*)-isomer was always the major product under the conditions employed. It is also important to note that the stereoselectivities in acetonitrile became low in both excitation modes, presumably due to the less tightly bound radical ionic excited species, but the both excitation modes still gave the distinctly different linear Eyring plots, implying that the same diastereodifferentiation mechanism operativing in this solvent.

(d) Differential Activation Parameters for the Diastereodifferentiation. To more quantitatively discuss the solvent effect on the two excited-state complex species, the Eyring analyses[24] were performed for the de's obtained at different temperatures in various solvents. By plotting the ln{[(1′*S*,2*S*)-**3a**]/[(1′*S*,2*R*)-**3a**]} values against the reciprocal temperature (1/*T*), we obtained the differential activation enthalpy ($\Delta\Delta H^\ddagger$) and entropy ($\Delta\Delta S^\ddagger$) values (Table 3). As each Eyring plot gave a nice straight line of different slope and intercept (Figure 1), operation of a single, but distinct, diastereodifferentiation mechanism is confirmed for each excitation mode in all the solvents examined. In this Paternó−Büchi reaction occurring in the singlet manifold, the photocyclization is likely to proceed thorough the concerted or short-lived 1,4-biradical mechanism, and hence, the diastereoface-differentiating complexation of chiral alkyl cyanobenzoate with olefin donor is solely responsible for the observed de values, as the subsequent ring-closure process is very fast.

A careful comparison of the activation parameters obtained in both excitation modes reveals the contrasting nature of the two excited-state complex species as indicated below.

(1) Consistently larger $|\Delta\Delta H^\ddagger|$ and $|\Delta\Delta S^\ddagger|$ values were obtained in nonpolar methylcyclohexane and toluene than in polar THF and acetonitrile, irrespective of the excitation mode. This implies that the two excited-state complexes, generated by direct and CT excitation, share a common feature to certain degree, being more or less polarized than the relevant ground-state species and therefore better solvated in polar solvents to make the critical diastereodifferentiation less efficient.

(2) The changes in $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ do not behave independently but compensate each other (vide infra). As a natural consequence of the $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ values with the same sign and the differential Gibbs−Helmholtz equation, $\Delta\Delta G^\ddagger = \Delta\Delta H^\ddagger - T\Delta\Delta S^\ddagger$, the dominant diastereomer is switched at a critical temperature (i.e., equipodal temperature, T_0), as exemplified in Figure 1. As shown in Table 3, the equipodal temperature T_0 is a critical function of the irradiation conditions, i.e., the excitation mode and solvent. This analysis reveals that the observed preference for a specific diastereomer is just an incidental result obtained in a given solvent and at a given temperature, and therefore, a comparison of the differential activation parameters for both excitation modes is more crucial for elucidating the nature of the two distinct excited species.

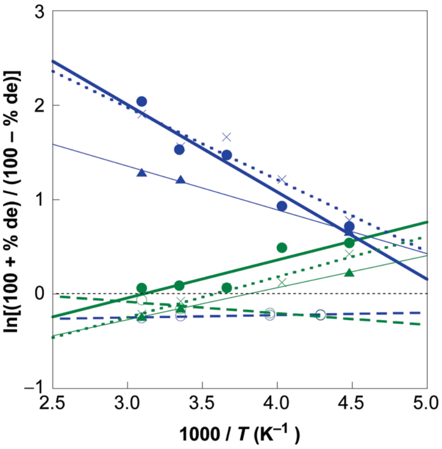

FIGURE 1. Temperature dependence of the de of **3a** obtained upon direct (blue) and CT (green) excitation in methylcyclohexane (filled circle), toluene (cross), tetrahydrofuran (triangle), and acetonitrile (open circle). The regression lines were obtained by the least-squares fitting.

(3) The direct and CT excitation constantly led to the oppositely signed $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ in all the solvents employed. This clearly designates that the two excited-state complexes formed via direct and CT excitation are completely distinct species in structure and reactivity and, more importantly, that despite the same chirogen introduced to the substrate, the diastereoface selectivity is inverted for the two complex species in terms of the activation parameters.

(4) The $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ values are sensitive to solvent polarity and gradually decrease with increasing polarity to eventually be inverted in sign in acetonitrile, irrespective of the excitation mode. This suggests the role of specific solvation of polar solvents to the excited species in the critical diastereodifferentiating step. More intriguingly, the direct and CT excitation in methylcyclohexane containing 2% acetonitrile led to contrasting behavior of the activation parameters (Table 3), showing smaller decreases (than in acetonitrile)

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(24) Eyring, H. *J. Chem. Phys.* **1935**, *3*, 107–115.

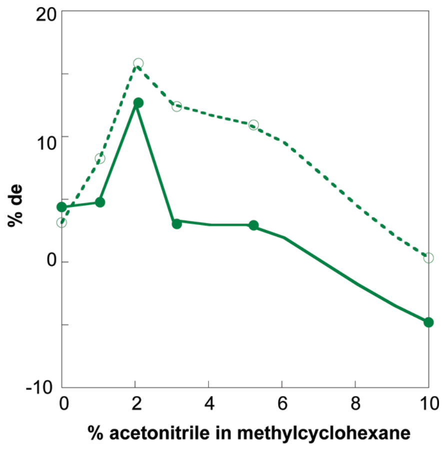

FIGURE 2. Effect of acetonitrile content on the de of **3a** produced upon CT excitation of **1a** and **2** in methylcyclohexane at 25 °C (solid line) and at 50 °C (dashed line).

upon direct excitation versus further augmentation upon CT excitation. These results indicate that the degree and impact of selective solvation are significantly different for the two excited-state complex species, probably due to the difference in dipole moment and polarizability.

(5) The $\Delta\Delta H^\ddagger$ and $T\Delta\Delta S^\ddagger$ values obtained for the CT excitation balance to each other at $T = 298$ K, while the entropic contribution ($T\Delta\Delta S^\ddagger$) overwhelms the enthalpic contribution ($\Delta\Delta H^\ddagger$) upon direct excitation, as can be seen from Table 3. This means that the diastereoface selectivity upon photocycloaddition is controlled almost equally by the enthalpic and entropic factors in the excited CT complex generated by CT excitation but is more critically controlled by the entropic factor in the conventional exciplex formed via direct excitation. Furthermore, both the absolute $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ values are larger for the direct excitation than for the CT excitation, indicating that the conventional exciplex is more susceptible to the temperature and solvent than the excited CT complex. This seems reasonable because the exciplex is a species formed dynamically in the excited state with significant desolvation and solvent reorganization, while the CT complex which is originally solvated in the ground state suffers only modest solvent reorganization after excitation.

(e) Specific Solvation by Acetonitrile. In both excitation modes, the use of polar acetonitrile solvent led to the sign inversion of the $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ values (Table 3). We therefore examined the effects of acetonitrile (1−10%) added to methylcyclohexane on the photocycloaddition of **1a** to **2**. In the presence of acetonitrile, the photoreaction was more or less decelerated but gave **3a** in modest to good yields (Table S2, Supporting Information). However, the de of **3a** obtained upon direct irradiation decreased abruptly from 64% to −3% upon addition of only a small portion (1%) of acetonitrile and stayed at low values, ranging from +2 to −8%, in methylcyclohexane solutions containing 2−10% acetonitrile, which are comparable to the −12% de obtained in 100% acetonitrile. This result indicates the strong preferential solvation of acetonitrile molecules to the conventional exciplex.

In the CT excitation, the effect of added acetonitrile was more modest and not uniform. As shown in Figure 2, a small amount of acetonitrile (up to 2%) added to the methylcyclohexane solution at 25 °C appreciably enhanced the de of **3a** from 4% to 13%, but further addition lowered the de and eventually switched the chiral sense of product to give **3a** in −5% de, which is comparable to that (−8% de) obtained in pure acetonitrile. A parallel trend, including the de values optimized in 2% acetonitrile and the inverted chiral sense of product in 100% acetonitrile, was observed for the CT excitation at 50 °C (Figure 2). These results are accounted for in terms of the specific solvation to the excited CT complex, as proposed previously for a polarized exciplex species involved in the polar photoaddition of alcohols to aromatic olefins.[25] The different solvent dependence behavior and activation parameters observed upon direct versus CT excitation confirm that the conventional exciplex and the excited CT complex produced in each excitation mode do not interconvert or share common geometry, polarity/polarizability, or reactivity.

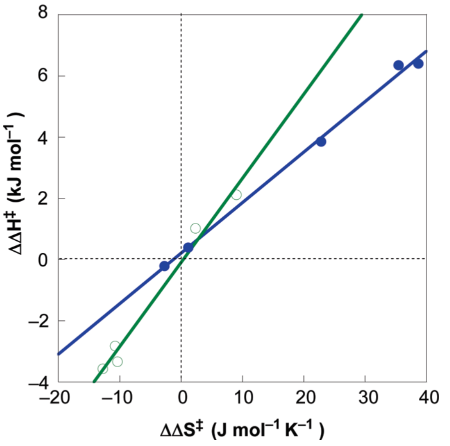

FIGURE 3. Enthalpy−entropy compensation plots of the activation parameters obtained upon direct (blue closed circle) and CT (green open circle) excitation in a variety of solvents shown in Table 3.

(f) Enthalpy−entropy Compensation. The compensatory enthalpy−entropy relationship[26] is a widely observed phenomenon in chemistry and biochemistry, and the origin and physical meanings of the extrathermodynamic relationship have been a target of much debate.[27] Figure 3 shows the enthalpy−entropy compensation plots for the differential activation parameters obtained upon direct and CT excitation of a mixture of **1a** and **2** in various solvents, including methylcyclohexane containing 2% acetonitrile. In all of the cases examined, a good linear regression line that passes through the origin was obtained for each of the two excitation modes, indicating that a single mechanism is operative in the critical diastereodifferentiating step. The slope of the $\Delta\Delta S^\ddagger-\Delta\Delta H^\ddagger$ plot, having the dimension of temperature, is called the "isokinetic," or "isodiastereodifferentiating," temperature (β), since the de value becomes identical at this specific temperature, regardless of the solvent used.[28] The smaller slope (β) for formation of **3a** means heavier contribution of the entropy factor than the enthalpy factor to the diastereodifferentiation in the direct rather than CT excitation (Table 4).

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TABLE 4. Comparison of Isodiastereodifferentiating Temperature β Obtained from the Entropy−Enthalpy Compensation Plot for the Direct versus Charge Transfer Band Photoexcitation of 1a or 1b with 2[a]

substrate	β_{direct} (K)	β_{CT} (K)	$\Delta\beta^{b}$ (K)
1a	177	275	98
1b	79	436	357

[a] The values were obtained by the slope of plots in Figures 3 and S4 (Supporting Information). [b] $\Delta\beta = \beta_{\text{CT}} - \beta_{\text{direct}}$.

The β values for the formation of **3b** are also tentatively evaluated using the data in methylcyclohexane for a comparison purpose. These observations reinforce the above-mentioned conclusions that the exciplex and the excited CT complex differ in structure and reactivity and such a difference in slope is consistent with a greater flexibility in the conventional exciplex than the excited CT complex (vide infra).

(g) Substituent Effects. Photocycloaddition of cyanobenzoate **1a** to more electron-rich 1,1-bis(*p*-methoxyphenyl)ethene under comparable conditions was unsuccessful, although the diarylethene was completely consumed to give the corresponding dimer and other unidentified products, which is probably attributable to an efficient electron-transfer quenching by this donor. The free energy changes (ΔG) of the electron transfer from diarylethenes to excited **1a** in toluene and acetonitrile were estimated by the Rehm−Weller equation.[29] Using the oxidation potentials of the ethenes (E_{ox} = 1.32 and 1.88 V for methoxy- and parent diphenylethene, respectively),[30] the reduction potential and the singlet energy of acceptor (E_{red} = −1.85 V for methyl *p*-cyanobenzoate[31] and $\Delta E_{0,0}$ = 411 kJ mol^{-1} of **1a** from its absorption spectrum), intensely negative ΔG values were obtained for 1,1-bis(*p*-methoxyphenyl)ethene; i.e., ΔG = −58 and −112 kJ mol^{-1} in toluene and acetonitrile, respectively. It is to be noted, however, that the Paternó−Büchi reaction of **1a** with **2** underwent at comparative efficiencies in acetonitrile and in toluene, where the $|\Delta G|$ value is much smaller (ΔG = −30 and +25 kJ mol^{-1}, respectively).

A further mechanistic support for the distinction between the conventional exciplex and the excited CT complex came from the differential activation parameters obtained upon photocycloaddition of **1b**, which possesses a slightly bulkier chiral group.[10] Note that two additional methyl groups are introduced at a peripheral position of the chiral group in **1b**. Thus, the irradiation of a mixture of **1b** and **2** at 290 or 330 nm afforded the corresponding oxetane **3b** as a sole product in a good yield. The absolute configurations of diastereomeric **3b** isomers were tentatively assigned by the comparison of their retention times with those of **3a** upon HPLC analysis on the same reversed-phase column, assuming that the elution order is preserved for both **3a** and **3b**.

The temperature-dependence behavior of de of **3b** was similarly investigated and analyzed by using the Eyring analysis,[10] and the differential activation parameters obtained in various solvents were examined to give excellent straight lines of significantly different slopes or β for direct and CT excitation (Figure S4, Supporting Information). The modification of the chiral ester moiety at a remote position caused the dramatic changes in differential activation parameters for the direct excitation. In the direct excitation, both parameters became smaller, but the effect was more pronounced on the enthalpic term. The relatively smaller effects were found for the CT excitation, where the $\Delta\Delta H^{\ddagger}$ was slightly decreased while the $\Delta\Delta S^{\ddagger}$ was practically unaffected (Table 3). This contrasting behavior of the activation parameters upon direct versus CT excitation indicates that the peripheral part of the chiral group is more closely located to the reaction partner **2** and hence more influential in the exciplex than in the excited CT complex. The smaller changes found for the parameters in the CT excitation may be ascribed to the diastereodifferentiation that principally occurred at the stage of the complexation in the ground state.

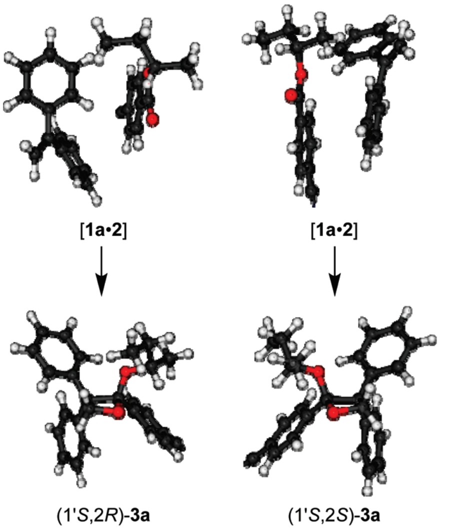

FIGURE 4. Optimized geometries of (1′*S*,2*R*)- and (1′*S*,2*S*)-**3a** at the B-LYP/TZVP level and their precursors (i.e., complex between (*S*)-**1a** with **2**) at the DFT-D-B-LYP/TZVP level. The most abundant *Tg*$^{+}$ conformers are shown.

Quantum Chemical Investigation of the Diastereomeric Complexes. To theoretically estimate the structural and energetic (enthalpic) differences between the diastereomeric complexes of **1a** with **2**, all possible conformations of the complex, taking into account the nine rotamers about the C*−O and C*−C bond in **1a** (see Chart S1 in the Supporting Information), were calculated by the recently developed dispersion-corrected DFT method.[32] A pair of diastereomeric [**1a**·**2**] complexes, which are precursors to (1′*S*,2*R*)- and (1′*S*,2*S*)-**3a**, were optimized at the DFT-D-B-LYP/TZVP level,[33] starting from the hypothetical complexation of **1a** and **2** with a separation of 3.4 Å. As can be seen from Figure 4, the optimized structures obtained sustain the $\pi-\pi$ stacking between the aromatic rings of the donor and acceptor. In general, the π overlap between the donor and acceptor molecules is maximized in the CT complex to give a conformationally rigid stacked structure.[34] Since the second aromatic ring in diphenylethene is almost perpendicular

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[29] (a) Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 259–270. (b) Weller, A. *Z. Phys. Chem. Neue Folge* **1982**, *133*, 93–98.

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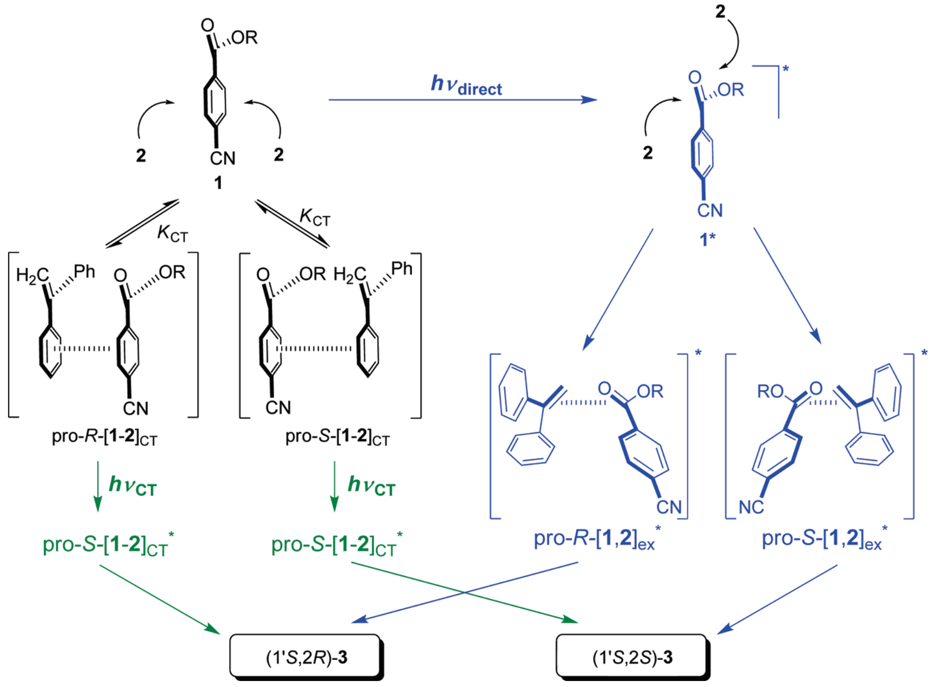
SCHEME 2. **Mechanisms of Diastereodifferentiating [2 + 2] Photocycloaddition of Chiral Alkyl Benzoate 1 to 1,1-Diphenylethene 2 via Conventional Exciplex (Blue) and Excited CT Complex (Green) Formed, Respectively, upon Direct and Charge-Transfer Band Excitation (Black Indicates Ground-State Events)**[a]



[a]The ester substituent R contains a chiral group.

to the first π-stacked ring, the whole molecule is twisted in the CT complex. The calculated structures are for the ground-state complexes, but we assume that these structures are more or less relevant to the excited CT complexes. Due to the strong $\pi-\pi$ stacking, the excited CT complex will not be able to gain additional conformational freedoms upon excitation, and the entropic difference between the diastereomer pair should be much smaller than that for the exciplex, in nice agreement with the experimental results. The subsequent (COSMO)-SCS-MP2 energy calculations[35] revealed that the conformers are populated in a ratio of 55:45 in the gas phase or 54:46 in acetonitrile (Table S3, Supporting Information). This preference for the (1′*S*,2*R*)-isomer predicted by theory is in nice agreement with the experimental result obtained at temperatures lower than the equipodal temperature (T_0) in the CT excitation of **1a** with **2**. The solvent effect was not readily approximated by the current solvation model (conductor-like screening model) employed in our calculation.

The diastereomeric pairs of nine rotamers of photoproduct **3a** were computed by the standard DFT method at the B-LYP/TZVP level (Figure 4 and Table S3, Supporting Information). By weight-averaging the relative (COSMO)-SCS-MP2 energies of all possible conformers, (1′*S*,2*R*)-**3a** was found to be energetically more favored than (1′*S*,2*S*)-**3a** in a ratio of 58:42 (in gas phase) or 56:44 (in acetonitrile). The most favored conformation of the chiral group was calculated to be Tg^+ in (1′*S*,2*R*)-**3a**, which is consistent with the X-ray structure of (1′*S*,2*R*)-**3a**, and this conformation is also the predominant one in the parent ester **1a**.[10] It is to be noted that this conformer is slightly disfavored in diastereomeric (1′*S*,2*S*)-**3a**. In the direct excitation, the excited state of cyanobenzoate interacts with diphenylethene to form an exciplex, and the interaction is expected to occur near the carbonyl group. The conformation of the chiral group is expected to affect more dynamically on the more flexible exciplex structure but less effectively on the originally π-stacked, rigid CT complex. However, the present calculations do not take into account the entropic contributions, despite their critical roles in differentiating the two excited complex species. Since the reliable structural estimation of such excited species by theoretical calculation is not feasible at the current stage, our experimental procedures to obtain and analyze the activation parameters under a variety of conditions provide us with a wealth of information to elucidate the nature of the excited-state complex species generated via the two distinct excitation modes.

Summary and Conclusions

From the comprehensive analysis of the temperature and solvent effects on the diastereodifferentiating Paternó−Büchi reaction of chiral alkyl cyanobenzoates with 1,1-diphenylethene, we can contrast the two diastereodifferentiation mechanisms operative in direct versus CT excitation as illustrated in Scheme 2. Upon direct excitation of cyanobenzoate, the Paternó−Büchi reaction with diphenylethene proceeds in the singlet manifold to give a diastereomeric pair of excited-state complexes (i.e., "conventional" exciplex), the diastereomer ratio of which determines the product's de through the subsequent cyclodimerization reaction. The good linear Eyring plots obtained indicate that no switching of diastereodifferentiation mechanism, such as different cyclization rates for the diastereomeric exciplex pair, is involved in the present photocycloaddition reaction. The first

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[35] (a) Grimme, S. *J. Phys. Chem. A* **2005**, *109*, 3067–3077. (b) Grimme, S. *J. Chem. Phys.* **2003**, *118*, 9095–9102.

excited singlet state of cyanobenzoates is mostly $\pi-\pi^*$ in nature but borrows some intensity from the n$-\pi^*$ state,[10] and thus, the interaction is expected to occur near the carbonyl group in the exciplex formation. For this reason, the chiral substituent can more critically control the product's de upon direct, rather than CT, excitation in the Paternó−Büchi reaction. Exciplex formation is a dynamic process that involves the initial desolvation upon association and the subsequent structural relaxation of the collision complex with accompanying extensive solvent reorganization around it. In contrast, the ground-state CT complexation is mostly driven by the $\pi-\pi$ stacking of donor and acceptor molecules to maximize the orbital overlap. Originally stacked to each other in the ground state, the excited CT complex is considered to be less flexible in structure and less extensive in desolvation and/or solvent reorganization. This makes the exciplex more susceptible to environmental factors such as temperature and solvent, relative to the excited CT complex. Indeed, the de of the oxetane produced upon direct excitation displayed larger (and oppositely signed) slope and intercept in the Eyring plot compared to those for CT excitation, supporting this view.

In this detailed mechanistic study on the Paternó−Büchi reaction of chiral cyanobenzoates with diphenylethene, we have demonstrated that the conventional exciplex (formed upon direct excitation) and the excited CT complex (formed upon CT-band excitation) are independent and noninterconvertible excited species that possess distinctly different structures and reactivities, which eventually afford the same diastereomeric oxetane pair in different diastreoselectivities. The two excited-state complex species were comparatively and quantitatively discussed for the first time in terms of the differential activation parameters and isokinetic temperatures. It is interesting and potentially useful that the excitation mode, manipulated simply by changing the irradiation wavelength, can switch the diastereofacial selectivities upon complex formation and the subsequent photocycloaddition process (at a very low or high temperature, where the major controlling factor is the enthalpy or entropy, respectively). This sort of stereochemical control by irradiation wavelength can be extended to other photoreactions if the excitation at the CT band affords the excited species different from the conventional exciplex. Further research along this line is currently underway in other photochemical systems.

Experimental Section

General Methods. Spectrophotometric-grade methylcyclohexane, toluene, tetrahydrofuran, and acetonitrile were used as received in the photoreactions and spectroscopic measurements. 1,1-Diphenylethene was purified by column chromatography over alumina under argon atmosphere before use, which completely eliminated the impurities absorbing at around 340 nm (presumably benzophenone) in the commercial samples.

Preparation of (*S*)-1b. Reaction of (*S*)-4-methyl-2-pentanol with 4-cyanobenzoyl chloride in pyridine gave (*S*)-**1b** as a colorless oil in 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (d, J = 3.6 Hz, 3H), 0.95 (d, J = 3.6 Hz, 3H), 1.35 (d, J = 6.2 Hz, 3H), 1.38−1.45 (m, 1H), 1.65−1.76 (m, 1H), 5.22−5.30 (m, 1H), 7.74 (AA′XX′, J_{AX} = 8.7 Hz, $J_{AA'}$ = 1.8 Hz, 2H), and 8.13 (AA′XX′, J_{XA} = 8.7 Hz, $J_{XX'}$ = 1.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.5, 22.4, 22.9, 24.9, 45.1, 71.4, 116.2, 118.1, 130.1, 132.2, 134.7, and 164.6. CI-MS *m*/*z* (relative intensity): 232 ($M^+ + 1$, 100), 85 (68). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.47; H, 7.12; N, 6.22.

Photolysis. All irradiations were performed under argon atmosphere at a given temperature in a temperature controller. The solution was irradiated in a 1-cm square cuvette with a 100-W xenon light source. For the band-selective excitations at direct (290 nm) and CT bands (330 nm), a UVB mirror module fitted with HQBP290-UVB filter and a UVA mirror module with HQBP330-UVA filter were employed, respectively. The product distribution and conversion of photolyzed samples were determined by HPLC fitted with a UV detector (254 nm) by monitoring each peak (relative to 3,5-dimethoxymethylbenzoate added as an external standard) on an ODS column (4.6 × 250 mm) eluted with a 65:35 mixture of acetonitrile and water, containing 0.5% (v/v) triethylamine, at a flow rate of 1 mL/min. The retention times of **1a**, **2**, (1′*S*,2*S*)-**3a**, (1′*S*,2*R*)-**3a**, and the standard were 10.1, 23.2, 47.3, 49.8, and 6.0 min, respectively. The photoproducts from the reaction of **1b** with **2** were not isolated but identified by GC−MS, and the diastereoselectivities were similarly determined by HPLC (monitor at 254 nm) under conditions identical to those employed for the reaction of **1a** with **2**.

Quantum Chemical Computations. All calculations were performed on Linux PCs using the TURBOMOLE 5.8 program suite.[36] Geometry optimizations were performed at the B-LYP/TZVP or dispersion-corrected DFT-D-B-LYP/TZVP level within the density functional theorem without any symmetry constraint (C_1) with a numerical quadrature multiple grid of m4. Subsequent single-point energy calculations were performed by the SCS-MP2 method with a TZVPP basis set. Further details of the calculation were described previously.[20,37] The effect of solvent on the conformer distribution was also evaluated by using the PCM model. Thus, single-point energy calculations were performed with the conductor-like screening model (COSMO)[38] as implemented in the TURBOMOLE program suite. The dielectric constant (ε) of 36.64 in acetonitrile and optimized atomic radii (C, 2.00; N, 1.83; O, 1.72; H, 1.30 Å) were used for the construction of the molecular cavity.

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Supporting Information Available: Details of the determination of the association constants in various solvents, CD spectra of the complex, the temperature dependence of de upon 254 and 313 nm irradiation, the enthalpy−entropy compensation plot for the photoreaction of **1b** with **2**, the detailed results of the photolysis in mixed solvents and in the presence of triplet quencher, the NMR spectra for **1b**, and the Cartesian coordinate for optimized geometries. This material is available free of charge via the Internet at http://pubs.acs.org.

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[36] Ahlrichs, R.; Bär, M.; Baron, H. P.; Bauernschmitt, R.; Böcker, S.; Crawford, N.; Deglmann, P.; Ehrig, M.; Eichkorn, K.; Elliott, S.; Furche, F.; Haase, F.; Häser, M.; Horn, H.; Hättig, C.; Huber, C.; Huniar, U.; Kattannek, M.; Köhn, A.; Kölmel, C.; Kollwitz, M.; May, K.; Nava, P.; Ochsenfeld, C.; Öhm, H.; Patzelt, H.; Rappoport, D.; Rubner, O.; Schäfer, A.; Schneider, U.; Sierka, M.; Treutler, O.; Unterreiner, B.; Arnim, M. v.; Weigend, F.; Weis, P.; Weiss, H. *TURBOMOLE,* version 5.8; Universität Karlsruhe: Karlsruhe, 2005. See also: http://www.cosmologic.de/QuantumChemistry/main_turbomole.html.

[37] For recent examples, see: (a) Nishizaka, M.; Mori, T.; Inoue, Y. *J. Phys. Chem. Lett.* **2010**, *1*, 1809–1812. (b) Nishizaka, M.; Mori, T.; Inoue, Y. *J. Phys. Chem. Lett.* **2010**, *1*, 2402−2405.

[38] (a) Tomasi, J.; Persico, M. *Chem. Rev.* **1994**, *94*, 2027–2094. (b) Sinnecker, S.; Rajendran, A.; Klamt, A.; Diedenhofen, M.; Neese, F. *J. Phys. Chem. A* **2006**, *110*, 2235–2245.