

Stereoselective *E/Z* photoisomerization of oxazolidinone functionalized enecarbamates: direct and triplet sensitized irradiation†

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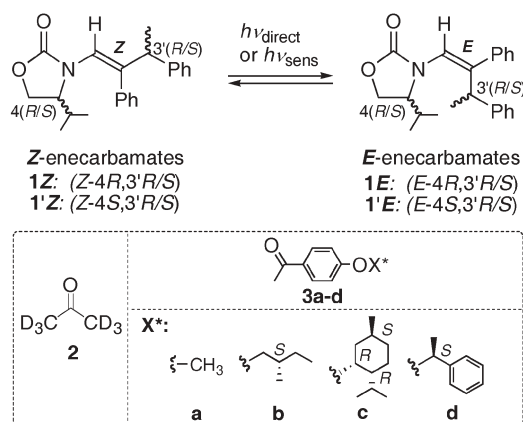
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Oxazolidinone-functionalized enecarbamates undergo diastereoselective *E/Z* photoisomerization upon direct and triplet sensitized irradiations with chiral/achiral sensitizers, showing that the enhanced product diastereoselectivity depends on the solvent and temperature.

Photochirogenesis or chirality control in photoreactions is one of the most challenging fields in photochemistry^{1–6} in which stereo-differentiation has to be imprinted within a short lifetime of an excited species. Oxazolidinone-functionalized enecarbamates **1** (Scheme 1) offer unusual opportunities to explore mechanistically versatile systems for the study of conformational, electronic, stereoelectronic, and steric effects.^{7–9} In this context, we recently observed high stereocontrol in the singlet-oxygen mediated oxidation of these enecarbamates (both in solution¹⁰ and organized media¹¹) by fine-tuning the alkene geometry. The dependence of the stereoselectivity on the alkene functionality prompted us to explore the photoisomerization processes. The elucidation of the intricacies involved in such a stereo-differentiating photoisomerization¹² would not only help to understand the stereochemical behavior of the enecarbamates, but also provide a versatile methodology to control the chirality of the photoproducts in photochemistry. For this purpose, the direct and sensitized photoisomerization of the enecarbamates were examined in various solvents as well as at a wide range of temperatures.



Scheme 1 *E/Z* photoisomerization of enecarbamates.

† Electronic supplementary information (ESI) available: reaction procedures, comparison of direct irradiation at different wavelength and synthesis of the chiral sensitizers. See <http://www.rsc.org/suppdata/cc/b5/04413h/>

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Direct irradiation of **1Z** at 254 nm was performed in various solvents and the observed diastereomeric excess (de) of the *E* and *Z* isomers at the photostationary state are listed in Table 1. Both *Z* and *E* isomers exhibit very low diastereoselectivities, and the configuration of the enhanced diastereomer depends on the solvent, but not on the temperature. The change of the irradiation wavelength from 254 to 300 nm has a negligible influence on the de values, but there is a noticeable change in the photostationary state. This may be attributed to the difference in optical density of the enecarbamate diastereomers at the different excitation wavelengths (see Supporting Information†).

To explore the triplet-sensitized photoisomerization of the enecarbamates, acetone-*d*₆ **2** (Scheme 1; E_T 339 kJ mol⁻¹) was employed both as solvent and sensitizer, as the triplet energy (E_T) of **1Z** is approximately 307 kJ mol⁻¹ (Fig. 1, estimated from phosphorescence spectra). Facile isomerization occurred and the photostationary state was reached within 15 min of irradiation (Table 2). Inspection of Table 2 reveals that diastereoselectivities observed with both the *Z* and *E* isomers are decreased on prolonged irradiation.

To examine the sensitizations with chiral triplet sensitizers, 4'-alkoxyacetophenone derivatives (E_T = 301 kJ mol⁻¹ for **3a**; Scheme 1) with chiral/achiral alkoxy groups were employed (**3a-d**). First, triplet sensitization was performed in CD₃CN with the achiral sensitizer **3a** (Scheme 1) at various time intervals for both *E* and *Z* isomers (Table 3). As in the case of the sensitization with **2**, facile photoisomerization was observed and the photostationary state was reached within 5 min. Evidently, the rate of the *Z*-to-*E* photoisomerization is slower than the *E*-to-*Z* one; i.e., the

Table 1 Photoisomerization of **1Z** by direct irradiation^a

Solvent	Temp/°C	Irdn/min	%de (1E) ^b	%de (1Z) ^b	Z:E
CD ₃ CN	20	2	6 (S)	4 (R)	62:38
		5	7 (S)	3 (R)	53:47
		10	1 (S)	4 (R)	52:48
CD ₃ OD	-40	10	6 (S)	8 (R)	55:45
		20	4 (R)	1 (S)	53:47
		40	2 (R)	2 (S)	56:44
CD ₂ Cl ₂	20	10	6 (R)	3 (S)	53:47
		40	3 (R)	2 (S)	56:44
		10	3 (S)	3 (R)	54:46
C ₆ D ₆	20	10	3 (S)	3 (R)	54:46
		10	3 (S)	3 (R)	54:46

^a [**1Z**] = 4.3 mM. A diastereomeric mixture of **1Z** (3'*R*:3'*S* = 50:50) employed. Irradiations performed at 20 °C at 254 nm in quartz NMR tubes under a N₂ atmosphere. *Z/E* ratios and de values determined by ¹H-NMR spectroscopy. ^b Diastereomeric excess (de) of the product. The configuration of the 3' epimer shown in a parenthesis. Mass balance >98%; error limit ±3%; mass balance decreased on prolonged irradiation (>20 min) presumably due to side reactions.

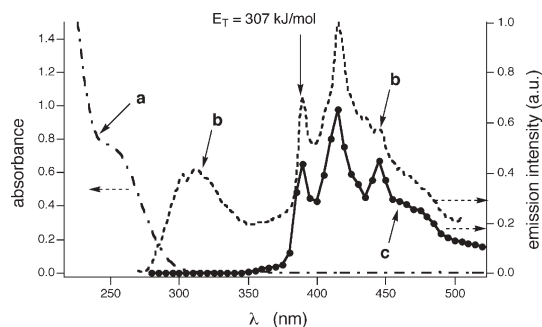


Fig. 1 Absorption (a), steady-state emission (b), and time-resolved phosphorescence (c) spectra of **1Z** (2.0×10^{-4} M) in CH_3CN at 23°C (a) or ethanol glass at 77 K (b, c). The time-resolved phosphorescence spectrum was recorded $1\ \mu\text{s}$ after an excitation pulse of $360\ \text{nm}$.

Table 2 Sensitized photoisomerization of **1Z**, **1'Z**, **1E** and **1'E** in acetone- d_6 **2**^a

Compound	Irdn/min	%de (1E) ^b	%de (1Z) ^b	Z:E
1Z	2	9 (S)	6 (R)	83:17
	5	9 (S)	3 (R)	76:24
	10	6 (S)	2 (R)	76:24
	15	8 (S)	1 (R)	77:23
1'Z	2	10 (R)	4 (S)	87:13
	5	10 (R)	6 (S)	77:23
	10	9 (R)	3 (S)	76:24
1E	2	9 (R)	1 (S)	77:23
	5	3 (S)	3 (R)	56:44
	10	6 (S)	0	76:24
1'E	2	3 (S)	0	76:24
	5	2 (S)	1 (R)	77:23
	10	2 (S)	1 (R)	77:23
	15	2 (S)	1 (R)	77:23
1E	2	3 (S)	3 (R)	56:44
	5	6 (S)	0	76:24
	10	3 (S)	0	76:24
	15	2 (S)	1 (R)	77:23
1'E	2	2 (R)	0	57:43
	5	5 (R)	2 (S)	74:26
	10	1 (R)	1 (S)	75:25
	15	3 (R)	2 (S)	75:25

^a [**1Z**] = [**1'Z**] = [**1E**] = [**1'E**] = $4.3\ \text{mM}$ in acetone- d_6 **2**. A diastereomeric mixture of **1** ($3'R:3'S = 50:50$) employed. Irradiations performed at 20°C ; $>300\ \text{nm}$ in pyrex NMR tubes under a N_2 atmosphere. Z/E ratios and de values were determined by $^1\text{H-NMR}$ spectroscopy. ^b Diastereomeric excess (de) of the product. The configuration of the $3'$ -epimer shown in a parenthesis.

3a-sensitized photoisomerization of **1Z** gave a Z:E ratio of 85:15 after 2 min compared to 71:29 for **1E**. This is presumably due to the larger steric hindrance in the *E*-isomer than that in the *Z*-isomer. The de values for **1E** and **1Z** are clearly different, which suggests the significance of the starting alkene geometry of the encarbamate. The general trend that the de values of the product were higher upon photoisomerization of **1Z** than that of **1E** may be ascribed to the reactivity-selectivity principle,^{13–15} in which the fast reaction (photoisomerization) of the *E* isomer to the photostationary state results accordingly in lower de values. Next, the chiral triplet sensitizers **3b–d** were employed for the diastereoselective *E/Z* photoisomerization in a variety of solvents at various temperatures (Table 4 and 5). As in the case of the **3a** sensitization (Table 2), the *E* isomers displayed again higher stereoselectivities than those of the corresponding *Z* isomers (Table 4). The subtle solvent dependence of the *E/Z* photoisomerization suggests that entropic factors might play a role in the stereodifferentiation process. For this reason, the temperature effects were also assessed in various solvents.¹⁶ Inspection of Table 5 shows that the sense of chirality in the enhanced *E* diastereomer at the $C-3'$ position depends once again on

Table 3 Sensitized photoisomerization of **1Z**, **1'Z** and **1E** with **3a**^a

Compound	Irdn/min	%de (1E) ^b	%de (1Z) ^b	Z:E
1Z	2	17 (R)	2 (R)	85:15
	5	15 (R)	0	83:17
	10	14 (R)	0	84:16
	15	13 (R)	0	84:16
1'Z	2	20 (S)	2 (S)	85:15
	5	20 (S)	3 (S)	84:16
	10	15 (S)	4 (S)	84:16
	15	16 (S)	2 (S)	84:16
1E	2	3 (R)	3 (S)	71:29
	5	9 (R)	5 (S)	84:16
	10	3 (R)	6 (S)	84:16
	15	0	4 (S)	84:16

^a [**1Z**] = [**1'Z**] = [**1E**] = $\sim 8\ \text{mM}$, and [**3a**] = 4 equivalence relative to [**1Z**] in CD_3CN . A diastereomeric mixture of **1** ($3'R:3'S = 50:50$) employed. Irradiations performed at 20°C ; $>300\ \text{nm}$ in pyrex NMR tubes under a N_2 atmosphere. Z/E ratios and de values were determined by $^1\text{H-NMR}$ spectroscopy. ^b Diastereomeric excess (de) of the product. The configuration of the $3'$ epimer shown in a parenthesis.

temperature, whereas the enhanced *Z* isomer is insensitive to the temperature variation. For the starting *Z* isomers in CD_3OD , the $C-3'S$ configuration of the *E* diastereomer was favored at 20°C , whereas the $C-3'R$ configuration was preferred on lowering the temperature. In contrast, photosensitization of the *Z* isomer in CD_2Cl_2 at different temperatures does not display such a variation and the $C-3'S$ configuration of the *E* diastereomer is enhanced at each temperature. The change of the sense at the $C-3'$ position on lowering the temperature in CD_3OD was observed for both achiral and chiral sensitizers **3a–d**, which indicates that the chirality did not play any significant role in asymmetric induction at the range of temperature employed.

To have more quantitative insight into the stereodifferentiation process, the differential Eyring equation¹⁷ was applied to analyze

Table 4 Solvent effect: isomerization of **1Z** with triplet sensitizers^a

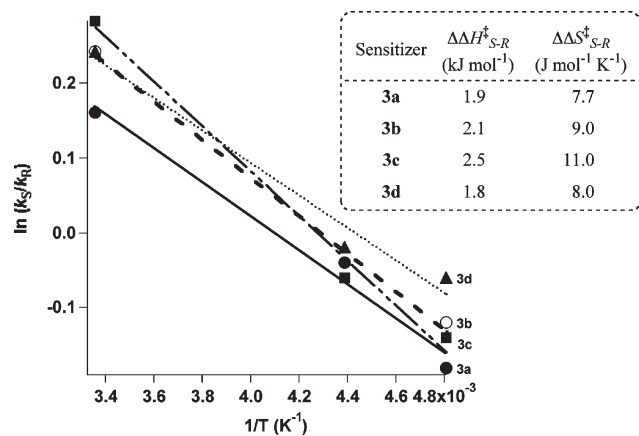
Sens	Solvent	%de (1E) ^b	%de (1Z) ^b	Z:E
3a	CD_3CN	15 (R)	0	83:17
	CD_3OD	8 (S)	3 (S)	83:17
	CD_2Cl_2	8 (S)	3 (S)	80:20
	CDCl_3	15 (R)	6 (S)	81:19
	C_6D_6	9 (R)	6 (S)	84:16
3b	CD_3CN	2 (S)	1 (S)	80:20
	CD_3OD	12 (S)	5 (S)	83:17
	CD_2Cl_2	8 (S)	9 (S)	83:17
	CDCl_3	8 (R)	9 (S)	83:17
	C_6D_6	18 (R)	9 (S)	82:18
3c	CD_3CN	7 (R)	5 (S)	86:14
	CD_3OD	14 (S)	4 (S)	86:14
	CD_2Cl_2	7 (S)	5 (S)	86:14
	CDCl_3	5 (R)	10 (S)	80:20
	C_6D_6	12 (R)	4 (S)	79:21
3d	CD_3CN	4 (S)	0	79:21
	CD_3OD	12 (S)	4 (S)	81:19
	CD_2Cl_2	6 (S)	6 (R)	73:27
	CDCl_3	7 (R)	8 (S)	77:23

^a [**1Z**] = $4.3\ \text{mM}$, [**3a**] \sim [**3d**] = ~ 8 equivalence relative to [**1Z**]. A diastereomeric mixture of **1Z** ($3'R:3'S = 50:50$) employed. 5 min-irradiations ($>300\ \text{nm}$) performed at 20°C in pyrex NMR tubes under a N_2 atmosphere. Z/E ratios and de values were determined by $^1\text{H-NMR}$ spectroscopy. ^b Diastereomeric excess (de) of the product. The configuration of the $C-3'$ position of the encarbamate shown in a parenthesis.

Table 5 Temperature effect in the isomerization of **1Z** with triplet sensitizers^a

Sens	Solvent	Temp/°C	%de (1E) ^b	%de (1Z) ^b	Z:E
3a	CD ₃ OD	20	8 (S)	3 (S)	83:17
		-45	2 (S)	1 (S)	80:20
		-65	9 (R)	0	85:15
	CD ₂ Cl ₂	20	8 (S)	3 (S)	80:20
		-45	12 (S)	3 (S)	83:17
		-65	6 (R)	3 (S)	77:23
3b	CD ₃ OD	20	12 (S)	5 (S)	83:17
		-45	2 (R)	5 (S)	81:19
		-65	6 (R)	3 (S)	77:23
	CD ₂ Cl ₂	20	8 (S)	9 (S)	83:17
		-45	8 (S)	2 (S)	83:17
		-65	7 (S)	5 (S)	86:14
3c	CD ₃ OD	20	14 (S)	4 (S)	86:14
		-45	3 (R)	1 (S)	88:12
		-65	7 (R)	5 (S)	78:22
	CD ₂ Cl ₂	20	7 (S)	5 (S)	86:14
		-45	7 (S)	5 (S)	86:14
		-65	7 (S)	5 (S)	86:14
3d	CD ₃ OD	20	12 (S)	4 (S)	81:19
		-45	1 (R)	7 (S)	79:21
		-65	3 (R)	4 (S)	78:22
	CD ₂ Cl ₂	20	6 (S)	6 (R)	73:27
		-45	4 (S)	11 (S)	86:14
		-65	4 (S)	11 (S)	86:14

^a [**1Z**] = 4.3 mM. [**3a**], [**3b**], [**3c**] and [**3d**] were ~8 equivalents relative to [**1Z**]. A diastereomeric mixture of **1Z** (3'R:3'S = 50:50) employed. 5 min-irradiations (>300 nm), performed in pyrex NMR tubes under a N₂ atmosphere. Reaction temperature was controlled in a methanol/dry-ice bath. Z/E ratios and de values were determined by ¹H-NMR spectroscopy. ^b Diastereomeric excess (de) of the product. The configuration of the 3' epimer shown in a parenthesis.

**Fig. 2** Eyring plot of the de values for **1E** obtained upon triplet photosensitization with sensitizers **3a** (●), **3b** (○), **3c** (■), and **3d** (▲) in CD₃OD.

the data. The plot of the logarithm of the relative rate constant, $\ln(k_S/k_R)$, against the reciprocal temperature, yielded the contributions from the differential activation enthalpy ($\Delta\Delta H_{S-R}^\ddagger$) and entropy ($\Delta\Delta S_{S-R}^\ddagger$) for the formation of the diastereomeric *E* enecarbamates (*E-4R3'R/S*) upon photoisomerization of **1Z** (Fig. 2). The observed temperature effect reflects a significant contribution from the differential entropy ($\Delta\Delta S_{S-R}^\ddagger$) for both the achiral and chiral sensitizers **3a-d**. The de values of **1E** decreased by lowering the temperature and reversed the selectivity to give a good straight line for each sensitizer, which evidently indicates that a single diastereo-differentiating mechanism operates in this *E/Z* photoisomerization.

Our present study on the *E/Z* photoisomerization of the enecarbamates by direct and triplet-sensitized irradiations discloses that the entropic control is not only displayed in the bimolecular reaction of singlet oxygen with the enecarbamates, but also an inherent feature of the *E/Z* photoisomerization. The solvent and temperature effects for the **1E** in this isomerization process complement the photooxidation results.^{10,11} The poor diastereoselectivities observed for the enecarbamates with the chiral triplet sensitizers may be attributed to the electron-exchange mechanism in such triplet sensitizations, in which only a long-distance collision complex is involved in excited states,¹⁸ as well as the fact that the chiral centers located in the *para*-position of the acetophenone-derived sensitizers are too far from the “reactive center” to enhance the diastereoselectivities of the products.

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