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Planar-to-Planar Chirality Transfer in the Excited State. Enantiodifferentiating Photoisomerization of Cyclooctenes Sensitized by Planar-Chiral Paracyclophane

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Ⓢ *Supporting Information*

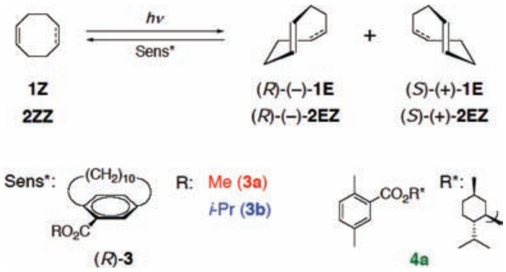
ABSTRACT: Photochemical *planar-to-planar* chirality transfer was effected by using (*R*)-[10]paracyclophane-12-carboxylates as a planar-chiral sensitizer and (*Z*)-cyclooctene and (*Z*,*Z*)-1,5-cyclooctadiene as prochiral substrates to give a planar-chiral (*E*)- and (*E*,*Z*)-isomer in up to 44% and 87% enantiomeric excess, respectively, the latter of which being the highest ever reported for a sensitized photochirogenic reaction.

Photochirogenesis, or chiral photochemistry, has been a target of intensive studies in recent years, and a variety of molecular and supramolecular approaches have hitherto been proposed and examined.[1] Of these strategies, asymmetric photosensitization, requiring a minimal amount of a chiral source, is the most straightforward, chirogen-efficient method to achieve photochirogenesis. Thus, a great deal of effort has been devoted to the study of the enantiodifferentiating photoisomerization of (*Z*)-cycloalkenes[2−5] sensitized by point-chiral (ar)alkyl benzene(poly)carboxylates to afford the planar-chiral (*E*)-isomers in good enantiomeric excesses (ee's) of up to 77%, despite the short-lived sensitizer-substrate interactions in the excited state. It was further revealed that the product's ee is a critical function of various entropy-related environmental variants, such as temperature,[2] pressure,[3] and solvation.[4]

Small- and large-sized cyclophanes attracted much attention primarily as deformed π-systems[6] and supramolecular hosts, respectively.[7] Planar-chiral cyclophanes were employed as chiral ligands, reagents, and catalysts[8−13] in the catalytic alkynylation of aldehydes with [2.2]paracyclophane-based ligands,[9] the cyclopropanation with bridged pyridinium ylides,[10] and the biomimetic reduction with [10]parapyridinophanes used as bridged NADHs.[11] Optically active cyclophanes have also been applied successfully to metal-mediated stereoselective synthesis[12] and dynamic asymmetric transformation.[13]

In this first study to explore the *planar-to-planar* chirality transfer in the excited state, we employed methyl and isopropyl (*R*)-[10](5,6)paracyclophane-12-carboxylates (**3a**, **b**)[13a] as planar-chiral sensitizers to effect the enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**) and (*Z*,*Z*)-1,5-cyclooctadiene (**2ZZ**) to the corresponding planar-chiral (*E*)-isomer (**1E**, **2EZ**) (Scheme 1). We further elucidated the mechanisms of energy and chirality transfer in the excited state and optimized the product's ee by manipulating environmental variants.

Scheme 1. *Planar-to-Planar* Chirality Transfer upon *Z*-to-*E* Photoisomerization of 1Z and 2ZZ Sensitized by Planar-Chiral Paracyclophanes 3a,b and Point-Chiral Reference Sensitizer 4a



A solution containing **1Z** or **2ZZ** (5 mM) and (*R*)-**3** (1 mM) was irradiated at temperatures ranging from +25 to −140 °C. The irradiated solutions were analyzed by GC first on a CBP20 column to give the *E*/*Z* ratio, and then the (*E*)-isomer, **1E** or **2EZ**, selectively extracted by aqueous silver nitrate, was analyzed on a Supelco β-DEX 225 column to give the ee value.[2−5]

The photoisomerization proceeded smoothly to give the photostationary *E*/*Z* ratios of ca. 0.01 upon prolonged irradiations (Table 1), which is much smaller than those (0.1−0.4) reported for conventional benzene(poly)carboxylate sensitizers.[2−4] Notably, (−)-menthyl 2,5-dimethylbenzoate (**4a**), employed as an electronically equivalent noncyclophane sensitizer, also gave a low *E*/*Z* ratio of 0.03. It is likely therefore that the steric bulk of the 2,5-substituents hinders the sensitization of **1Z** rather than **1E** (which is more constrained and easier to be excited)[2b] to give the low *E*/*Z* ratios for both **3** and **4**, the former of which may have additional hindrance caused by the conformationally locked benzylic methylenes. Planar-chiral **3a** and **3b**, rather than point-chiral **4a**, showed better photochirogenic performance to give (*R*)-**1E** in 10% and 13% ee, respectively, upon irradiation at room temperature, while **4a**

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Table 1. Enantiodifferentiating Photoisomerization of 1Z and 2ZZ Sensitized by Paracyclophane 3 or Reference Sensitizer 4[a]

substrate	sensitizer	solvent[b]	temp/°C	*E*/*Z*	% ee
1Z	**3a**	P	25	0.007	−9.7
			−40	0.002	−24.5
			−110	[c]	−41.7
	3b	M	25	0.010	−13.2
			−40	0.010	−31.6
			−110	0.005	−42.9
	4a	P	25	0.028	−3.1
			−40	0.030	−6.9
			−110	0.007	−13.0
2ZZ	**3a**	M	25	[c]	−43.2
			−40	[c]	−56.1
			−110	0.007	−75.3
		IM	−140	0.019	−87.4
	3b	M	25	0.002	−36.9
			−40	0.008	−56.9
			−110	0.012	−76.5
		IM	−140	0.010	−84.8

[a] [**1Z**] or [**2ZZ**] = 5 mM; [sensitizer] = 1 mM; irradiated for 30 min (only for **4a**) or 60 min under Ar with a 500-W high-pressure Hg lamp fitted with a UV-27 filter. [b] Solvent: P, pentane; M, methylcyclohexane (MCH); IM, a 3:1 (v/v) mixture of isopentane and methylcyclohexane. No precipitation observed even at −140 °C. [c] Value not determined.

afforded 3% ee under the same conditions. The ee of **1E** gradually increased by decreasing the irradiation temperature to give 42% ee for **3a** and 43% ee for **3b** at −110 °C, whereas **4a** afforded **1E** in 13% ee. As shown in Figure 1, all of the ee's obtained fell on a single straight line upon Eyring analysis,[2−5] indicating operation of a sole enantiodifferentiation mechanism over the entire temperature range employed. It is noteworthy that the temperature dependence behaviors for methyl and isopropyl esters are very similar (Figure 1), indicating that the peripheral modification is not an effective tool for manipulating the photochirogenic process.

Possessing an additional double bond at the transannular position, 1,5-cyclooctadiene **2ZZ** was a better substrate, affording (*R*)-**2EZ** in 43% and 37% ee even at 25 °C upon sensitization with **3a** and **3b**, respectively. Remarkably, the ee was steadily enhanced up to 87% (for **3a**) and 85% (for **3b**) by reducing the temperature down to −140 °C to give nice linear Eyring plots (Figure 1); these ee's are the highest ever reported for an enantiodifferentiating photosensitized reaction.

The differential enthalpy ($\Delta\Delta H^{\ddagger}$) and entropy ($\Delta\Delta S^{\ddagger}$) of activation were calculated from the slope and intercept of the plot, according to the established procedures.[2−4] The activation parameters shown in Table 2 reveal that the consistently higher ee's of **1E** obtained with **3**, rather than **4**, are attributed to the almost tripled $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ for the cyclophane sensitizers, while the further enhanced ee's for **2EZ** are mostly enthalpic in origin, probably as a result of the stronger interaction of the excited sensitizer with the more donating substrate **2ZZ**, rather than **1Z**.

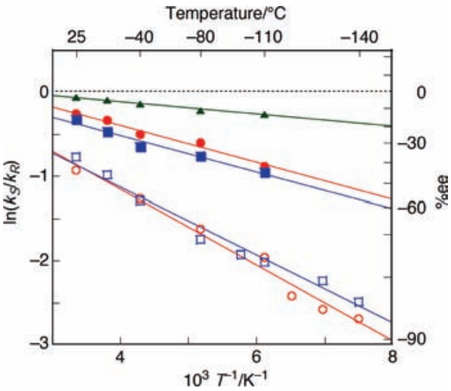

Figure 1. Eyring plots for the ee of **1E** (closed symbols) and **2EZ** (open symbols) produced in the enantiodifferentiating photoisomerization of **1Z** and **2ZZ** sensitized by **3a** (circles), **3b** (squares), and **4a** (triangle).

Table 2. Differential Enthalpy ($\Delta\Delta H^{\ddagger}$) and Entropy ($\Delta\Delta S^{\ddagger}$) of Activation for Enantiodifferentiating Photoisomerization of 1Z and 2ZZ Sensitized by 3 or 4

substrate	sensitizer	solvent[a]	$\Delta\Delta H^{\ddagger}$	$\Delta\Delta S^{\ddagger}$
1Z	**3a**	P	0.44	0.98
	3b	M	0.44	0.95
	4a	P	0.15	0.35
2ZZ	**3a**	M or IM	0.91	1.4
	3b	M or IM	0.78	0.89

[a] Solvent: P, pentane; M, methylcyclohexane; IM, a 3:1 (v/v) mixture of isopentane and methylcyclohexane (used only for irradiation at −140 °C).

To better understand the excitation process, we examined the fluorescence quenching behavior of **3a**, **3b**, and **4b** (R = Me) upon addition of **1Z**. As shown in Figure 2a, the fluorescence of **3a** at 334 nm was slowly reduced in intensity by adding **1Z** (0−0.8 M) to give a weak emission at 398 nm with an isoemissive point (Figure 2a, inset), suggesting the intervention of an exciplex in the photosensitization of **1Z** with paracyclophane. Similar behavior was observed upon fluorescence quenching of **3b** and **4b** by **1Z**. Quantitative analyses of the quenching data gave the Stern−Volmer constants ($k_q\tau$) listed in Table 3. The fluorescence lifetimes (τ) determined independently by using the single-photon-counting technique allow us to calculate the quenching rate constants (k_q) for **1Z** as (1.5−2.1) × 10^8 M^{-1} s^{-1} (Table 3), which are 1 order of magnitude smaller than those reported for less-hindered sensitizers, i.e. (1−3) × 10^9 M^{-1} s^{-1}.[2b] The appreciably larger k_q of 3.3 × 10^8 M^{-1} s^{-1} for **4b** may reflect the dual accessible noncyclophane structure. These small k_q values for both cyclophanebenzoates **3** and disubstituted benzoate **4** indicate that the ortho/meta substitution causes steric hindrance to decelerate the quenching by **1Z**.

Cyclooctadiene **2ZZ** also slowly quenched the fluorescence of **3a** and **3b** at (0.7−0.9) × 10^8 M^{-1} s^{-1} (Table 3), which are slightly smaller than those for **1Z**. Interestingly, the exciplex emission appeared at appreciably longer wavelengths of 417−418 nm (Figure 2b, inset). Probably due to the higher electron-donating ability, **2ZZ** forms a better stabilized (by 3.3 kcal mol^{-1}) and more intimately interacting exciplex than **1Z** to afford **2EZ** in higher ee's of up to 87%.

In this study, we have expanded the scope of photochirogenesis to the *planar-to-planar* chirality transfer in the excited state by employing planar-chiral paracyclophane sensitizers and prochiral cyclooctene substrates to produce planar-chiral (*E*)-isomers in the highest ee's ever reported for a sensitized photochirogenic

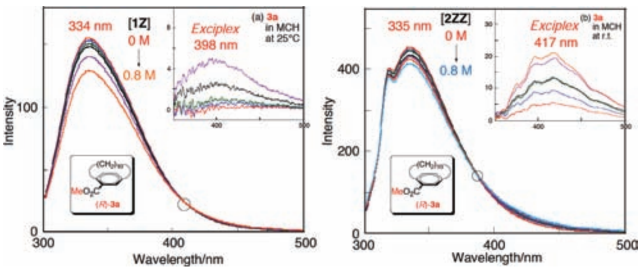

Figure 2. Fluorescence spectra of (a) **3a** (0.038 mM) in the presence of 0−0.8 M **1Z** (λ_{ex} 270 nm) and (b) **3a** (0.027 mM) (λ_{ex} 290 nm) in the presence of 0−0.8 M **2ZZ** in MCH at room temperature. Inset: exciplex emission obtained by spectral subtraction.

Table 3. Fluorescence Quenching of 3a, 3b, and 4b by 1Z or 2ZZ

sensitizer	λ_{max}/nm	τ/ns	quencher	$k_q\tau$/M^{-1}	$k_q/10^8$ M^{-1} s^{-1}	$\lambda_{exciplex}$/nm
3a	334	1.3[a]	**1Z**[b]	0.27	2.1	398
			2ZZ[c]	0.12	0.9	417
3b	333	1.1[d]	**1Z**[e]	0.17	1.5	401
			2ZZ[f]	0.08	0.7	418
4b	313	0.6[g]	**1Z**[h]	0.20	3.3	—

[a] [**3a**] = 0.27 mM in MCH at 25 °C. [b] [**3a**] = 0.038 mM in MCH at 25 °C. [c] [**3a**] = 0.027 mM in MCH at room temperature. [d] [**3b**] = 0.25 mM in MCH at 25 °C. [e] [**3b**] = 0.025 mM in MCH at 25 °C. [f] [**3b**] = 0.025 mM in MCH at room temperature. [g] [**4b**] = 0.61 mM in MCH at room temperature. [h] [**4b**] = 0.061 mM in MCH at room temperature.

reaction. The major difference from the conventional point-chiral photosensitization systems is the selective shielding of one of the enantiotopic faces of chiral cyclophanes **3** by the decamethylene bridge, which both enthalpically and entropically renders the approach and the subsequent geometrical isomerization of substrate **1Z** or **2ZZ** more enantioface-selective to give high ee's. The inherently low *E*/*Z* ratios obtained upon paracyclophane sensitization may be readily overcome by continuously circulating the photolyzed solution through a column loaded with $AgNO_3/SiO_2$ to selectively extract the (*E*)-isomer from the *E*/*Z* mixture during the period of irradiation.[14] Chiral cyclophane sensitizers are more suitable for the photoisomerization of smaller-sized cycloalkenes that afford highly strained (*E*)-isomers stabilized only at low temperatures but are expected to experience less steric hindrance upon exciplex formation giving higher *E*/*Z* ratios. It is also interesting to note that strained (*E*)-cyclooctenes **1E** and **2EZ** are potent inhibitors of the ripening action of ethylene as a plant hormone and (*R*)-**1E** is more effective than the antipode,[15] rendering the present method attractive in relevant research. The concept of *planar-to-planar* chirality transfer in the excited state has established a new scope of photochirogenesis and can be a useful and powerful tool in a more general context of (supra)molecular photochirogenesis.

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Experimental details and a comprehensive list of the original data used in Figure 1. This material is available free of charge via the Internet at http://pubs.acs.org.

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