

Diastereodifferentiating *Z-E* Photoisomerization of 3-Benzoyloxycyclooctene: Diastereoselectivity Switching Controlled by Substrate Concentration through Competitive Intra- vs Intermolecular Photosensitization Processes

Toru Inoue, Keisuke Matsuyama, and Yoshihisa Inoue*

*Inoue Photochirogenesis Project, ERATO, JST
4-6-3 Kamishinden, Toyonaka 565-0085, Japan*

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The mechanism and application of asymmetric photochemical reactions sensitized by optically active compounds have recently attracted the interest of organic (photo)chemists as a novel methodology for transferring and multiplying molecular chirality through the electronically excited state.^{1,2} In particular, the enantiodifferentiating *Z-E* photoisomerization of unsubstituted (*Z*)-cyclooctene sensitized by optically active polyalkyl benzene-polycarboxylates is one of the most successful and intriguing examples.^{2–6} When this enantiodifferentiating photoisomerization is carried out at varying temperatures and pressures, the product chirality switches at a specific temperature or pressure in several cases.^{3–6} This unusual switching behavior allows us to selectively obtain both enantiomers by changing the reaction temperature or pressure upon photosensitization with a single enantiomer.

In contrast, the photosensitized isomerization of substituted cyclooctenes has been scarcely reported, except for 1-substituted cyclooctenes.^{7–10} Introduction of a substituent at other positions renders the substituted (*Z*)-cyclooctene chiral, and the photosensitization of such a substrate leads to a diastereodifferentiating isomerization. In the present study, we introduced a benzoate moiety at the 3-position of cyclooctene, anticipating a highly efficient intramolecular diastereodifferentiating photosensitization. However, the direct photolysis of (*Z*)-3-benzoyloxycyclooctene (**1Z**) gave unexpected results, showing that the intramolecular photosensitization was not efficient in this case and, interestingly, that the major diastereomer obtained is switched by changing the substrate concentration. Although diastereoselectivity of the product is known to be altered by employing different additives^{11,12} or protective groups,¹³ to the best of our knowledge, this is the

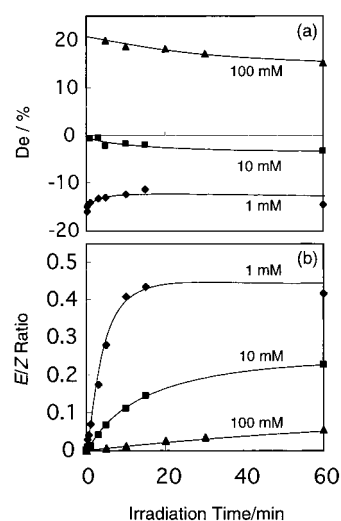
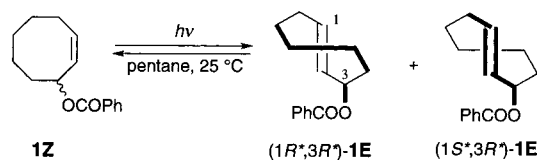


Figure 1. (a) Diastereomeric excess and (b) *E/Z* ratio in the photoisomerization of **1Z** at different concentrations in pentane at 25 °C.

Scheme 1



first example in which such a switch is caused by a change in the substrate concentration. We now wish to report the mechanistic details of this unprecedented concentration-dependent diastereodifferentiating photoisomerization of **1Z** and further to propose a potentially general method to control the diastereoselectivity of the product through competing intra- and intermolecular photosensitization processes.

The irradiation of **1Z** at different concentrations (1, 10, and 100 mM) was conducted at 254 nm in pentane at 25 °C with frequent monitoring of the *E/Z* ratio and the diastereomeric excess (de) of the (*E*)-isomer (**1E**) by capillary GC, using a Hewlett Packard HP-5 column. In all runs, the major course of photoreaction was the geometrical isomerization, leading to a diastereomeric mixture of **1E** (Scheme 1), and no byproducts were detected in the GC analysis.

As shown in Figure 1b, the *E/Z* ratio gradually increases with increasing irradiation time, and the rate of increase is strongly dependent on the substrate concentration employed. Irradiation times of up to 60 min lead to distinctly different photostationary states (pss) for the *E/Z* mixture, at least for the dilute solutions (1 and 10 mM), while the *E/Z* ratio of the 100 mM solution continues to increase. This contrasting behavior of the *E/Z* ratio at the pss cannot be rationalized by the conventional singlet sensitization mechanism that involves only one sensitizing species.^{3–6}

A more dramatic effect of a change in the concentration of the substrate was observed in the de of the product, as illustrated in Figure 1a, where positive and negative de values represent the predominant formation of (1*R**,3*R**)- and (1*S**,3*R**)-**1E**,¹⁴ respectively. Unexpectedly, the initial de of -17%,¹⁵ which was obtained in the photolysis of a 1 mM solution of **1Z**, was observed to be almost zero at 10 mM and +21% at 100 mM.¹⁶ Thus, the

(14) The asterisk represents the relative configuration of the two stereogenic centers.

(15) The initial de value was estimated by extrapolating the de values observed at shorter irradiation periods to time zero.

* Contact address: Prof. Yoshihisa Inoue, Department of Molecular Chemistry, Faculty of Engineering, Osaka University, 2-1 Yamada-oka, Suita 565-0871, Japan. Phone: +81-6-6879-7920. Fax: +81-6-6879-7923. E-mail: inoue@chem.eng.osaka-u.ac.jp.

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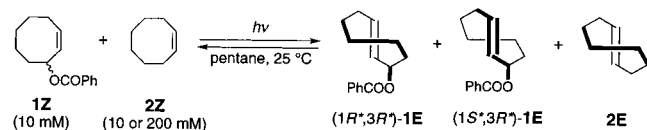
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Scheme 2



major diastereomer obtained was switched from **(1R*,3R*)-1E** to **(1S*,3R*)-1E** merely by increasing the substrate concentration from 1 to 100 mM. This seems to be specific to the present system, since we have never observed such a drastic concentration effect in the enantiomeric excess of the product in our previous studies concerning the enantiodifferentiating photosensitization of unsubstituted cyclooctene.^{3–6}

Taking into account the structural features of **1**, which carries the sensitizer (benzoate) and substrate (cyclooctene) moieties within the same molecule, the apparently unusual diastereoselectivity switching through a change in substrate concentration can be reasonably accounted for in terms of competing intra- and intermolecular photosensitizations of the cyclooctene moiety. To obtain further evidence to support this proposed competitive sensitization mechanism, we performed the photolysis of **1Z** in the presence of added cyclooctene (**2Z**) (Scheme 2).

A pentane solution of **1Z** (10 mM), containing **2Z** (10 or 200 mM), was irradiated under the conditions comparable to those used above, and the amounts of **1E** and **2E** and the de of **1E** were monitored by GC at several points during the irradiation. As can be seen in Figure 2, both **1E** and **2E** were efficiently produced during the initial stages of irradiation, indicating clearly that the intramolecular energy transfer from the excited benzoate moiety to the cyclooctene moiety of **1Z** is not the only process in operation and the intermolecular sensitization of added **2Z** can also occur. Almost equal amounts of **1E** and **2E** (~1.5 mM) were obtained at the pss in the presence of 10 mM **2Z** (Figure 2a), while a large amount (>20 mM) of **2E** was produced at the expense of **1E**, whose concentration was as low as 0.6 mM even at the pss, in the presence of 200 mM **2Z**.

Furthermore, the initial de was also changed significantly by the addition of **2Z**. In sharp contrast to the almost zero de obtained with a 10 mM solution of **1Z**, the initial de of **1E** was increased to -5% in the presence of **2Z** (Figure 2a, bottom). The addition of 200 mM **2Z** further enhanced the initial de to -17%, which is in good agreement with the value observed for the 1 mM solution of **1Z**, where intermolecular sensitization was not expected to occur effectively. This coincidence suggests that the intermolecular sensitization process is practically suppressed by the addition of 200 mM cyclooctene. However, the use of a very high concentration of **1Z** up to 100 mM should minimize the contribution of the intramolecular sensitization, and the initial de of +20% obtained above may be attributable therefore to intermolecular sensitization.

As illustrated in Scheme 3, the unprecedented diastereoselectivity switching phenomenon observed in the photoisomerization of 3-benzoyloxycyclooctene (**1**) described above has been shown to originate from competing intra- and intermolecular photosensitization processes that give rise to opposite diastereomers. Probably, the diastereoface of the olefin moiety, which is preferred

(16) It is also noted that the de of the product deviated slightly from the initial value in each run, approaching the photostationary state upon prolonged irradiation. Judging from the similarity in the time profiles of the de and E/Z ratios, this deviation may be attributable to the diastereodifferentiating $E-Z$ photoisomerization, in which the preferential diastereomer of **1E** has a tendency to undergo the reverse process slightly more effectively.

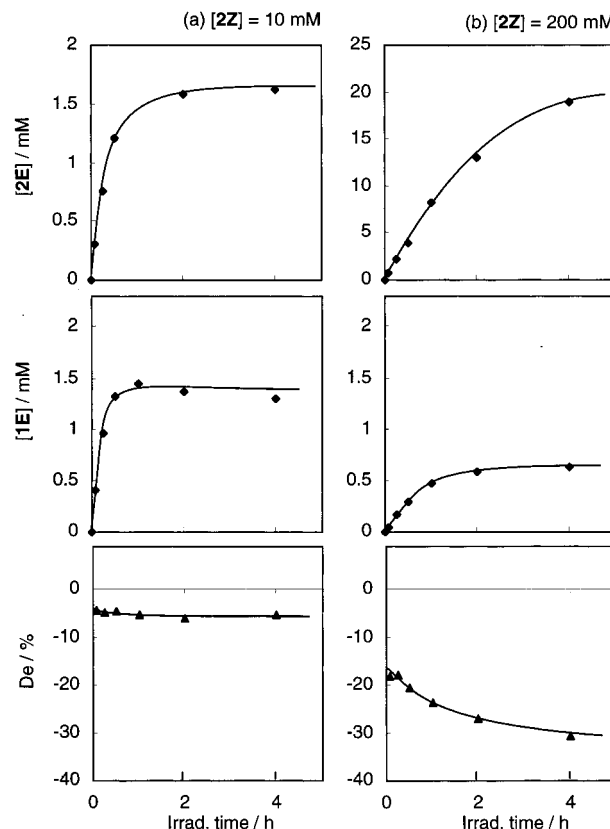
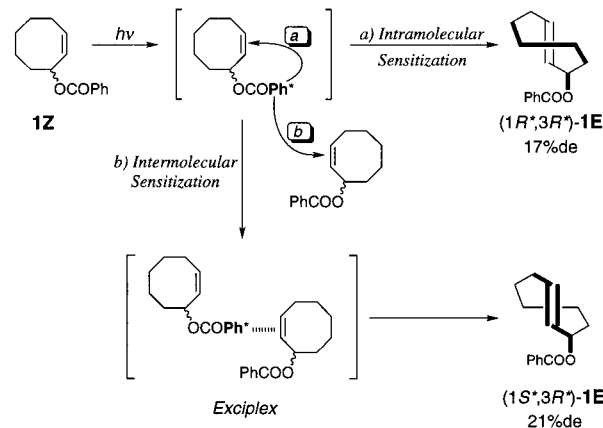


Figure 2. Effect of adding (Z)-cyclooctene **2Z** (a, 10 mM; b, 200 mM) on the diastereodifferentiating photoisomerization of **1Z** (10 mM) in pentane at 25 °C.

Scheme 3



upon intramolecular sensitization, is conversely hindered by the benzoate substituent upon intermolecular sensitization. It should be emphasized that this methodology is not restricted to the present system, and the basic concept should be applied to a wide variety of photosensitized diastereodifferentiating reactions of chiral substrates.

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