Efficient Diastereodifferentiating *E-Z* Photoisomerization of Cyclooctene Tethered to Intramolecular Sensitizer through Optically Active Pentane-2,4-diyl Unit

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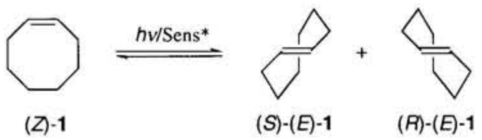
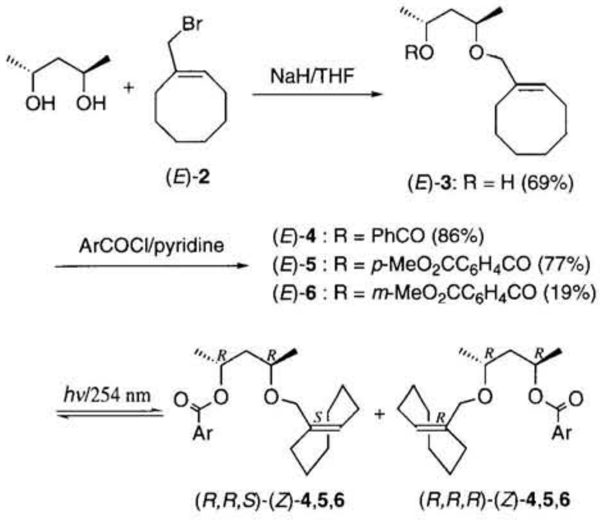
Photolysis of a tethered cyclooctene (*E*)-**4**, in which the sensitizer benzoate is connected to the olefin moiety through a chiral 2,4-pentanediol tether, afforded the *Z/E* ratios up to 0.8 and the diastereomeric excess of 33% at –65 ℃, while the terephthalate analogue (*E*)-**5** gave higher de of 44% at the same temperature.

After several attempts to accomplish chirality multiplication in the excited state through asymmetric photosensitization with a catalytic amount of chiral sensitizer,[1] it has been shown that the enantiodifferentiating photoisomerizations of cyclooctene (**1**) with optically active benzenepolycarboxylates give satisfactory enantiomeric excesses (ee) of 53-64% at -89 ℃.[2] However, the efficiencies of *Z*-to-*E* conversion are fairly low (<10%) for these sensitizers.



Mechanistically, the intervention of an exciplex intermediate between the chiral sensitizer singlet and the substrate has been proved by the efficient quenching of sensitizer fluorescence accompanied by intense exciplex emission.[2b] The geometry of singlet exciplex involved plays a crucial role in determining the enantiomeric fate of cyclooctene. The importance of exciplex geometry has also been demonstrated in the enantiodifferentiating photoisomerization of (*Z*)-**1** included and sensitized by β-cyclodextrin 6-*O*-monobenzoate, which leads to high *E/Z* ratios up to 0.8 but relatively low ee of 6% at the photostationary state (pss).[3]



Scheme 1.

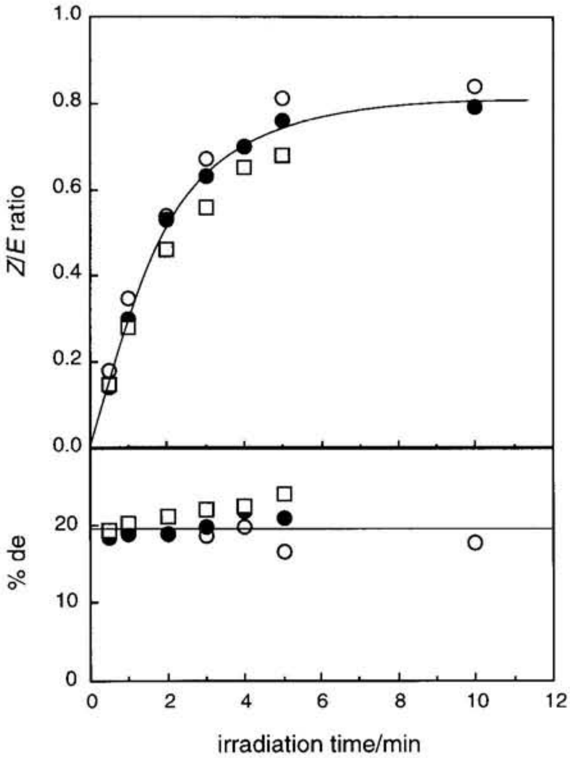


Figure 1. *Z/E* ratio and diastereomeric excess (% de) as a function of irradiation time in photolysis of (*E*)-**4** in pentane (○), acetonitrile (●) and methanol (□) at 25 °C.

A straightforward and effective method to control the exciplex geometry is to connect the cyclooctene moiety to the sensitizer unit with a chiral tether, which facilitates the intramolecular sensitization, producing a stereochemically well-defined exciplex. In this communication, we wish to demonstrate that this simple strategy works quite well and leads not only to high conversion but also to good diastereomeric excess (de).

The tethered cyclooctene (*E*)-**4** was prepared by the reaction of 1-bromomethylcyclooctene (*E*)-**2** with monosodium salt of (2*R*,4*R*)-2,4-pentanediol giving (*E*)-**3** in 69% yield and the subsequent esterification with benzoyl chloride in 86% yield. The tere- and isophthalate analogues (**5** and **6**) were similarly synthesized in 77% and 19% yields, respectively.

A solution of (*E*)-**4** (0.5 mM) was irradiated under argon in pentane, acetonitrile or methanol at 25 ℃ with a low-pressure mercury lamp (30 W). The reaction was monitored by HPLC on an ODS column with a methanol-water (85/15) eluent; the geometrical and diastereomeric isomers of (*E*)- and/or (*Z*)-**4** were completely separated under these conditions. In Figure 1, the *Z/E* ratio and de value of the product in the irradiated solution were plotted as a function of the irradiation time. Irrespective of the solvent employed, the *Z/E* ratio and the de of (*Z*)-**4** showed quite similar time profile. Thus, the *Z/E* ratio gradually increased with increasing irradiation time to give a plateau of 0.8 at pss, although some decomposition products were detected upon extended irradiations up to 10 min. On the other hand, the de was kept constant at 19 ± 2% from the very initial stages to the pss in all solvents employed. The *Z/E* ratios and de values independent of the solvent polarity clearly rule out the intervention of a radical ionic intermediate even in the highly polar and/or protic solvents and confirm the exciplex mechanism as was the case with the photosensitization of the untethered **1**. The constant de values throughout the irradiation period indicate that the forward *E*-to-*Z* isomerization is the only diastereodifferentiating process, while the back reaction is not diastereoselective at all. Hence, the diastereoface selectivity in the (*E*)-isomer is fairly high but practically no diastereomer selection is achieved with the (*Z*)-isomer, probably due to the very fast intramolecular quenching accelerated by its high strain.

Since the product's ee has been shown to depend significantly on temperature in the asymmetric photosensitization of **1**,[2] the photolysis of (*E*)-**4** was carried out at some different temperatures ranging from +85 to –65 °C.[4] In this temperature range, the *Z/E* ratio at pss was constant of 0.8, but the de of (*Z*)-**4** was increased with decreasing temperature and reached to 33% at –65 °C. The natural logarithm of the relative rate constant k_{R*}/k_{S*} for the production of (*R*)- and (*S*)-(*Z*)-**4**, where $k_{R*}/k_{S*} = (100 + \%de)/(100 - \%de)$, was plotted against the reciprocal reaction temperature to give a straight line shown in Figure 2.

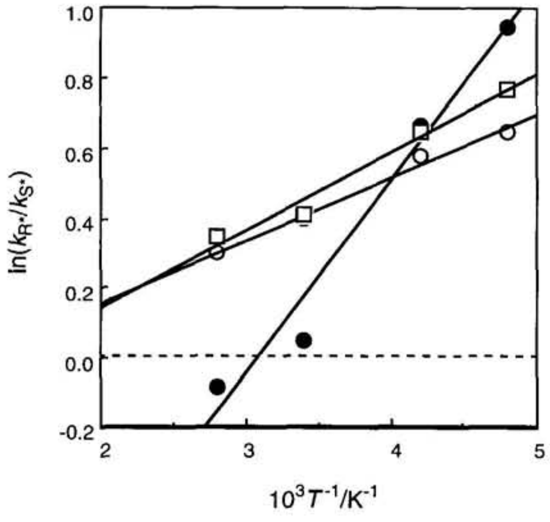


Figure 2. Plot of ln(*k*R*/*k*S*) as a function of reciprocal temperature for the photolyses of (*E*)-**4** (○), (*E*)-**5** (●) and (*E*)-**6** (□).

Similar experiments with tere- and isophthalate derivatives (*E*)-**5** and (*E*)-**6** also gave good straight lines with larger slopes, and the highest de of 44% was obtained for (*Z*)-**5** at –65 °C,[5] although the *Z/E* ratios are 0.06 and 0.15 for **5** and **6**, respectively. It should be noted that the intermolecular sensitizations of **1** with a variety of chiral benzoates, including (*R,R*)-2,4-pentanediol dibenzoate,[6] never exceed 7% ee and the ee is not greatly improved by lowering the reaction temperature.[2] However, a more interesting feature of the present intramolecular sensitization is the inversion of the product's de by changing temperature, as can be seen from the plot for terephthalate **5** shown in Figure 2.

From the slope and intercept, we can calculate the differential enthalpy ($\Delta\Delta H^\ddagger$) and entropy ($\Delta\Delta S^\ddagger$) for the diastereodifferentiating isomerization from excited (*E*)-isomers, as listed in Table 1. Although these $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ are not specifically large, it is emphasized that the diastereomeric inversion is observed indeed in the temperature range employed or expected by extrapolation to higher temperatures in all cases examined.

Table 1. Differential enthalpy ($\Delta\Delta H^\ddagger$) and entropy ($\Delta\Delta S^\ddagger$) for diastereodifferentiating photoisomerization of (*E*)-**4**, (*E*)-**5** and (*E*)-**6**

Substrate	$\Delta\Delta H^\ddagger$ /kcal mol^{-1}	$\Delta\Delta S^\ddagger$ /cal mol^{-1} K^{-1}
Benzoate (*E*)-**4**	0.095	0.11
Terephthalate (*E*)-**5**	0.28	0.85
Isophthalate (*E*)-**6**	0.11	0.12

In conclusion, we have demonstrated that the efficiencies of both photosensitization and stereodifferentiation can be enhanced considerably by connecting the substrate and sensitizer moieties through a chiral tether to give the high *Z/E* ratio up to 0.8 and good de of 44%, even if the intermolecular asymmetric photosensitizations with, for example, chiral benzoates fail to give high *Z/E* ratio and/or ee.

References and Notes

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4 The photolysis at 85 °C was carried out in octane.
5 Stereochemistries of the major diastereomers of (*Z*)-**4**, (*Z*)-**5** and (*Z*)-**6** were unknown, but were determined to be same by hydrolysis and re-esterification experiments.
6 Unpublished result: the photosensitization of **1** with (*R,R*)-2,4-pentanediol dibenzoate gave 0.8% ee in pentane at 25 °C.