Singlet- *versus* triplet-sensitized enantiodifferentiating photoisomerization of cyclooctene: remarkable effects of spin multiplicity upon optical yield

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Photosensitized enantiodifferentiating geometrical isomerizations of (*Z*)-cyclooctene (1Z), producing the chiral (*E*)-isomer (1E), were performed in triplet, as well as singlet, states in order to clarify the effects of spin multiplicity upon the product's enantiomeric excess (ee) or optical purity (op). In sharp contrast to the moderate and highly temperature-dependent ee/op values, up to 10%, of 1E produced in the singlet sensitization with (−)-menthyl benzene(di)carboxylates, much lower and temperature-independent ee/op values around 1%, were obtained by using the structurally related chiral aromatic ethers as formal 'triplet' sensitizers. The ee/op values obtained in the 'triplet' sensitizations decreased significantly with decreasing substrate concentration, approaching nearly zero at extremely low 1Z concentrations, while the photostationary *E*/*Z* ratio, $(E/Z)_{pss}$, increased dramatically from 0.013 to 0.22 in the same range of concentration. Both concentration dependences of ee/op and $(E/Z)_{pss}$ were shown to originate from the concurrent operation of the singlet sensitization at higher concentrations as evidenced by fluorescence quenching experiments. The authentic triplet sensitization was demonstrated to be totally ineffective as a method of asymmetric induction at least for the present system, probably owing to the lack of formation of a structurally well defined triplet exciplex.

Enantiodifferentiating photosensitization, requiring only a catalytic amount of a chiral source, is one of the most mechanistically and synthetically intriguing methodologies with which to induce chirality into prochiral substrates through the electronically excited state.[1,2] Historically, Hammond and Cole demonstrated for the first time that (+)-(*R*)-[1-(*N*-acetylamino)ethyl]naphthalene can be used as a singlet sensitizer to effect enantiodifferentiating *cis–trans* photoisomerization of 1,2-diphenylcyclopropane, affording an optical purity (op) of 6.7%,[3,4] although our own attempts to reproduce this relatively high op value under comparable conditions were not very successful, but gave the *trans*-isomer with 3–4% op.[5] Employing the same substrate, Ouannès *et al.*[6] and Kagan *et al.*[7] showed that triplet sensitizations with optically active 3-methylindan-1-one and 4-methyl-1-tetralone can also give the *trans*-isomer with 1–3% op. More recently,[5] we have obtained somewhat higher op values, up to 10%, with this substrate by using optically active (poly)alkyl benzene- and naphthalene(poly)carboxylates as singlet sensitizers.

We have reported also that the enantiodifferentiating photoisomerizations of cyclooctene, employing a variety of optically active benzene(poly)carboxylates as singlet sensitizers, give moderate to good values of op up to 64%.[8,9] Judging from the efficient fluorescence quenching and the concomitant exciplex emission observed, it is obvious that the sensitization with these benzene(poly)carboxylates takes place through the formation of a singlet exciplex in which the steric and electronic interactions between the excited chiral sensitizer and the substrate are intimate and sufficiently long-lived to attain such high op values. A more interesting feature of this enantiodifferentiating photosensitization is the dramatic switching of product chirality by changing irradiation temperature, which is peculiar to the singlet sensitizations with sterically congested *o*-benzenepolycarboxylates. This unprecedented phenomenon has been reasonably accounted for in terms of the significant contribution of the entropy term, which probably originates from the dynamic structural changes incorporating the sensitizer's conformational motions synchronized with the enantiodifferentiating rotation of cyclooctene molecule within the exciplex intermediate.[8,9]

By contrast, the photosensitized enantiodifferentiation in the triplet state, although not sufficiently explored with 1,2-diphenylcyclopropane[5] and cyclooctene,[8] does not appear to be particularly advantageous, presumably because triplet sensitization is believed to proceed through the electron exchange mechanism, without forming a long-lived, structurally well defined triplet exciplex, but involving a short-lived collision complex.[10] However, the enormous temperature dependence of op, found in the singlet photosensitization of cyclooctene particularly with *o*-benzenedicarboxylates, prompted us to explore more closely the effect of spin multiplicity upon enantiodifferentiating photoisomerization of cyclooctene sensitized by triplet, as well as singlet, sensitizers.

In the present work, we synthesized some structurally related aromatic esters and ethers carrying the same chiral moiety(ies) at the pertinent position(s), and employed these compounds as comparative singlet and triplet sensitizers in the enantiodifferentiating photoisomerization of cyclooctene at varying temperatures in order to elucidate explicitly the effect of spin multiplicity upon the enantiodifferentiation efficiency in the excited state.

Experimental

General

IR spectra were recorded on a JASCO A-202 instrument. ^1H NMR spectra were obtained on a JEOL GX-400 spectrometer in [^{2}H]chloroform. Mass spectra were recorded on a JEOL JMS-DX-303 instrument. Optical rotations were measured in a thermostatted conventional 10 cm cell, using a Perkin-Elmer polarimeter model 243B. Fluorescence spectra were obtained in aerated pentane solutions at room temperature on a JASCO

FP-777 instrument. The fluorescence lifetime was determined in an aerated pentane solution at room temperature by the single photon counting technique using a Horiba NAES-550 instrument; the excitation of the sample was conducted at 270 nm and the emission was detected with a Toshiba UV-29 filter.

Gas chromatographic (GC) analyses of the photolysed mixtures were performed on a 1 m packed column of 40%-bis(2-cyanoethyl)ether at 65 °C with a Shimadzu GC-6A instrument. Capillary GC analyses of chiral photoproduct **1E** were carried out on a Supelco 25 m β-DEX 120 capillary column at 60 °C, using a Shimadzu GC-14B instrument. In all GC analyses, the temperatures of injection and detector ports were kept at 120 and 150 °C, respectively, in order to prevent any thermal isomerization or decomposition of highly strained **1E**. All GC peaks were integrated with Shimadzu C-R6A integrators connected to the GC instruments. The GC response for each enantiomer peak was calibrated by using several authentic samples of optically active **1E** of given op values determined by the polarimeter; an excellent linear relationship of unit slope was obtained between the ee and op values under the conditions employed.

It may be useful to note that the amount of **1E** in a sample solution injected into the capillary column should be kept in a certain range in order to attain good peak separation and excellent ee reproducibility. In our case using the above combination of a Supelco capillary column and Shimadzu instruments, the best separation and reproducibility were attained when the integrated area of **1E** was less than 10^5; the error in ee < ±0.3%.

Materials

(−)-Menthyl benzoate (**2a**), terephthalate (**2b**) and phthalate (**2c**) were synthesized from the corresponding acid chlorides and (−)-menthol according to the procedure reported previously.[8] Benzyl and *o*- and *p*-xylylene (−)-menthyl ethers (**3a–c**) were prepared similarly from the corresponding chlorides and (−)-menthol.[8]

(−)-1,2-Bis(menthyloxymethyl)benzene (3c). $[\alpha]_D^{20}$ −127.8° (*c* 0.97, benzene); *m/z* 415 (M − 1); ν(neat)/cm^{-1} 2925, 2870, 1460, 1375, 1350, 1190, 1125, 1110, 1090, 1070, 1055 and 755; δ_H(CDCl$_3$) 0.70 (d, *J* = 6.8 Hz, 6 H), 0.88 (d, *J* = 6.8 Hz, 6 H), 0.95 (d, *J* = 6.8 Hz, 6 H), 0.84–0.99 (m, 5 H), 1.25–1.31 (m, 3 H), 1.34–1.43 (m, 2 H), 1.60–1.64 (m, 4 H), 2.22–2.29 (m, 4 H), 3.18 (dt, *J* = 4.2, 10.6 Hz, 2 H), 4.42 (d, *J* = 11.7 Hz, 2 H), 4.77 (d, *J* = 11.7 Hz, 2 H), 7.25–7.29 (m, 2 H) and 7.39–7.41 (m, 2 H).

Photolysis

All irradiations were carried out in temperature-controlled water (25 °C) or methanol (−25 to −78 °C) bath. A solution (3 or 300 cm^3) containing **1Z** (0.63–400 mmol dm^{-3}), optically active sensitizer (1–5 mmol dm^{-3}) and cyclooctane or cycloheptane added as an internal standard was irradiated at 254 nm under an argon atmosphere in a quartz tube (1 cm i.d.) for analytical scale irradiation (3 cm^3) or in an annular vessel for preparative scale irradiation (300 cm^3) with a 30 W mercury resonance lamp (Eikosha) fitted with a Vycor sleeve.

Product isolation

In a typical preparative scale run, photoproduct **1E** was selectively extracted at < 5 °C from the irradiated pentane solution with three 30 cm^3 portions of 20% aqueous silver nitrate solution.[11] The combined aqueous extracts were washed with two 25 cm^3 portions of pentane and then added dropwise with stirring into a concentrated aqueous ammonia solution at 0 °C. The resulting mixture was extracted with three 25 cm^3 portions of pentane, and the combined pentane extracts were dried over magnesium sulfate and concentrated at a reduced pressure (50–100 Torr). The residue obtained was subjected to bulb-to-bulb distillation *in vacuo* to give pure **1E**; the op value was then determined using a polarimeter.

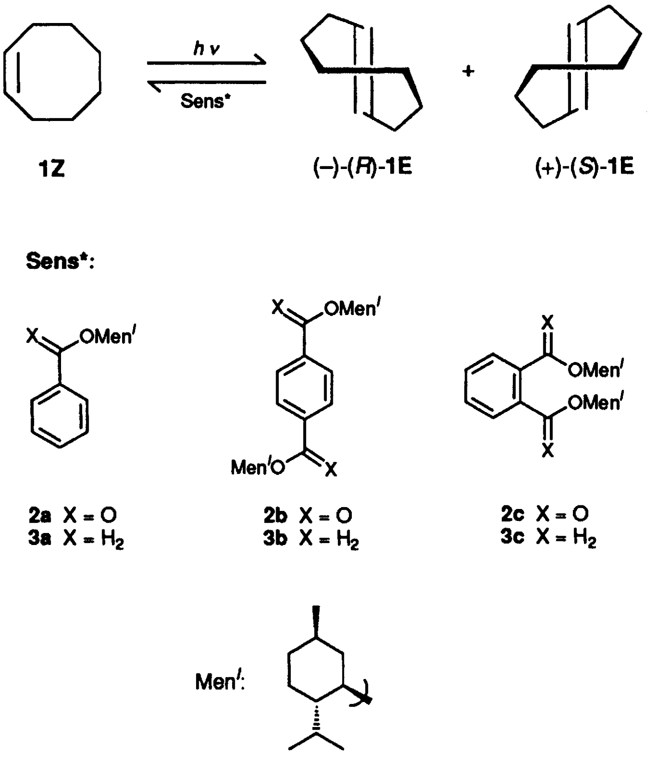
In the analytical runs with 3 cm^3 solutions, the irradiated solution was treated as above to give a pentane solution of pure **1E**, the ee value of which was then determined by chiral GC analysis. Since the GC analysis requires only a very small amount of the photoproduct **1E**, the irradiation periods employed in the analytical scale runs were much shorter than that required in the preparative scale runs.

In the calibration experiments, it was demonstrated that the ee values determined by chiral GC are in excellent agreement with the op values determined from the optical rotation of the same sample.

Results and discussion

Enantiodifferentiating photosensitization

The sensitized photoisomerizations of (*Z*)-cyclooctene (**1Z**, 200 mmol dm^{-3}) were performed in pentane at 25 °C in the presence of some structurally related optically active aromatic esters and ethers (Scheme 1). In these experiments, (−)-menthyl benzene(di)carboxylates (**2a–c**) were employed as singlet sensitizers,[8,9,12] while (−)-menthyl benzyl and xylylenyl ethers (**3a–c**) were expected to act as triplet sensitizers upon intersystem crossing from the excited singlet generated initially.



Scheme 1

The photostationary *E*/*Z* ratio, $(E/Z)_{pss}$ and the optical purity (op) or enantiomeric excess (ee) of **1E** isolated from the photolysates are summarized in Table 1, where the % ee/op value and the optical rotation of the product **1E** possess the same sign, *i.e.* if (*R*)-(−)-**1E** is produced in excess, the ee/op value is headed by a minus sign, while a positive ee/op value indicates the formation of (*S*)-(+)-**1E** as the dominant enantiomer.

It is noted that the sensitizations with aromatic esters **2** and ethers **3** lead to striking differences in the $(E/Z)_{pss}$ ratio under the conditions employed. Triplet sensitizations are known in general to afford relatively low $(E/Z)_{pss}$ ratios as compared with the singlet sensitizations with aromatic esters.[13] However, the low $(E/Z)_{pss}$ ratios obtained upon sensitization with the ethers

3a–c are not necessarily attributable only to the triplet state but rather rationalized by the incorporation of a singlet mechanism particularly at such a high substrate concentration (200 mmol dm^{-3}). This will be discussed below in conjunction with the concentration dependence of ee/op. Similarly, the ee/op values obtained in the singlet sensitization with aromatic esters **2** are appreciably higher than the corresponding values from the formal 'triplet' sensitization with aromatic ethers **3**, although the differences in the ee/op values obtained upon singlet and 'triplet' sensitizations would not appear to differ significantly at this temperature and substrate concentration.

The differences in ee/op values between the singlet and 'triplet' sensitizations are exaggerated in the low-temperature irradiations, as shown in Table 2. In the singlet sensitizations with esters **2**, the ee/op values are highly temperature-dependent and are substantially enhanced up to 10% at −60 °C for the phthalate sensitizer **2c**. On the other hand, the 'triplet' sensitizations with ethers **3** show only negligible temperature dependence, affording extremely low ee/op values below 2% for the *ortho*-substituted diether **3c** and at low temperatures. Consequently, the differences in ee/op between the singlet and 'triplet' sensitizations increase rapidly by lowering the temperature. These results clearly indicate that there exists intimate steric interactions between **1** and singlet sensitizer **2** within the exciplex intermediate, whereas the substrate–sensitizer interactions in the 'triplet' sensitization are much weaker. This is probably due to the lower charge-transfer character of **1–3** compared with the **1–2** pair in the excited state and also to the lower degree of organization in the interacting pair. However, even the low ee/op values obtained upon 'triplet' sensitization turned out to originate from the incorporation of the singlet state of the formal 'triplet' sensitizer.

Table 1 Enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**, 200 mmol dm^{-3}) sensitized by the structurally related aromatic esters and ethers (**2a–c** and **3a–c**, 5 mmol dm^{-3}) in pentane at 25 °C

Sensitizer	Irradiation time/h	Conversion (%)	Yield (%)[a]	$(E/Z)_{pss}$[b]	ee/op (%)	Ref.
2a	28	21	17	0.22	−2.72	*c*
2b	24	25	8	0.22	−5.96	*c*
2c	23	9	5	0.058	3.80	*c*
3a	2.5	4.3	1.5	0.015	−1.3	*d*
3b	23	3.0	1.0	0.013	−1.85	*c*
3c	8	4.2	2.1	0.021	0.5	*d*

[a] Chemical yield based on use of **1Z**. [b] Photostationary state *E*/*Z* ratio. [c] %op determined by optical rotation of product **1E** produced in preparative scale irradiation. [d] %ee determined by chiral GC analysis of product **1E** produced in analytical scale irradiation.

Effects of substrate concentration

Close examination of the effects of substrate concentration upon ee/op revealed that, even in the formal 'triplet' sensitization with **3**, the singlet sensitization cannot rigorously be ruled out, especially at high substrate concentrations. The comparative singlet and 'triplet' sensitizations with **2a** and **3a** were carried out at a variety of substrate concentrations to give the $(E/Z)_{pss}$ and ee/op values shown in Table 3. As illustrated in Fig. 1, the $(E/Z)_{pss}$ and ee/op values upon singlet sensitization are kept constant over the entire concentration range employed, whereas the values obtained in the 'triplet' sensitization vary critically with the substrate concentration. Thus, the $(E/Z)_{pss}$ ratio obtained upon 'triplet' sensitization increases with decreasing concentration of **1Z**, approaching the ultimate value of 0.22 at concentrations lower than 2.5 mmol dm^{-3}. On the contrary, the ee/op value decreased gradually from 1.3% at 40–400 mmol dm^{-3} to 0.4% at 2.5 mmol dm^{-3}.†

As has been demonstrated already,[14] the decreasing $(E/Z)_{pss}$ ratio at higher substrate concentrations indicates the concurrent operation of the singlet mechanism in the triplet sensitization of cyclooctene. In the present study, incorporation of the singlet mechanism at higher concentrations was proved experimentally by the fluorescence quenching of **3a**. As demonstrated in Fig. 2, the addition of **1Z** to a solution of **3a** led to fairly efficient quenching of fluorescence at 296 nm at high **1Z** concentrations, but no additional emission assigned to the exciplex was observed at longer wavelengths. However, it is noted that only negligible quenching takes place up to the substrate concentrations of 10 mmol dm^{-3}. As shown in Table 3 and Fig. 1, the $(E/Z)_{pss}$ ratio obtained upon sensitization with the 'triplet' sensitizer **3a** finally reaches a plateau of 0.22 at substrate concentrations below 2.5 mmol dm^{-3}, indicating that the sensitization with **3a** proceeds exclusively through the triplet mechanism at the low concentration. Unfortunately, the ee/op value obtained in 'triplet' sensitization decreases with decreasing concentration and the ultimate ee/op value

Table 2 Temperature effects upon enantiomeric excess (ee) or optical purity (op) in enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**, 200 mmol dm^{-3}) sensitized by aromatic esters or ethers (**2a–c** or **3a–c**, 5 mmol dm^{-3}) in pentane

Sensitizer	Temperature/ °C	Irradiation time/h	Conversion (%)	Yield (%)[a]	$(E/Z)_{pss}$[b]	ee/op (%)	Ref.
2a	25	28	21	17	0.22	−2.72	*c*
	−25	60	20	15	*d*	−2.97	*c*
2b	25	24	25	8	0.22	−5.96	*c*
	−25	63	24	19	0.23	−7.18	*c*
	−40	64	24	18	0.22	−8.16	*c*
2c	25	23	9	5	0.058	3.80	*c*
	−25	70	17	9	*d*	6.63	*c*
	−60	70	18	9	*d*	10.3	*c*
3a	25	2.5	4.3	1.5	0.015	−1.3	*e*
	−40	6	3.1	1.4	0.014	0.5	*e*
	−78	18	3.2	1.4	0.014	1.0	*e*
3b	25	23	3.0	1.0	0.013	−1.85	*c*
	−60	62	3.0	1.0	0.008	−0.56	*c*
3c	25	8	4.2	2.1	0.021	0.5	*e*
	−40	8	4.1	1.7	0.018	−0.7	*e*
	−78	12	4.6	1.7	0.018	−0.4	*e*

[a] Chemical yield based on **1Z** used. [b] Photostationary state *E*/*Z* ratio. [c] %op determined by optical rotation of product **1E** produced in preparative scale irradiation. [d] Not determined. [e] %ee determined by chiral GC analysis of product **1E** produced in analytical scale irradiation.

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† In Fig. 1, the ee/op and *E*/*Z* plots do not give exactly consistent mid-points, for which the inaccuracy of the experimental ee/op values, especially at low ee/op values, would be responsible, although the relevant errors are generally smaller than the possible deviations: ±0.3% in ee, < ±0.1% in op, and < ±0.1 in $(E/Z)_{pss}$. At present, we have no clear explanation for the inconsistent mid-points for the ee/op and *E*/*Z* plots.

Table 3 Effect of substrate concentration upon photostationary-state **1E**/**1Z** ratio, $(E/Z)_{pss}$, and enantiomeric excess (ee) or optical purity (op) in enantiodifferentiating photoisomerization of (*Z*)-cyclooctene (**1Z**) sensitized by aromatic ester (**2a**) or ether (**3a**) in pentane at 25 °C

Sensitizer	[**1Z**]/mmol dm^{-3}	Irradiation time/h	Conversion (%)	Yield (%)^a	$(E/Z)_{pss}$	ee/op (%)	Ref.
2a	5	2	21.7	20.8	0.24	−2.5	*b*
	30	2	23.1	18.5	0.24	−2.5	*b*
	200	28	21	17	0.22	−2.72	*c*
	500	9	9.6	9.0	*d*	−2.6	*b*
3a	0.63	0.5	*d*	*d*	0.22	*d*	
	2.5	3	*d*	*d*	0.22	−0.44	*c*
	10	6	30	11	0.17	−0.90	*c*
	40	10	19	7	0.089	−1.29	*c*
	200	2.5	4.3	1.5	0.015	−1.3	*b*
	400	28	5	1	0.013	−1.28	*c*

[a] Chemical yield based on amount of **1Z** used. [b] %ee determined by chiral GC analysis of product **1E** produced in analytical scale irradiation. [c] %op determined by optical rotation of product **1E** produced in preparative scale irradiation. [d] Not determined.

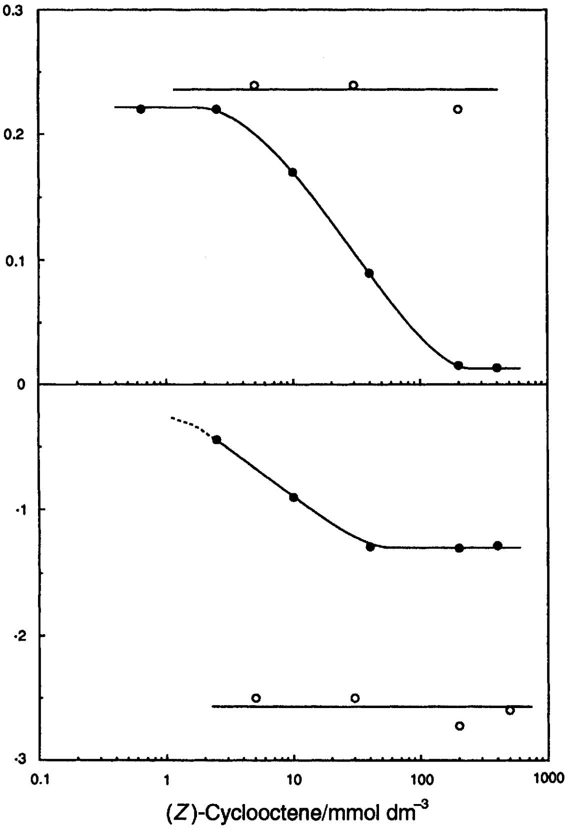

Fig. 1 Photostationary state **1E**/**1Z** ratio, $(E/Z)_{pss}$, and enantiomeric excess (ee) or optical purity (op) as functions of substrate concentration in enantiodifferentiating photoisomerization of (*Z*)-cyclooctene **1Z** sensitized by aromatic ester **2a** (○) or ether **3a** (●) in pentane at 25 °C

extrapolated to the zero substrate concentration appears to be well less than 0.5%.

According to the Stern–Volmer treatment, the relative fluorescence intensity (F_0/F) was plotted as a function of **1Z** concentration to give a good straight line with a Stern–Volmer constant $(k_q\tau)$ of 3.86 dm^3 mol^{-1}, as shown in Fig. 3. Since the fluorescence lifetime of **3a** was independently determined as 4.9 ns under comparable conditions by the single photon counting technique, the quenching rate constant k_q is calculated as 7.9×10^8 dm^3 mol^{-1} s^{-1}. This value is unexpectedly low compared with that for benzenecarboxylates that are quenched by **1Z** as fast as 3.2×10^{10} dm^3 mol^{-1} s^{-1}.[8,9] The lower ee/op values and slower quenching rate in the present case may be attributed to the low charge-transfer character and therefore weak steric interactions in the singlet sensitization with ethers **3** rather than esters **2**.

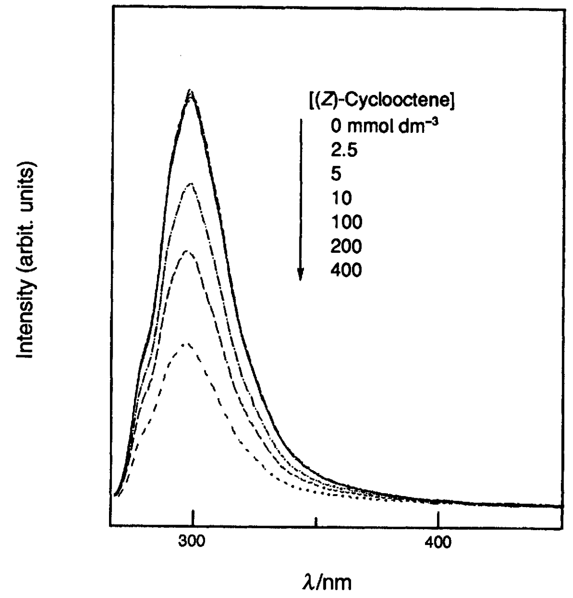

Fig. 2 Fluorescence quenching of (−)-menthyloxymethylbenzene **3a** (1.46 mmol dm^{-3}) with **1Z** (2.5–400 mmol dm^{-3}) in aerated pentane at 23 °C

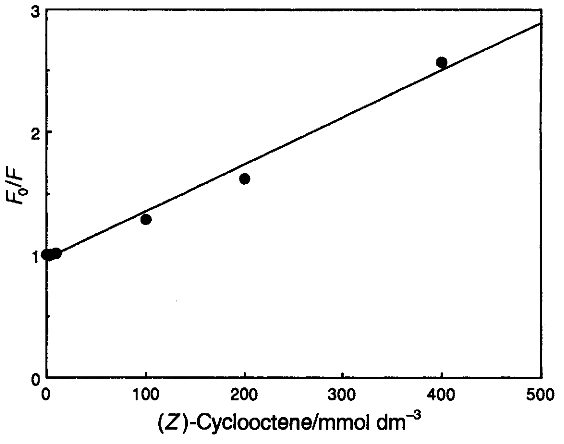

Fig. 3 Stern–Volmer plot for the fluorescence quenching of (−)-menthyloxymethylbenzene **3a** with **1Z**

We may conclude therefore that the use of a chiral triplet sensitizer is not specifically advantageous and the intervention of an intimately interacting singlet exciplex formed through a moderate charge-transfer interaction is one of the most crucial conditions required to produce efficient enantiodifferentiating photosensitization systems.

Acknowledgements

This work was supported in part by grants from the Ministry of Education, Science, Sports, and Culture of Japan (Nos. 06650990 and 07228239), the Japan Securities Scholarship Foundation and the Sumitomo Foundation.

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Paper 6/01275B
Received 22nd *February* 1996
Accepted 11*th April* 1996