PERKIN 2

Geometrical photoisomerization of (*Z*)-cyclooctene sensitized by aromatic phosphate, phosphonate, phosphinate, phosphine oxide and chiral phosphoryl esters

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Received (in Cambridge) 10th July 1998, Accepted 8th September 1998

Aromatic phosphate, phosphonate, phosphinate and phosphine oxide have been used as effective sensitizers for the geometrical photoisomerization of (*Z*)-cyclooctene (**1*Z***) to its highly strained (*E*)-isomer (**1*E***). Photosensitizations with phosphate and phosphonate gave moderate photostationary-state *E*/*Z* ratios of 0.14–0.17. A comparative study of the fluorescence quenching experiments and kinetic analysis of the product yield demonstrate that the photosensitized isomerization proceeds through a mixed mechanism that involves both singlet and triplet excited states. Triphenylphosphine oxide is not fluorescent and gave a low photostationary-state *E*/*Z* ratio of 0.05. Using (−)-menthyl or (−)-bornyl phosphate, phosphonate and phosphinate as chiral sensitizers, the enantiodifferentiating photoisomerization of **1*Z*** was performed to afford optically active **1*E*** in enantiomeric excesses ≤5%.

Introduction

We have been interested in the geometrical photoisomerization of medium-sized cycloalkenes and the nature of the thermally labile (*E*)-isomers generated photochemically.[1] Of these, (*E*)-cyclooctene (**1*E***) is of particular interest to us, since it is more strained, by *ca.* 40 kJ mol^{-1}, than the (*Z*)-isomer (**1*Z***)[2] and is inherently chiral[3] as a result of the restricted rope-jumping motion of the methylene bridge connecting the *trans* double bond. This constrained, but moderately stable, **1*E*** can be prepared conveniently and efficiently through a photochemical[1,4] rather than a thermal route.[5] Hence, we have investigated both direct photolysis at 185 nm and singlet- and triplet-sensitized photoisomerizations of **1*Z***,[1] as well as the enantiodifferentiating photosensitization with a variety of optically active sensitizers.[6] The direct excitation at 185 nm, generating an excited singlet state, affords an ultimate *E*/*Z* ratio at the photostationary state [$(E/Z)_{pss}$] of 0.96, which is exceptionally high for such a constrained (*E*)-cycloalkene. On the other hand, the triplet sensitizations with ketones and alkylbenzenes give a much lower $(E/Z)_{pss}$ of 0.02–0.2, while the singlet sensitization with benzenepolycarboxylates leads to intermediate $(E/Z)_{pss}$ ratios of 0.1–0.6.[1] Recently, we have demonstrated that the enantiodifferentiating photoisomerization of **1*Z*** can be effected by chiral polyalkyl benzenepolycarboxylates, affording optically active **1*E*** in moderate to good enantiomeric excesses (ee).[6] However, the sensitizers employed in the previous studies were restricted to conventional ketones, alkylbenzenes, and benzenepolycarboxylates and no systematic survey for other effective sensitizers has been carried out to date.

In the course of the exploration for novel photosensitizers, we found that some aromatic phosphoryl compounds can also be used as efficient sensitizers for this photoisomerization reaction. Herein, we wish to report the photochemical behaviour of **1*Z*** upon sensitization with dimethyl phenyl phosphate (**2a**), dimethyl phenylphosphonate (**3a**), methyl diphenylphosphinate (**4a**), and triphenylphosphine oxide (**5**). In sharp contrast to the corresponding benzoates and (tere)phthalates which do not fluoresce in fluid solutions, these aromatic phosphates and phosphonates emit fairly strong fluorescence and the excited-state behaviour of the sensitizers can be investigated in more detail in order to elucidate the sensitization mechanism as well as the quenching parameters.

Since asymmetric photochemical reactions are of current interest,[7] we further introduced some chiral auxiliaries to the ester moiety of the phosphate and phosphonate and investigated the enantiodifferentiating photoisomerization of **1*Z*** sensitized by (−)-dimenthyl phenyl phosphate (**2b**), (−)-dimenthyl 2-methoxyphenyl phosphate (**2c**), (−)-dimenthyl 4-(−)-bis(menthyloxy)phosphinoyloxyphenyl phosphate (**2d**), (−)-dibornyl phenylphosphonate (**3b**), (−)-tetramenthyl benzene-1,2-diphosphonate (**3c**), and (−)-menthyl diphenylphosphinate (**4b**) (see Scheme 1). In this paper, we also discuss the relationship between the multiplicity of excited state involved and the product's ee.

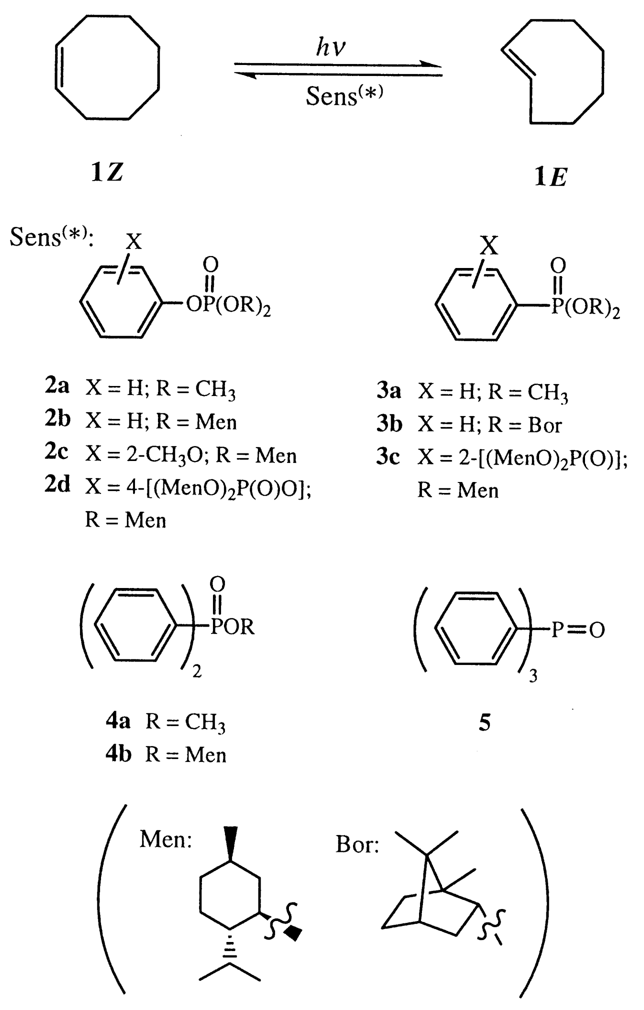
Results and discussion

Photoisomerization

Photosensitized isomerizations of (*Z*)-cyclooctene **1*Z*** (5 mM) were carried out under an argon atmosphere in pentane or pentane–ether (1 : 1) solution at 25 °C in the presence of achiral aromatic phosphoryl sensitizers **2a**, **3a**, **4a** and **5** (1 mM). The only major photochemical reaction detected by gas chromatography is the *Z*–*E* isomerization affording **1*E*** as the only detectable product. Upon prolonged irradiations, up to 2–3 h, an apparent photostationary-state mixture of **1*Z*** and **1*E*** was obtained for each sensitizer. The ultimate $(E/Z)_{pss}$ ratio, conversion of **1*Z***, and chemical yield of **1*E*** are summarized in Table 1. The phosphoryl esters **2a**, **3a** and **4a** gave moderate $(E/Z)_{pss}$ values of 0.14–0.17, which are comparable to those obtained upon photosensitizations with aromatic hydrocarbons[1] or benzenepolycarboxylates.[1,6] However, triphenylphosphine oxide **5** afforded a much lower $(E/Z)_{pss}$ of 0.05, which would be accounted for in terms of the possible operation of the triplet sensitization mechanism, simply because **5** possesses an electronic structure which resembles benzophenone and is likely to undergo fast intersystem crossing, giving the triplet state.

Fluorescence quenching

In order to elucidate the excited state involved in photosensitization processes using phosphate **2a** and phosphonate **3a**, the fluorescence spectra of the photosensitizers were measured and fluorescence quenching experiments were performed with **1*Z*** both in aerated and argon-saturated pentane at 20 °C. As can



Scheme 1 Geometrical photoisomerization of cyclooctene sensitized by (chiral) aromatic phosphoryl esters and phosphine oxide.

Table 1 Photoisomerization of cyclooctene sensitized by aromatic phosphate (**2a**), phosphonate (**3a**), phosphinate (**4a**), and phosphine oxide (**5**) at 25 °C

Sensitizer	Solvent	Time/h	*E*/*Z*	% Conversion	% Yield
2a	Pentane	1.0	0.155	28.9	11.0
3a	Pentane	2.0	0.168	28.8	12.0
4a	Pentane	1.3	0.142	26.8	10.4
5	Pentane–ether (1 : 1)	0.7	0.054	11.5	4.8

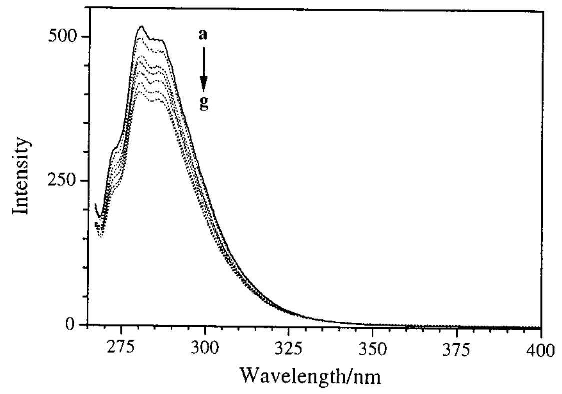


Fig. 1 Fluorescence spectra of **2a** (0.2 mmol dm^{-3}) excited at 265 nm in aerated pentane in the absence/presence of (*Z*)-cyclooctene (**1*Z***) of varying concentrations: (a) 0, (b) 10.24, (c) 20.51, (d) 30.76, (e) 40.96, (f) 51.20, (g) 61.44 mmol dm^{-3}.

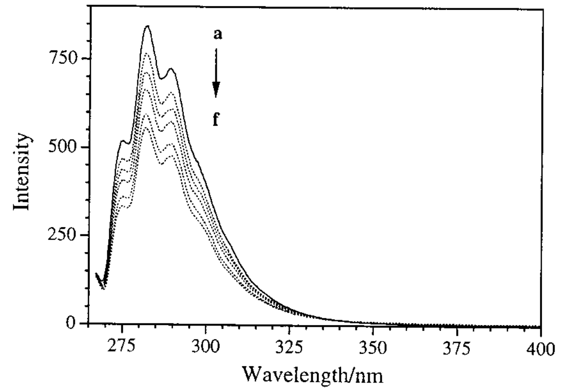


Fig. 2 Fluorescence spectra of **3a** (0.2 mmol dm^{-3}) excited at 265 nm in aerated pentane in the absence/presence of (*Z*)-cyclooctene (**1*Z***) of varying concentrations: (a) 0, (b) 2.56, (c) 7.69, (d) 12.80, (e) 20.51, (f) 30.76 mmol dm^{-3}.

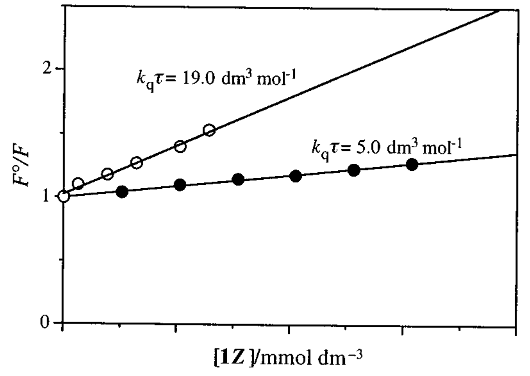


Fig. 3 Stern–Volmer plots for fluorescence quenching of **2a** (closed circle) and **3a** (open circle) by **1*Z*** in aerated pentane.

be seen from Fig. 1 and 2 (solid lines), both sensitizers show relatively strong fluorescence with vibrational fine structures, which are the exact mirror images of the absorption and excitation spectra (not shown). Triphenylphosphine oxide **5** is not fluorescent.[8]

The fluorescence of **2a** and **3a** was quenched moderately by adding the substrate **1*Z***, but no appreciable emission attributable to an exciplex intermediate was observed at longer wavelengths. According to the conventional Stern–Volmer treatment of the quenching data,[9,10] the relative fluorescence intensity ($F°/F$) was plotted as a function of the concentration of added **1*Z*** to give a good straight line for both **2a** and **3a**, as shown in Fig. 3. The Stern–Volmer constants ($k_q\tau_0$) were obtained as slopes of the plots, while the fluorescence lifetimes (τ_0) of **2a** and **3a** in the absence of quencher were independently determined in aerated and argon-saturated pentane by the single-photon-counting technique using a pulsed H_2 light source. The absorption and fluorescence spectral properties and the relevant kinetic parameters for the fluorescence quenching processes are summarized in Table 2.

As can be seen from Table 2, the Stokes shifts are very small (3 nm or 5 kJ mol^{-1}) and the vibrational fine structures are well preserved in the fluorescence spectra. These results indicate that the excited singlets of these aromatic phosphoryl compounds suffer minimal energetic and conformational relaxations on the singlet energy surface. In spite of the relatively high singlet energy (440 kJ mol^{-1}) estimated from the fluorescence 0–0 bands, the fluorescence quenching of **2a** and **3a** with **1*Z*** occurs only with moderate efficiency at 1–4 × 10^9 dm^3 mol^{-1} s^{-1}, which is one order of magnitude slower than the diffusion-controlled rate in pentane (2.8 × 10^{10} dm^3 mol^{-1} s^{-1}).[11]

To confirm the excited state involved, the photosensitization

Table 2 Absorption, fluorescence and quenching behaviour of dimethyl phenyl phosphate **2a** and dimethyl phenylphosphonate **3a** upon addition of (*Z*)-cyclooctene **1*Z*** in pentane

	Absorption	Fluorescence		$k_q\tau_0$/dm^3 mol^{-1}		k_q/dm^3 mol^{-1} s^{-1}	
Sensitizer	$\lambda_{0\text{–}0}$/nm^a (kJ mol^{-1})	$\lambda_{0\text{–}0}$/nm^a (kJ mol^{-1})	τ_0/ns^b	Fluorescence quenching	Product analysis	Fluorescence quenching	Product analysis
2a	268.4 (446)	271.5 (441)	6.7^c (4.8)^d	5.0^d	85^c	1.0×10^9	$(1.3 \times 10^{10})^e$
3a	270.0 (443)	273.1 (438)	4.1^c (4.3)^d	19.0^d	^{f}	4.4×10^9	^{f}

[a] Absorption fluorescence 0–0 band. [b] Fluorescence lifetimes of sensitizer measured by single photon counting method in the absence of quencher **1*Z***. [c] Determined under argon. [d] Determined under air. [e] Inconsistent quenching rate constant; see text. [f] Curved plot obtained (Fig. 5); see text.

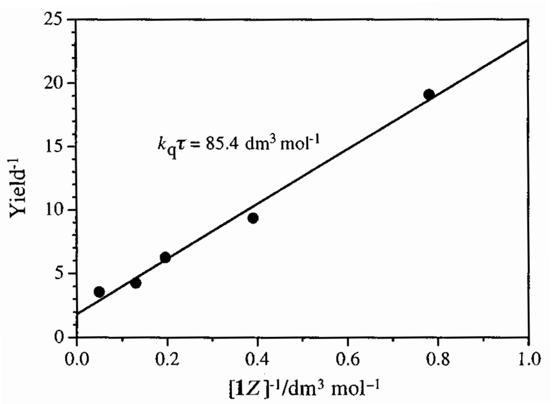


Fig. 4 Reciprocal yield of **1*E*** *versus* reciprocal concentration of **1*Z*** upon *Z*–*E* photoisomerization of **1*Z*** sensitized by **2a** in pentane under argon atmosphere.

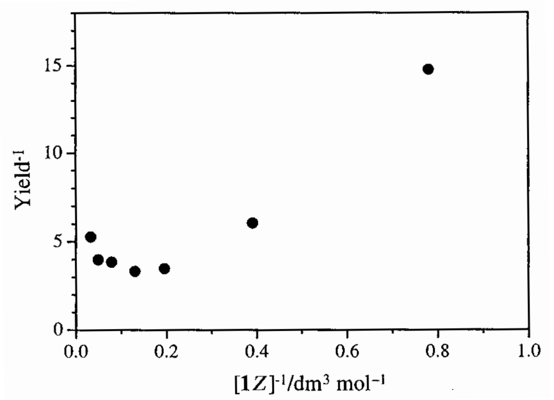


Fig. 5 Reciprocal yield of **1*E*** *versus* reciprocal concentration of **1*Z*** upon *Z*–*E* photoisomerization of **1*Z*** sensitized by **3a** in pentane under argon atmosphere.

with **2a** (1 mmol dm^{-3}) was carried out using various concentrations of **1*Z*** (1.28–76.9 mmol dm^{-3}) in a merry-go-round apparatus. A Stern–Volmer treatment of the product yield,[9,10] in which the reciprocal yield of **1*E*** is plotted against the reciprocal concentration of **1*Z***, afforded a good straight line shown in Fig. 4. However, there is a large discrepancy between the rate constants obtained from the fluorescence quenching (1.0×10^9 dm^3 mol^{-1} s^{-1}) and the product analysis (1.3×10^{10} dm^3 mol^{-1} s^{-1}), as can be seen from Table 2. A possible reason for these differences is discussed below.

In contrast, a similar experiment with **3a** gave a curved plot (Fig. 5), which is linear only at low concentrations of **1*Z***, but seriously deviates from an extrapolated straight line plot at higher concentrations. This result clearly indicates that at least two different excited states, most probably singlet and triplet, are involved in the sensitization process,[9] depending on the concentration of **1*Z***. It is inferred that, at low substrate concentrations, inefficient trapping of the excited singlet sensitizer by **1*Z*** leads to the intersystem crossing of phenylphosphonate **3a** to the triplet species, which in turn sensitizes the *E*–*Z* isomerization of **1*Z***. Similar behaviour, *i.e.* switching of the mechanism from singlet to triplet by lowering the substrate concentration, has been reported upon sensitization of **1*Z*** with aromatic hydrocarbons such as benzene and toluene.[1]

In this context, the discrepancy observed upon sensitization with **2a**, *i.e.* the much larger quenching rate constant obtained from the product analysis *versus* that from the fluorescence quenching, may be attributable to the dominant contribution of the triplet sensitization to the photoisomerization process. Although the direct observation of the triplet state was not possible in the present case, it seems likely that the less efficient quenching efficiency observed for **2a** ($k_q = 1.0 \times 10^9$ dm^3 mol^{-1} s^{-1}), as compared with that for **3a** (4.4×10^9 dm^3 mol^{-1} s^{-1}), facilitates the intersystem crossing to the triplet state. Thus, sensitization of **1*Z*** with **3a**, and probably **2a** as well, seems to be complicated by the mixed mechanism involving both excited singlet and triplet states.

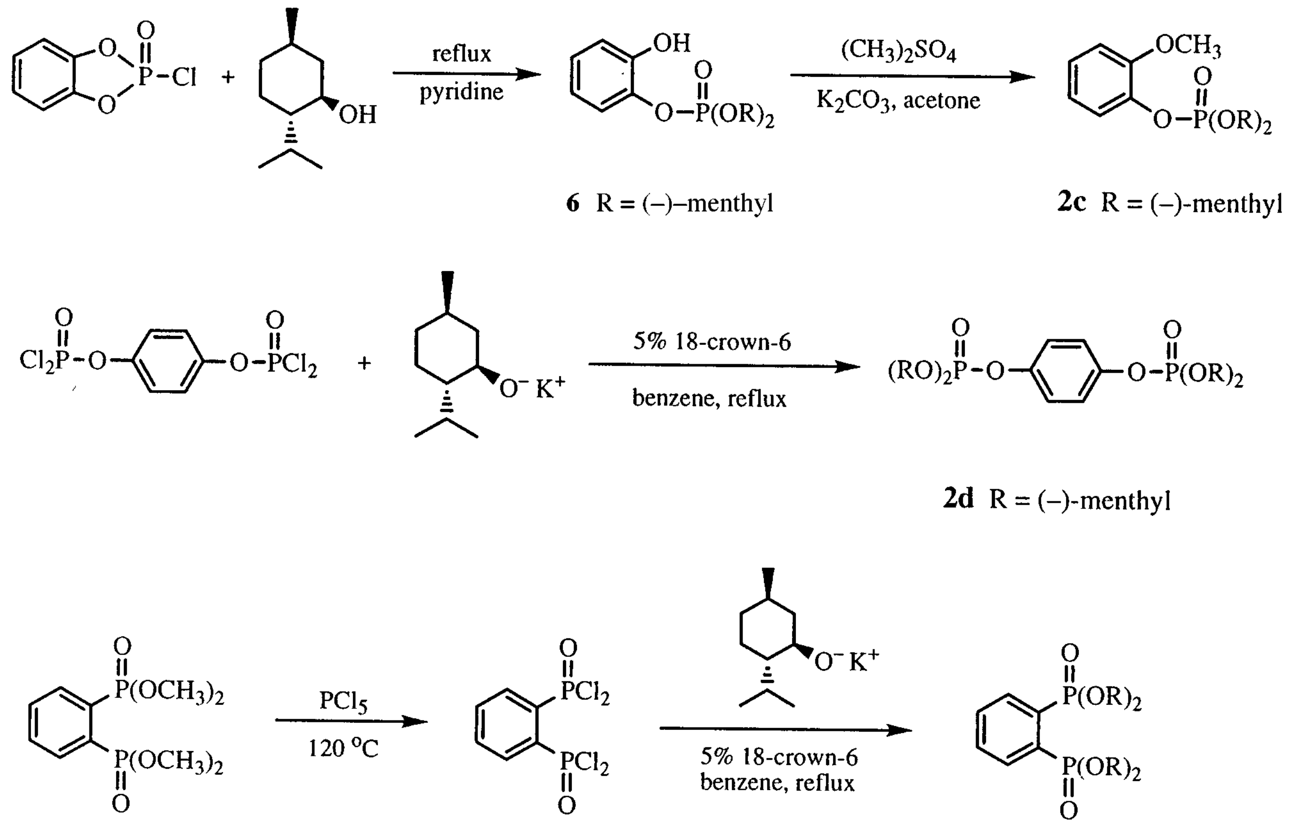
In summary, the *Z*–*E* photoisomerization of **1*Z*** can be carried out with good efficiency using phenyl phosphate, phenylphosphonate, or triphenylphosphine oxide as a sensitizer. However, the excited state involved depends critically on the sensitizer structure and the substrate concentrations employed, which is typically demonstrated by the sensitization of **1*Z*** with phosphonate **3**.

Enantiodifferentiation and temperature effects

We further explored the potentially enantiodifferentiating photoisomerization of **1*Z*** sensitized by the novel chiral aromatic phosphoryl esters shown below. Chiral aromatic phosphoryl sensitizers **2b**, **3b** and **4b** with one chiral ester moiety were prepared by the reaction of the corresponding aromatic phosphoryl chloride with (−)-menthol or (−)-borneol in pyridine. The *ortho*- or *para*-substituted chiral aromatic phosphoryl sensitizers **2c**, **2d** and **3c** were synthesized according to the methods shown in Scheme 2, and full details of the reaction procedures are summarized in the Experimental section.

The photosensitization of **1*Z*** with these chiral phosphoryl sensitizers was performed under comparable conditions to those employed above giving apparent photostationary-state mixtures upon prolonged irradiation. The ee of **1*E*** produced did not show any appreciable changes over a wide range of irradiation time or conversion. The results of enantiodifferentiating photosensitization of **1*Z*** are summarized in Table 3, where the ee value has the same sign as the product's optical rotation.

In comparison with the highly efficient enantiodifferentiating photoisomerization of **1*Z*** upon sensitization with chiral arenecarboxylates,[6] the product's ee's obtained in this study were generally very low. Thus, the sensitizations with simple menthyl or bornyl esters **2b**, **3b** and **4b** resulted in practically no enantiodifferentiation, even at a low temperature, as shown in Table 3. The highest ee of −5% was attained by using the menthyl bearing chiral *o*-benzenediphosphonate **3c** at −52 °C, while the other *ortho*- or *para*-substituted chiral phosphates **2c** and **2d**, possessing the auxiliaries gave very low ee's, around 1–2%. The ee appears to increase on decreasing the irradiation temperature and also on using a chiral sensitizer possessing adjacent ester



6 R = (–)-menthyl

2c R = (–)-menthyl

2d R = (–)-menthyl

3c R = (–)-menthyl

Scheme 2 Synthesis of chiral phosphoryl esters.

Table 3 Enantiodifferentiating photoisomerization of cyclooctene sensitized by chiral phosphoric acid esters in pentane

Sensitizer	Temperature/°C	Time/h	*E*/*Z*	% Conversion	% Yield	% ee[a]
2b	25	1.0	0.112	16.7	9.4	−0.4
	−52	1.5	0.220	21.6	17.2	−0.6
2c	25	2.0	0.064	15.4	5.4	+0.5
	−52	7.0	0.022	8.3	2.0	+1.0
2d	25	2.0	0.052	10.7	4.6	−1.0
	−52	6.0	0.071	13.5	6.2	−2.0
3b	25	1.3	0.179	23.8	13.6	−1.4
	−56	3.0	0.284	31.2	19.6	−0.2
3c	25	4.0	0.053	9.8	4.8	−2.5
	−52	14.0	0.100	21.0	7.8	−5.0
4b	25	0.8	0.143	20.8	11.2	−0.7
	−52	2.0	0.258	32.1	17.5	+0.6

[a] Enantiomeric excess; the sign coincides with that of the product's optical rotation.

groups, such as **3c**. Similar behaviour has been observed in the enantiodifferentiating photosensitization with chiral benzenepolycarboxylates,[6] although the ee's achieved are moderate to high in the previous cases. Furthermore, no temperature switching of product chirality, which is observed upon sensitization with benzenepolycarboxylates, is observed at all.

In earlier studies,[6] we have suggested that the interaction between the π bond of **1*Z*** and the sensitizer's carboxylic C=O bond—rather than its aromatic C=C bonds—plays an important role in the enantiodifferentiating photoisomerization of **1*Z*** using chiral polyalkyl benzenepolycarboxylates. We have also indicated that such an unusual behaviour of product chirality and fairly high ee's up to 64% arise as a result of dynamic conformational changes of the adjacent ester moieties of the *ortho*-substituted benzenepolycarboxylates, which synchronize with the enantiodifferentiating rotational relaxation of **1*Z*** around the double bond within the exciplex intermediate. Such dynamic structural changes lead to the anomalously high differential entropy of activation, which plays a crucial role in determining the product's ee, and also explain its temperature dependence.

The phosphoryl esters, possessing two alkyl groups in an ester moiety, are more bulky than the corresponding benzenecarboxylates. Hence, the adjacent phosphoryl ester moieties in **3c** are likely to offer severe steric hindrance which will act against the dynamic conformational changes, thus reducing temperature-dependence of the product's ee. Furthermore, the electronic spectrum of **3** is very similar in shape to those of simple alkylbenzenes, indicating the lack of conjugation between the P=O bond and the phenyl ring, although they are connected to one another. It is thus inferred that the sensitizer–substrate interaction in the excited state does not occur at the P=O bond, but at the aromatic ring that is located far away from the chiral groups. Although the ee's obtained are low and no definitive conclusions on the enantiodifferentiation mechanism can be drawn at the present stage, it should be emphasized that the enantiodifferentiating photoisomerization of **1*Z*** can be effected by using chiral arylphosphoryl sensitizers, and a sterically well-designed photosensitizer is expected to achieve higher ee's in the future. Synthetic and mechanistic investigations are currently in progress to reveal the enantiodifferentiating mechanism, and also to enhance the product's ee.

Experimental

General

Melting points were determined with a Yanaco MP-500D apparatus and are uncorrected. ^{1}H NMR spectra were obtained in CDCl$_3$ with tetramethylsilane (TMS) as an internal standard on a JEOL JNM-EX400 spectrometer. Mass spectra were recorded on a JEOL JMS DX-303 instrument. Optical rotation was determined at 589 nm in a thermostatted conventional 10 cm cell, using a Perkin-Elmer Model 341 polarimeter. All compounds reported in this paper gave satisfactory CHN microanalyses with a Perkin-Elmer Model 240 analyzer.

Gas chromatographic analyses of the geometrical isomers of **1** in photolyzed solutions were performed on a 50 m capillary column (Shimadzu CBP-20) at 65 °C with a Shimadzu 14A instrument. Enantiomeric excesses of **1*E***, isolated through selective extraction with 20% aqueous silver nitrate,[1,5] were determined by gas chromatography over a 60 m chiral capillary column (Supelco β-DEX 120) at 70 °C, using a Shimadzu 14A instrument. Compounds **2d** and **3c** were purified using a JAI LC-908 recycling preparative HPLC equipped with a GPC column JAIGEL 1H+2H (Japan Analytical Industry Co).

Stern–Volmer studies

Irradiations of a series of pentane solutions containing sensitizer (**2a** or **3a**, 1 mM) and pure **1*Z*** at various concentrations (1.28–76.9 mM) were performed in a merry-go-round apparatus in a water bath at 25 °C, using a 60 W low pressure mercury lamp. Subsequent data treatment gave the Stern–Volmer plot of reciprocal yield *versus* reciprocal concentration for the *Z*–*E* photoisomerization of **1*Z*** sensitized by **2a** or **3a**. Since the conversions were kept low (<5%) in order to avoid the effect of reverse *E*-to-*Z* photoisomerization, no corrections have been made for the back reaction.

Lifetime measurements

Fluorescence lifetimes were measured with 0.2 mmol dm^{-3} solutions of **2a** or **3a** in aerated pentane at 20 °C by means of the time-correlated single-photon-counting method on a Horiba NAES-550 instrument equipped with a pulsed H$_2$ light source. The radiation from the lamp was made monochromatic by a 10 cm monochromator, and the emission from the sample was detected through an appropriate filter (UV-29).

Photolyses

All irradiations were carried out in a temperature-controlled water (25 °C) or propan-2-ol (−25 to −78 °C) bath. A pentane solution (3 cm^3) containing **1*Z*** (5 mmol dm^{-3}), optically active sensitizer (1 mmol dm^{-3}) and cycloheptane (5 mmol dm^{-3}) added as an internal standard was irradiated at 254 nm under an argon atmosphere in a quartz tube using a 120 W low pressure mercury lamp (Eikosha) fitted with a Vycor sleeve.

Synthesis of photosensitizers

Although the methyl esters **2a**, **3a** and **4a** are known compounds, the spectroscopic and elemental analyses were carried out in order to confirm the purity.

Dimethyl phenyl phosphate (2a). 2a was prepared by the reaction of phenyl dichlorophosphate (1.0 g, 4.74 mmol) with methanol (used as solvent) in the presence of pyridine. After workup, the residue was subjected to flash column chromatography over silica gel with an ethyl acetate-hexane (1 : 4) eluent to give **2a** as colourless oil: yield 0.78 g (80%); UV (pentane) $\lambda_{max} = 262$ nm ($\varepsilon = 576$ dm^3 mol^{-1} cm^{-1}); IR (neat) v 1295 cm^{-1} (P=O); ^{1}H NMR (CDCl$_3$) δ 3.87 (6H, d, $J = 11.2$ Hz, OCH$_3$), 7.18 (3H, m, Ar), 7.30–7.40 (2H, m, Ar); MS (FAB) *m*/*z* 203 (M$^+$ + 1); anal. calc. for $C_8H_{11}PO_4$ (202.1467): C, 47.54; H, 5.49. Found: C, 47.39; H, 5.41%.

Dimethyl phenylphosphonate (3a). 3a was prepared by the reaction of phenylphosphonic dichloride (1.0 g, 5.12 mmol) with methanol (used as solvent) in the presence of pyridine. After workup, the residue was subjected to flash column chromatography over silica gel with an ethyl acetate–hexane (1 : 4) eluent to give **3a** as colourless oil: yield 0.76 g (81%); UV (hexane) λ_{max} 263 nm ($\varepsilon = 465$ dm^3 mol^{-1} cm^{-1}); IR (neat) v 1250 cm^{-1} (P=O); ^{1}H NMR (CDCl$_3$) δ 3.76 (6H, d, $J = 10.8$ Hz, OCH$_3$), 7.40–7.62 (3H, m, Ar), 7.75–7.83 (2H, m, Ar); MS (FAB) *m*/*z* 187 (M$^+$ + 1); anal. calc. for $C_8H_{11}PO_3$ (186.1473): C, 51.62; H, 5.96. Found: C, 51.54; H, 5.95%.

Methyl diphenylphosphinate (4a). 4a was prepared by the reaction of diphenylphosphonic chloride (1.0 g, 4.24 mmol) with methanol (used as solvent) in the presence of pyridine. After workup, the residue was subjected to flash column chromatography over silica gel with an ethyl acetate–hexane (1 : 4) eluent to give **4a** as a white solid: yield 0.79 g (80%); mp 58–60 °C; UV (pentane) λ_{max} 265 nm ($\varepsilon = 673$ dm^3 mol^{-1} cm^{-1}); IR (KBr) v 1230 cm^{-1} (P=O); ^{1}H NMR (CDCl$_3$) δ 3.76 (3H, d, $J = 11.2$ Hz, OCH$_3$), 7.40–7.56 (6H, m, Ar), 7.80–7.86 (4H, m, Ar); MS (FAB) *m*/*z* 233 (M$^+$ + 1); anal. calc. for $C_{13}H_{13}PO_2$ (232.2185): C, 67.24; H 5.64. Found: C, 66.97; H, 5.60%.

(−)-Dimenthyl phenyl phosphate (2b). 2b was prepared by the reaction of phenyl dichlorophosphate (1.27 g, 6 mmol) with (−)-menthol (1.56 g, 10 mmol) in the presence of pyridine (12 ml) under reflux for 24 h. After workup, the residue was subjected to flash column chromatography over silica gel with an ethyl acetate–hexane (1 : 4) eluent to give **2b** as colourless oil: yield 1.7 g (76%); $[\alpha]_D^{20}$ −68.9 ($c = 1.0$, CH$_2$Cl$_2$); UV (pentane) $\lambda_{max} = 263$ nm ($\varepsilon = 660$ dm^3 mol^{-1} cm^{-1}); IR (neat) v 1295 cm^{-1} (P=O); ^{1}H NMR (CDCl$_3$) δ 0.68 (3H, d, $J = 6.8$ Hz), 0.81 (3H, d, $J = 6.8$ Hz, CH$_3$), 0.82 (3H, d, $J = 6.8$ Hz, CH$_3$), 0.88 (3H, d, $J = 6.8$ Hz, CH$_3$), 0.91 (6H, d, $J = 6.8$ Hz, CH$_3$), 0.90–1.80 (14H, m), 1.90–2.10 (1H, m), 2.15–2.20 (2H, m), 2.20–2.30 (1H, m), 4.20–4.30 (2H, m), 7.10–7.40 (5H, m, Ar); MS (FAB) *m*/*z* 451 (M$^+$ + 1); anal. calc. for $C_{26}H_{43}PO_4$ (450.5988): C, 69.31; H, 9.62. Found: C, 69.39; H, 9.54%.

(−)-Dibornyl phenylphosphonate (3b). 3b was prepared by the reaction of phenylphosphonic dichloride (1.24 g, 6.36 mmol) with (1*S*)-*endo*-(−)-borneol (1.58 g, 10.26 mmol) in the presence of pyridine (15 ml) under reflux for 18 h. After workup, the residue was subjected to flash column chromatography over silica gel with an ethyl acetate–hexane (1 : 4) eluent to give **3b** as a white solid: yield 1.5 g (68%); mp 83–84 °C; $[\alpha]_D^{20}$ −24.3 ($c = 0.71$, CH$_2$Cl$_2$); UV (hexane) $\lambda_{max} = 264$ nm ($\varepsilon = 591$ dm^3 mol^{-1} cm^{-1}); IR (KBr) v 1250 cm^{-1} (P=O); ^{1}H NMR (CDCl$_3$) δ 0.72 (3H, s, CH$_3$), 0.83 (3H, s, CH$_3$), 0.84 (3H, s, CH$_3$), 0.85 (3H, s, CH$_3$), 0.87 (3H, s, CH$_3$), 0.93 (3H, s, CH$_3$), 1.0–1.40 (8H, m, CH$_2$), 1.60–1.80 (2H, m), 1.90–2.02 (2H, m), 2.10–2.22 (1H, m), 2.20–2.40 (1H, m), 4.60–4.75 (2H, m, O–CH), 7.40–7.62 (3H, m, Ar), 7.75–7.83 (2H, m, Ar); MS (FAB) *m*/*z* 431 (M$^+$ + 1); anal. calc. for $C_{26}H_{39}PO_3$ (430.5676): C, 72.53; H, 9.13. Found: C, 72.46; H, 9.17%.

(−)-Menthyl diphenylphosphinate (4b). 4b was prepared by the reaction of diphenylphosphonic chloride (1.6 g, 6.78 mmol) with (−)-menthol (1.0 g, 6.4 mmol) in the presence of pyridine (6 ml) under reflux for 24 h. After workup, the residue was subjected to flash column chromatography over silica gel with an ethyl acetate–hexane (1 : 4) eluent to give **4b** as a white solid: yield 0.8 g (32%); mp 71–72 °C; $[\alpha]_D^{20}$ −69.1 ($c = 1.0$, CH_2Cl_2); UV (pentane) $\lambda_{max} = 265$ nm ($\varepsilon = 1883$ dm^3 mol^{-1} cm^{-1}); IR (KBr) ν 1230 cm^{-1} (P=O); ^{1}H NMR ($CDCl_3$) δ 0.52 (3H, d, $J = 6.8$ Hz, CH_3), 0.84 (3H, d, $J = 6.3$ Hz, CH_3), 0.87 (3H, d, $J = 6.8$ Hz, CH_3), 0.90–1.10 (2H, m), 1.14–1.50 (4H, m), 2.00–2.20 (2H, m), 4.20–4.30 (1H, m), 7.40–7.60 (6H, m, Ar), 7.78–7.96 (4H, m, Ar); MS (FAB) *m*/*z* 357 ($M^+ + 1$); anal. calc. for $C_{22}H_{29}PO_2$ (356.4448): C, 74.13; H, 8.20. Found: C, 73.84; H, 8.12%.

1,2-Phenylene bis(phosphonic dichloride). This precursor in the subsequent synthesis was prepared by the reaction of 1,2-phenylene bis(dimethyl phosphonate)[12] (5.2 g, 18 mmol) with phosphorus pentachloride (14.6 g, 70 mmol) at 120 °C for 12 h. The phosphorus oxychloride formed was removed under reduced pressure, and the residue was used for the subsequent reaction without further purification: yield 5.1 g (90%); ^{1}H NMR ($CDCl_3$) δ 7.90–8.10 (2H, m, Ar), 8.32–8.46 (2H, m, Ar).

Tetramenthyl benzene-1,2-diphosphonate (3c). **3c** was synthesized in the reaction of 1,2-phenylene bis(phosphonic dichloride) (3.35 g, 10.7 mmol) with potassium menthoxide in the presence of 5% 18-crown-6 in benzene under reflux for 24 h [potassium menthoxide was prepared from menthol (10.05 g, 65 mmol) and potassium hydride (2.48 g, 62 mmol) in benzene under reflux for 16 h]. After workup, the residue was purified by silica gel column chromatography and JAI LC-908 recycling preparative HPLC (eluted with chloroform) to give **3c** as a white solid which forms an inclusion compound with one molecule of chloroform: yield 2.2 g (26%); mp 58–64 °C; $[\alpha]_D^{20}$ −55.8 ($c = 0.81$, CH_2Cl_2); UV (hexane) $\lambda_{max} = 279$ nm ($\varepsilon = 4853$ dm^3 mol^{-1} cm^{-1}); IR (KBr) ν 1240 cm^{-1} (P=O); ^{1}H NMR ($CDCl_3$) δ 0.60–2.0 (68H, m), 2.30–2.42 (4H, m), 4.30–4.43 (4H, m), 7.58–7.62 (2H, m, Ar), 8.20–8.40 (2H, m, Ar); MS (FAB) *m*/*z* 791 ($M^+ + 1$); anal. calc. for $C_{46}H_{80}O_6P_2\cdot CHCl_3$ (791.0851 + 119.3771): C, 62.00; H, 8.96. Found: C, 61.99; H, 8.94%.

1,4-Phenylene bis(dichlorophosphate). This precursor in the subsequent synthesis was prepared by the reaction of hydroquinone (5.1 g, 46.4 mmol) with phosphorus oxychloride (64 g, 0.42 mol) at 120 °C for 12 h in the presence of aluminium chloride (10 mg, 0.08 mmol).[13] The unreacted phosphorus oxychloride was removed under reduced pressure and the residue was used in subsequent reactions without further purification: yield 14.4 g (90%).

(−)-Dimethyl (−)-4-bis(menthoxyl)phosphinyloxyphenyl phosphate (2d). **2d** was synthesized by the reaction of 1,4-phenylene bis(dichlorophosphate) (1.4 g, 4.1 mmol) with potassium menthoxide (prepared using the method given above) in the presence of 5% 18-crown-6 in benzene under reflux for 24 h. After workup, the residue was purified by silica gel column chromatography and JAI LC-908 recycling preparative HPLC (eluted with chloroform) to give **2d** as a white solid: yield 0.45 g (16%); mp 71–73 °C; $[\alpha]_D^{20}$ −36.8 ($c = 1.0$, CH_2Cl_2); UV (hexane) λ_{max} 268 nm ($\varepsilon = 891$ dm^3 mol^{-1} cm^{-1}); IR (KBr) ν 1220 cm^{-1} (P=O); ^{1}H NMR ($CDCl_3$) δ 0.60–1.80 (60H, m), 1.95–2.12 (4H, m), 2.12–2.42 (7H, m), 2.95–3.12 (1H, m), 4.20–4.43 (4H, m), 7.16–7.22 (4H, m, Ar); MS (FAB) *m*/*z* 822 ($M^+ + 1$); anal. calc. for $C_{46}H_{80}O_8P_2$ (823.0839): C, 67.13; H, 9.80. Found: C, 67.72; H, 9.76%.

(−)-Dimenthyl 2-hydroxyphenyl phosphate (6). **6** was prepared by the reaction of 1,2-phenylene phosphorochloridate (2.0 g, 10.5 mmol) with (−)-menthol (1.4 g, 9.0 mmol) in pyridine for 16 h at 100 °C. After workup, the residue was subjected to flash column chromatography over silica gel with an ethyl acetate–hexane (1 : 4) eluent to give **6** as a white solid: yield 0.84 g (20%); mp 92–94 °C; $[\alpha]_D^{20}$ −64.5 ($c = 0.5$, CH_2Cl_2); UV (pentane) $\lambda_{max} = 271$ nm ($\varepsilon = 1523$ dm^3 mol^{-1} cm^{-1}); IR (KBr) ν 1290 cm^{-1} (P=O); ^{1}H NMR ($CDCl_3$) δ 0.68 (3H, d, $J = 6.8$ Hz, CH_3), 0.81 (3H, d, $J = 6.8$ Hz, CH_3), 0.82 (3H, d, $J = 6.8$ Hz, CH_3), 0.88 (3H, d, $J = 6.8$ Hz, CH_3), 0.9 (6H, d, $J = 6.8$ Hz, CH_3), 0.90–1.80 (14H, m), 2.0–2.10 (1H, m), 2.13–2.30 (3H, m), 4.23–4.40 (2H, m), 6.80–6.85 (1H, m, Ar), 7.0–7.10 (3H, m, Ar), 8.60–9.0 (1H, s, OH); MS (FAB) *m*/*z* 467 ($M^+ + 1$); anal. calc. for $C_{26}H_{43}O_5P$ (466.5982): C, 66.93; H, 9.29. Found: C, 66.45; H, 9.22%.

(−)-Dimenthyl 2-methoxyphenyl phosphate (2c). **2c** was prepared by the reaction of **6** (220 mg, 0.47 mmol) with dimethyl sulfate (63 mg, 0.5 mmol) in the presence of potassium carbonate (86 mg, 0.62 mmol) in acetone. After workup, the residue was subjected to flash column chromatography over silica gel with an ethyl acetate–hexane (1 : 6) eluent to give **2c** as colourless oil: yield 181 mg (80%); $[\alpha]_D^{20}$ −70.3 ($c = 0.5$, CH_2Cl_2); UV (pentane) λ_{max} 271 nm ($\varepsilon = 1945$ dm^3 mol^{-1} cm^{-1}); IR (neat) ν 1290 cm^{-1} (P=O); ^{1}H NMR ($CDCl_3$) δ 0.68 (3H, d, $J = 6.8$ Hz, CH_3), 0.81 (3H, d, $J = 6.8$ Hz, CH_3), 0.82 (3H, d, $J = 6.8$ Hz, CH_3), 0.88 (3H, d, $J = 6.8$ Hz), 0.91 (6H, d, $J = 6.8$ Hz), 0.90–1.80 (14H, m), 1.90–2.10 (1H, m), 2.20–2.30 (3H, m), 3.83 (3H, s, OCH_3), 4.20–4.40 (2H, m), 6.80–6.92 (2H, m, Ar), 7.08–7.13 (1H, m, Ar), 7.30–7.40 (1H, m, Ar); MS (FAB) *m*/*z* 480 (M^+); anal. calc. for $C_{27}H_{45}O_5P$ (480.6251): C, 67.48; H, 9.44. Found: C, 67.34; H, 9.37%.

Acknowledgements

We thank Dr Simon Everitt at the Inoue Photochirogenesis Project, for discussions and insights, as well as corrections and improvements arising from preliminary reading of this manuscript.

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