

Mediation of Conformationally Controlled Photodecarboxylations of Chiral and Cyclic Aryl Esters by Substrate Structure, Temperature, Pressure, and Medium Constraints

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Abstract: An aryl alkanoate, 2,4,6-trimethylphenyl (*S*)-(+)-2-methylbutyrate, whose ester group has a chiral center alpha to the carbonyl carbon and in which photo-Fries rearrangements are blocked by methyl substituents, undergoes facile photodecarboxylation under a variety of conditions and with complete retention of configuration. In fact, the decarboxylation process has many of the attributes of a symmetry-allowed suprafacial [1,3]sigmatropic rearrangement. The process requires concerted extrusion of carbon dioxide in a spiro-lactonic transition state, which has been investigated using high level DFT and CIS calculations: thermally less stable *s-cis* conformers in the ground and excited singlet states play an important role in determining the competitive efficiency of the process. Conformational control has also been imposed by substrate structure, solvent interactions, temperature, and applying external pressure, as well as using constraining media such as cyclodextrins and polyethylene films. The results are correlated with steady-state and dynamic fluorescence measurements at various temperatures in order to investigate further degrees to which ground and excited singlet state conformations affect the different photoreactivity channels available to the aryl esters.

Introduction

Photo-Fries rearrangements (Scheme 1, paths A and A') are the most common and best investigated photoreactions of aryl alkanoates.^{1–9} The reaction is generally devoid of large amounts of side products (other than those from separation of the radical pair and subsequent H-atom abstractions), and the quantum yields are usually 0.1–0.3. CIDNP experiments indicate that aryloxy–carbonyl bond cleavage proceeds from excited singlet states, leading to acyl–aryloxy radical pairs.^{10–12} In simple

phenyl esters, the acyl radical then adds at the *ortho* or *para* position of phenoxy (based on their high spin densities) or reforms a bond with the phenoxy oxygen (regenerating the initial ester in its ground state). The so-formed *ortho* or *para* adducts are keto intermediates that tautomerize to the isolated acylphenol photoproducts: a flash photolysis study of phenyl acetate has detected the presence of two transient species (presumably the keto intermediates) whose different rates of decay can be correlated with the rates of appearance of the *o*- and *p*-acetylphenols.^{13,14}

Another potential photoreaction of aryl esters, decarboxylation (Scheme 1, path C), has been investigated to a much smaller extent, largely because it usually represents a minor reaction pathway during the photolyses. However, when the structures of aromatic esters or their environments are “engineered” correctly, photodecarboxylation can be an important reaction component.¹⁵ For example, irradiations of 2-*tert*-butylphenyl and 2,4,6-trimethylphenyl pivalates and 3,5-di-*tert*-butylphenyl benzoate have been reported to give 1%, 5%, and 7–14% yields, respectively, of the corresponding decarboxylation products.^{16,17}

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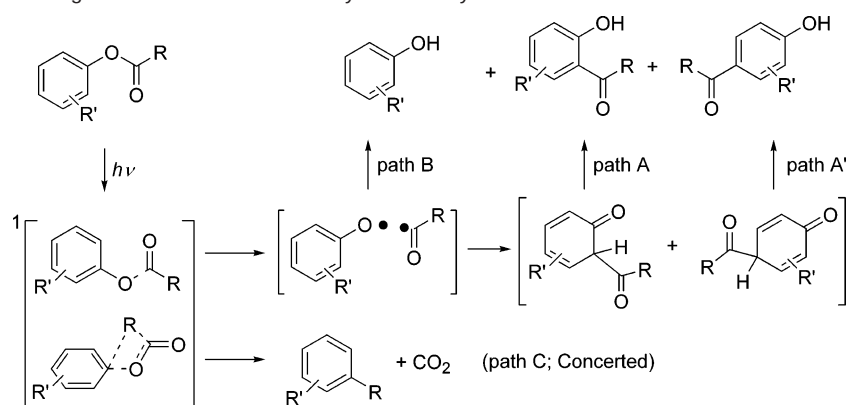
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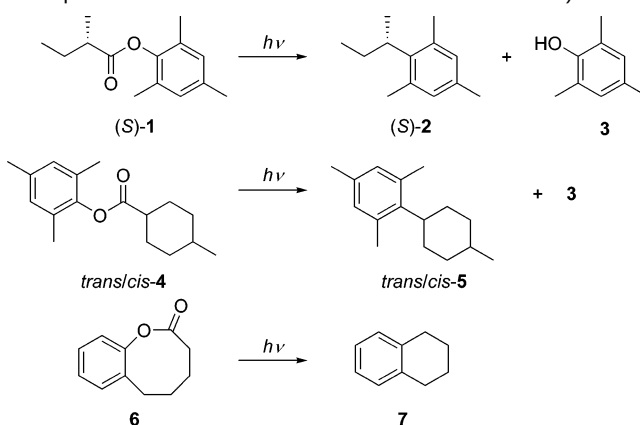
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Scheme 1. Photo-Fries Rearrangements and Photodecarboxylation of Aryl Esters

Prolonged irradiation of *p*-tolyl ferrocenoate also yielded ferrocenoic acid and *p*-tolylferrocene in 2% and 5% yields, respectively.¹⁸ Photoreaction of the coumarin derivative, diacetylhexahydromarmesin, in ethanol afforded 4% of decarboxylation product together with photo-Fries rearrangement and cage-escape products (30% and 13% yields, respectively).¹⁹ In all of these cases, the yield of photodecarboxylation is low, and concomitant formation of photo-Fries and cage-escape products were observed. Recently, we have prepared 2,4,6-trimethylphenyl (mesityl) esters, which generally provide good yields of decarboxylation products upon irradiation.^{20,21} For instance, photolysis of mesityl cyclohexanecarboxylate in acetonitrile affords the decarboxylation product in good yield in the absence of acid, while, in the presence of a catalytic amount of acid and alcohol, the same substrate undergoes efficient transesterification.²⁰

Here, we investigate the photodecarboxylation of chiral aryl ester mesityl (*S*)-(-)-2-methylbutanoate (**1**), 2,4,6-trimethylphenyl *trans*-4-methylcyclohexanecarboxylate (**4**), and a structurally constrained cyclic ester, 3,4,5,6-tetrahydro-2*H*-1-benzoxcin-2-one (**6**), under a variety of conditions to distinguish whether a concerted or a stepwise mechanism is operative and to determine how the photodecarboxylation pathway can be optimized by varying several environmental reaction conditions (e.g., temperature, solvent, pressure, and confinement in cyclodextrins and polyethylene films). We did not try to analyze for the other fragments from the cage escape products; we focused on the aromatic part of the fragments throughout the studies. The decarboxylation process has many of the attributes of a symmetry-allowed suprafacial [1,3]sigmatropic rearrangement.^{22–24} The natures and the divisions among the various photoreactions available to **1** (and to **4** and **6**) must depend on the ground and excited states conformational equilibria as well as the rates at which various conformers interconvert; in that regard, the *s-cis* conformer must be the immediate precursor of the decarboxylation if it is concerted and proceeds with retention of configuration of the chiral center (Scheme 1). It is the only conformation capable of attaining directly the spiro-lactonic transition state that allows expulsion of carbon dioxide while

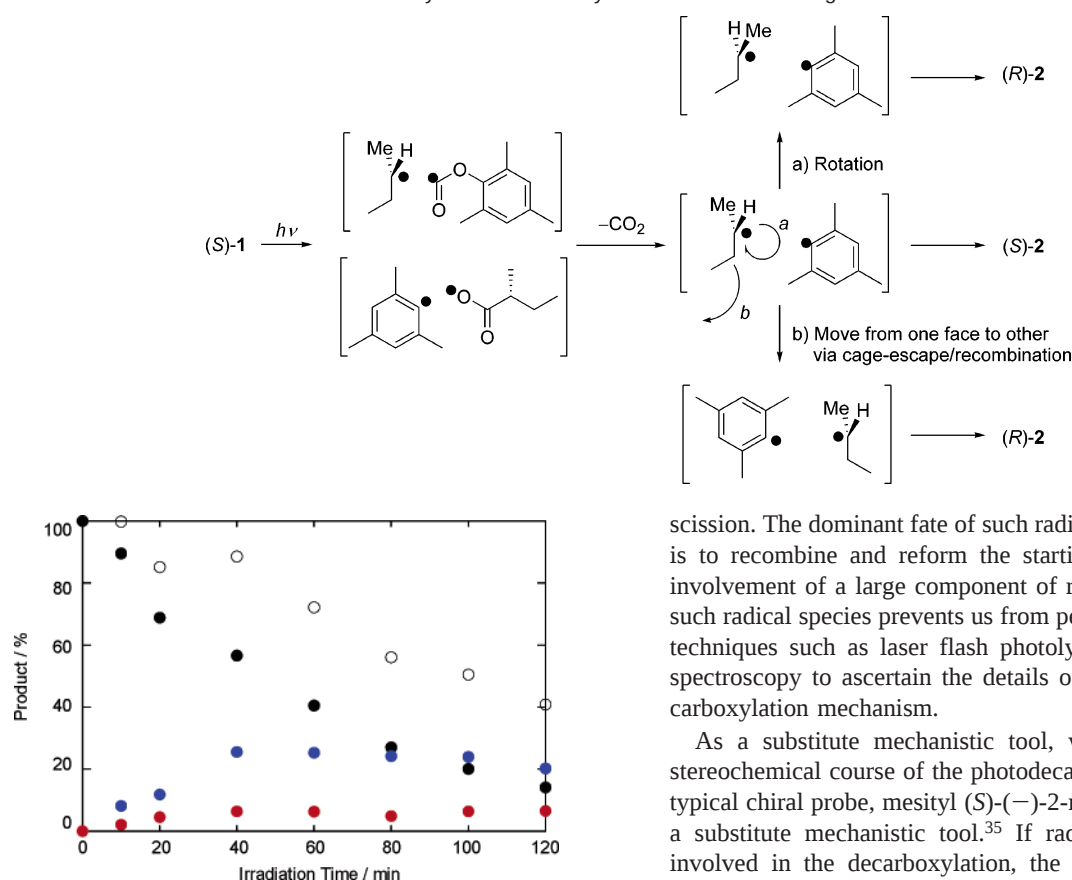
Scheme 2. Photodecarboxylation of Aryl Esters (Additional Photoproducts from Photo-Fries Reactions Are Not Shown)

retaining the stereochemical integrity of the chiral carbon center. The properties of the excited singlet state precursors to the reactions have been interrogated as well by steady-state fluorescence measurements at various temperatures and dynamics of the fluorescence, and their equilibria (especially between the key *s-cis* conformer and other conformers such as the *s-trans*) have been investigated computationally. Complete stereospecificity and reaction specificity, leading exclusively to the photodecarboxylation product, have been achieved during irradiation of **1** in unstretched high-density polyethylene films.

Results and Discussion

Irradiation at 254 nm of chiral ester **1** in acetonitrile at -25°C under an argon atmosphere leads to efficient decarboxylation to yield alkylmesitylene **2** in good yields. A smaller amount of 2,4,6-trimethylphenol (mesitol, **3**) was also obtained, in which the cage-escape process is also operative (Scheme 2). Time profiles for the distribution and appearance of the products (Figure 1) were monitored by GC. Prolonged irradiation (>40 min) did not increase the yield of photoproducts despite the continued loss of starting ester **1**. Secondary reactions, such as photoisomerization of the alkylbenzene²¹ or dimerization of the phenol, must become competitive with formation of additional **2** and **3** from remaining **1** under these conditions. Irradiations conducted for 1 h under a variety of experimental conditions (i.e., high conversions of **1**) resulted in poor material balances (30–60%) but did provide large amounts of photodecarboxylation product for stereochemical analyses; material balances were almost quantitative after 10-min irradiation periods and

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Scheme 3. Potential Routes for Loss of Chirality in the Decarboxylation Product Assuming a Radical Mechanism**Figure 1.** Product distribution from (S)-1 in acetonitrile under argon at $-25\text{ }^{\circ}\text{C}$ versus irradiation time. Black: (S)-1. Blue: 2. Red: 3. Open circle: material balance (1 + 2 + 3).

remained good ($>85\%$) after 20–40 min of photolysis. Therefore, irradiations where mechanistic information was sought from the product distributions were usually stopped after 10–20% conversions of ester, corresponding to 5–10 min of irradiation at room temperature and longer periods at subambient temperatures.

Retention of Chiral Configuration during Photodecarboxylation of 1. The mechanism of decarboxylation of benzylic-type molecules has been well documented, and the reaction has exploited to synthesize difficult to make species, such as cyclophanes.^{25–28} The mechanism involves homolysis to form benzyl radical pairs, most of which react within the solvent cage (to yield the decarboxylation product(s)) faster than escaping from it.^{29–32} In contrast, the mechanism of decarboxylation of aryl esters has been less investigated even though the photodecarboxylation has been observed, especially when the pathways leading to photo-Fries products are fully or partially blocked by substituents of the aryl portions of the esters. Even in those cases, the major process occurring in the excited singlet states remains the initial step in the photo-Fries reactions, β -bond

scission. The dominant fate of such radical pair intermediate(s) is to recombine and reform the starting esters.^{20,21,33,34} The involvement of a large component of reaction proceeding via such radical species prevents us from performing studies using techniques such as laser flash photolysis and transient EPR spectroscopy to ascertain the details of the (*minor*) photodecarboxylation mechanism.

As a substitute mechanistic tool, we have followed the stereochemical course of the photodecarboxylation of a prototypical chiral probe, mesityl (S)-(-)-2-methylbutanoate (**1**), as a substitute mechanistic tool.³⁵ If radical intermediates are involved in the decarboxylation, the resultant photoproduct should suffer loss of some chiral integrity. Such an approach was employed qualitatively by Finnegan and Knutson in 1967.³⁶ They isolated a 15–20% yield of the decarboxylation product after irradiating optically active 3,5-di-*tert*-butylphenyl (S)-(-)-2-methylbutanoate in dioxane. The optical rotatory dispersion (ORD) spectrum of the product was a positive curve, suggesting the (S)-(-) configuration (i.e., net retention) based on the ORD spectrum of the phenyl analogue. Although the authors suspected that the degree of optical purity of the decarboxylation product was high, no quantification was possible with the information available. Such an approach using a chiral probe to determine the nature of the involvement by the radical species has been recently adopted for other systems.^{37–39}

In the present system, if photodecarboxylation involves a radical pair (i.e., cleavage of **1**, loss of CO_2 from one of the fragments, and then recombination), the chiral purity of **2** should be less than that of **1** because some of the radicals are expected to rotate or move from one face to the other (without rotating) before combining (Scheme 3). There is ample precedent for loss of at least partial stereointegrity in analogous thermal and photochemical reactions.^{40–45} The enantiomeric excess (ee) of

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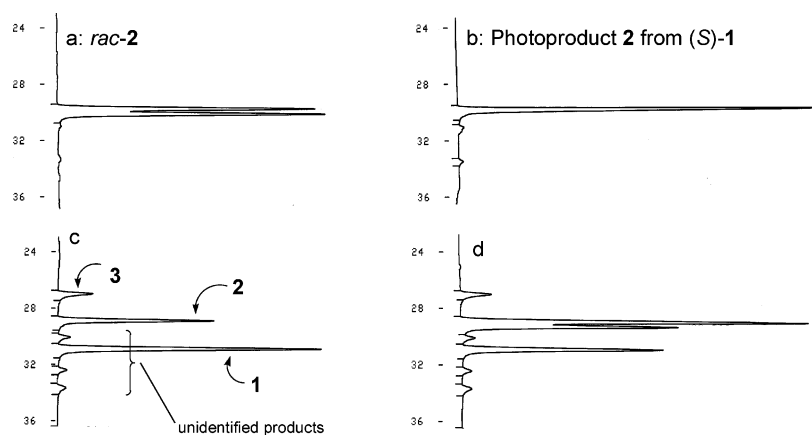


Figure 2. Chiral GC separation of **2** on a SUPELCO beta-DEX 325 column (30 m $\times$ 0.25 mm; thickness 0.25 μ m, column temp = 100 $^{\circ}$ C). For details, see Experimental Section in the Supporting Information. (a) Racemic **2**. (b) Photoproduct **2** obtained upon photolysis of (S)-**1**. (c) Typical chromatogram of photoproduct mixture. (d) Coinjection of racemic **2** and photolysis mixture. Note that the earlier retention time peak from **2** is the larger.

Table 1. Solvent and Temperature Effects on Irradiation of (S)-**1**^a

solvent	solvent properties ^b						[1] (mM)	T ($^{\circ}$ C)	irrad time (min)	conversion (%)	yields (%) ^c		2/3 ratio	ee of 2 (%) ^d	MB ^e
											2	3			
acetonitrile	0.34	1.344	35.94	3.95	45.6	14.1	2.0	-25	60	73	59	14	4.2	>99.5	48
							2.0	25	60	93	61	32	1.9	>99.9	39
							2.0	25	60	76 ^f	67	9	7.4	>99.5	32
							2.0	25	60	76 ^g	35	41	0.85	>99.5	61
							2.0	75	60	89	53	36	1.5	>99.5	28
							3.1	0	5.0	19.7 $\pm$ 0.7	78.8 $\pm$ 2.6	13.3 $\pm$ 1.0	5.92	>99	92
acetonitrile (purified) ^h	0.34	1.344	35.94	3.95	45.6	14.1	3.1	0	5.0	19.3 $\pm$ 0.5	58.9 $\pm$ 4.1	11.3 $\pm$ 1.2	5.21	>99	70
methylcyclohexane	0.73	1.423	2.02	0			3.1	-95	24 h	not detected	not detected	not detected	nd ^j	nd ^j	nd ^j
							3.1	-80	24 h	0.1 $\pm$ 0.1	not detected	not detected	nd ^j	nd ^j	nd ^j
								-45	30	8.9 $\pm$ 0.4	78.6 $\pm$ 11.6	19.5 $\pm$ 3.0	4.03	>99	98
								-25	10.0	7.3 $\pm$ 0.2	82.5 $\pm$ 5.0	15.5 $\pm$ 1.4	5.32	>99	98
								-10	10.0	14.4 $\pm$ 0.4	86.6 $\pm$ 2.7	12.7 $\pm$ 0.7	6.82	>99	99
								0	5.0	15.1 $\pm$ 0.4	82.9 $\pm$ 2.1	13.7 $\pm$ 0.6	6.05	>99	97
								+25	5.0	15.6 $\pm$ 0.4	76.5 $\pm$ 3.1	16.7 $\pm$ 0.5	4.58	>99	93
								+60	5.0	13.5 $\pm$ 0.3	68.0 $\pm$ 2.1	24.2 $\pm$ 1.6	2.81	>99	92
								+95	5.0	8.5 $\pm$ 0.2	60.3 $\pm$ 2.6	27.0 $\pm$ 3.2	2.23	>99	87
								0	5.0	15.8 $\pm$ 1.3	82.9 $\pm$ 2.1	13.7 $\pm$ 0.6	3.26	>99	98
diethyl ether	0.24	1.352	4.42	1.11	34.5	19.2	3.3	0	5.0	14.2 $\pm$ 0.8	74.7 $\pm$ 5.6	22.9 $\pm$ 1.5	4.08	>99	93
tetrahydrofuran	0.58	1.406	7.47	1.69	37.4	20	3.3	0	5.0	14.8 $\pm$ 0.1	58.0 $\pm$ 5.3	14.3 $\pm$ 0.2	4.70	>99	71
hexane (dried) ⁱ	0.31	1.375	1.89	0	31	0	3.1	0	5.2	26.4 $\pm$ 0.3	74.7 $\pm$ 4.7	18.3 $\pm$ 1.8	3.94	>99	47
methanol (dried) ⁱ	0.59	1.328	32.66	1.69	55.4	30	3.1	0	5.0	17.0 $\pm$ 0.5	37.8 $\pm$ 3.8	9.6 $\pm$ 0.4	4.06	>99	72
diglyme	0.46	1.408	7.3	1.92	38.6		3.1	0	5.0	12.6 $\pm$ 0.6	58.3 $\pm$ 4.1	12.4 $\pm$ 0.2	2.05	>99	83
propionitrile	0.41	1.366	28.86	4.04	43.6	16.1	3.4	0	5.0	16.9 $\pm$ 0.6	56.0 $\pm$ 13.8	27.3 $\pm$ 0.1	1.19	>99	72
dichloromethane	0.45	1.424	8.93	1.62	40.7	1	3.3	0	5.0	9.0 $\pm$ 0.3	39.3 $\pm$ 2.1	33.0 $\pm$ 1.1	7.12	>99	79
1,4-dioxane	1.44	1.422	2.27	0.46	36	14.3	3.1	+10	5.0	7.2 $\pm$ 0.8	69.1 $\pm$ 2.6	9.7 $\pm$ 1.0	1.44	>99	45
perfluorohexane	0.66	1.252	1.57				3.1	0	10.0						

^a All irradiations were carried out with a 30 W low-pressure mercury lamp (Eikosha PIL-type) in Pyrex tubes (diameter = 1 cm) under an argon atmosphere (λ = 254 nm), unless otherwise stated. ^b Solvent properties in reference shown: viscosity (mPa s), refractive index, permittivity, dipole moment, Reichardt's polarity $E_T(30)$, and donor number. From Abboud, J.-L. M.; Notario, R. *Pure Appl. Chem.* **1999**, *71*, 645–718. ^c Absolute yields of **2** and **3** based on consumed **1**, from an average of at least three separate experiments, except for 60-min irradiations. ^d %ee of product **2**, determined by chiral GC. Error = $\pm$ 0.2%. ^e Material balance (%). ^f Saturated with oxygen (ca. 8 mM). ^g In the presence of TEMPO (2.0 mM). ^h Acetonitrile (RdH, Chromasolv) was purified. See Experimental Section in the Supporting Information for details. ⁱ Hexane or methanol (RdH, Chromasolv) was distilled from CaH₂ under Ar. ^j Not determined.

the photodecarboxylation product **2** in our experiments was determined by chiral GC (Figure 2). A near baseline separation of the racemic product **2** was achieved and a <0.2% standard deviation of the error in the enantiomeric ratios could be maintained for the racemates. The detection limit of each enantiomer was $\sim$ 1% at the lower conversions of **1** and was 0.5% at higher conversions (e.g., 1-h irradiations). In some cases,

the product ee was also determined on a chiral HPLC (see Supporting Information for detailed conditions of analyses of ee's). None of the other isomers were detected, and the ee of **2** remained >99% when **1** was irradiated for 1 h in acetonitrile at temperatures between 75 and -25 $^{\circ}$ C. The addition of a radical trapping agent, TEMPO or molecular oxygen, to the acetonitrile solutions had no effect on the ee (Table 1). In one experiment at 25 $^{\circ}$ C, a known amount of racemic **2** was added and the mixture was analyzed by GC to ascertain the purity of the product **2**. The calculated ee of the photochemically produced **2** was >99.9%. The ee of **2** remained >99% regardless of the conversion of **1** and when any of the other experimental

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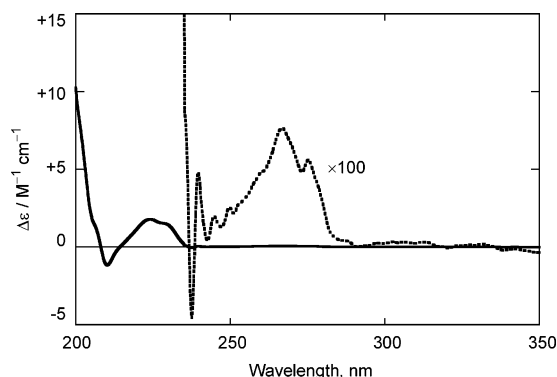


Figure 3. Circular dichroism spectrum of **2** from photolysis of (*S*)-**1** (1 mM) in hexane at 25 °C.

parameters (such as temperature, solvent, or pressure) was changed.

Although the data presented thus far demonstrate the stereospecificity of the photodecarboxylation reaction, they do not distinguish between complete retention and the less likely possibility, complete inversion. The specific rotation $[\alpha]_D$ in hexane of the photodecarboxylation product **2** (+11.9°) is nearly the same as that of (*S*)-(+)-**1** (+11.7° in chloroform), and although they depend somewhat on solvent,⁴⁶ they remain similar within any one solvent. This result suggests that the decarboxylation process occurs with *retention* of configuration. This assertion has been confirmed by circular dichroic (CD) spectroscopy of the product **2** in hexane (Figure 3). A weak positive Cotton effect in the 1L_b band region and fairly strong positive and negative Cotton effects at shorter wavelengths were found: molar circular dichroism ($\Delta\epsilon$) values were +0.063 (264 nm), +1.78 (224 nm), and -1.16 (210 nm) $M^{-1} cm^{-1}$, and these extrema correspond to the maxima in the UV absorption spectrum ($\log \epsilon = 3.35$ (268 nm), 4.68 (222 nm, sh), and 5.39 (203 nm)). According to the benzene chirality and benzene sector rules,^{47–52} a positive Cotton effect in the 1L_b band region must be from the (*S*)-isomer. The CD spectrum was also very similar to other chiral (*S*)-alkenylbenzenes.⁵³ Our conclusion that the photodecarboxylation proceeds with *net retention* of configuration is further demonstrated by the *diastereospecific* photodecarboxylation of **4** (vide infra). These results exclude involvement of radical pairs during the photodecarboxylation of aryl esters, at least those like the ones investigated here.

Solvent Effects on the Competition between Photodecarboxylation and Photo-Fries Processes. The distribution of photo-Fries products and the ratio of decarboxylation to Fries product yields are known to be solvent dependent.^{54,55} Table 1 summarizes the results from irradiations of **1** for 5 min at 0 °C (typically 10–20% conversions) in a variety of solvents; reaction was performed at 10 °C in 1,4-dioxane because of its melting

point. As reported previously,^{21,56} the photoproduct distributions from aryl esters can depend on the method that some solvents are purified. Indeed, the photoproduct distributions from **1**, **4**, and **6**, but not the enantio- or diastereo-purity of the decarboxylation products, did depend (reproducibly within the same solvent batch) on the source of some solvents or how they were purified. However, the results could be reproduced whenever a solvent from the same batch was employed for the photolysis. Except as indicated, the data reported here were obtained from one batch for each solvent. We suspect that the source of this dependence is trace impurities within the solvents that react rapidly with the radical intermediates, but the results indicate that “purification” increases the concentrations of these species!

The highest yields of **2** were obtained in methylcyclohexane and in acetonitrile, the 2/3 ratio being 6.1 and 5.9, respectively, at 0 °C. Purification of acetonitrile (see the Experimental Section in the Supporting Information for details) increased the relative yield of the cage-escape product slightly; the ratio of 2/3 was 5.2, but surprisingly, the material balance was significantly lower than that when the irradiation was conducted in nonpurified acetonitrile. Better yields of photo-Fries rearrangement products from 2-naphthyl esters have been reported in spectrograde hexane than in purified hexane.⁵⁶ Reaction of **1** in (nonpurified, not spectrograde) propionitrile afforded a lower 2/3 ratio with lower material balance than that in acetonitrile. Reaction in distilled hexane also afforded a lower relative yield of **2** and a much lower material balance (47%) than in undistilled hexane.

The highest 2/3 ratio from reaction in an isotropic solution, 7.1, was found in 1,4-dioxane (at 10 °C). In dichloromethane, the relative yields of **2** and **3** were almost equal and the yield of **3** was actually higher than that of **2** in perfluorohexane, where the material balance was poor. Although the ionic liquid, 1-ethyl-3-methyl-1*H*-imidazolium tetrafluoroborate, has been used as a “green” photochemical solvent for several transformations,^{57–59} no conversion of **1** was detected after prolonged irradiation, probably as a result of absorption of the radiation by the medium. No direct correlation between the product distributions and solvents parameters such as viscosity and polarity was obvious to us.

Like the photo-Fries rearrangement, the photodecarboxylation reaction is believed to occur from excited singlet states.^{31,60} Attempted triplet sensitization of **1** (3 mM) in acetone ($E_T = 332$ kJ/mol) as solvent and sensitizer, using >280 nm where acetone absorbs strongly and **1** does not, was unsuccessful. No conversion was detected even after 6 h of irradiation. After irradiation for 24 h, small amounts of unknown products were observed, but no **2** or **3** could be detected. The estimated triplet energy of the ester **1** is ~330 kJ/mol.⁶¹ Other triplet sensitizers whose energies are probably somewhat lower than the triplet of **1**, such as acetophenone ($E_T = 310$ kJ/mol) and benzophenone ($E_T = 287$ kJ/mol), were also unsuccessful. Similarly, reactions of aryl esters **1** and **4** were not hindered by addition of naphthalene ($E_T = 253$ kJ/mol, ca. 10 mM), a known quencher of triplet states of aromatic esters.⁶² Although these

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Table 2. Temperature Dependence on the Photochemistry of *cis/trans* Mixtures of **4** in Methylcyclohexane^a

T (°C)	irrad (min)	conversion ^b (%)	Z/E ratio of recovered 4	yields (%) ^c		5/3 ratio	Z/E ratio of 5	material balance (%)
				5	3			
−80	24 h	1.4 ± 0.1	63.7:36.3	not detected	not detected	n.d. ^d	n.d. ^d	98
−45	30	5.2 ± 0.1	63.2:36.8	92.4 ± 10.9	16.0 ± 9.2	5.78	66:34	104
−25	10	14.6 ± 0.6	63.2:36.8	78.9 ± 2.1	12.2 ± 0.7	6.47	63:37	91
−10	10	13.3 ± 0.5	63.4:36.6	77.9 ± 4.3	13.5 ± 0.9	5.77	64:36	91
+25	5	14.8 ± 0.6	63.7:36.3	75.1 ± 11.5	21.9 ± 0.9	3.43	64:36	97
+60	5	20.5 ± 1.4	63.8:36.2	61.9 ± 7.8	27.7 ± 1.5	2.23	63:37	90
+95	5	10.7 ± 0.3	63.5:36.5	57.6 ± 5.1	33.7 ± 0.9	1.71	64:36	91

^a Initial concentration of **4** was 3.6 mM (Z/E = 64.2:35.8). For irradiation conditions, see footnote a in Table 1. ^b All reactions were repeated at least 3 times, and the results were averaged. ^c Absolute yields based on consumed **1**. ^d Not determined.

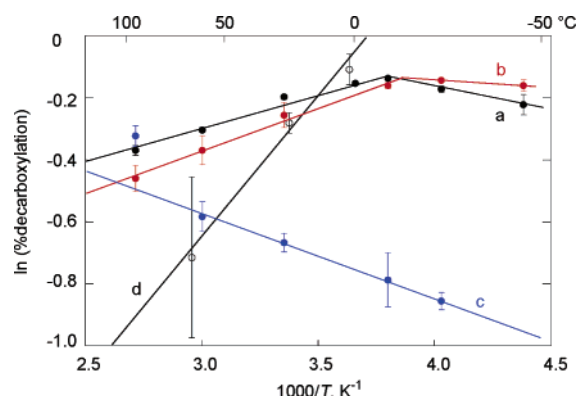


Figure 4. Arrhenius-type plots of the temperature dependence of relative yields of photodecarboxylation products from irradiations of (a) **1**, (b) **4**, and (c) **6** in methylcyclohexane solutions and (d) of **1** in PE46(u) film. Best linear fits are drawn as well. Data below and above −10 °C were used for individual fits for **1** and **4** in methylcyclohexane. The datum at 95 °C was omitted in fitting data from **6**.

experiments do not rule out a triplet photodecarboxylation mechanism, they and the complete retention of configuration of the decarboxylation products strongly implicate the singlet manifolds; only an adiabatic transformation of triplet **1** to triplet **2** could accommodate the stereochemistry of the reaction.

Influence of Temperature on the Competition between Photodecarboxylation and Photo-Fries Reactions of **1.** The dependence of temperature on the ratio of **2/3** was examined in (one batch of spectrograde) liquid methylcyclohexane between −95 and +95 °C. The temperature dependence of the fluorescence spectra of **1** was also studied in the same solvent between −120 and +100 °C (vide infra). Photolyses below −80 °C were extremely slow, and only trace conversions of **1** were observed at −80 °C after 24 h irradiation. By contrast, 15% conversion was achieved after 5-min irradiation at 0 °C. Reaction became faster as the temperature was increased, but it slowed slightly above 25 °C. Similarly, the highest **2/3** ratio, 6.8, was obtained at 0 °C, and a plot of the relative yield of **2** versus reciprocal temperature could be fitted to two linear segments (Figure 4). A change in the relative efficiencies of the two photoprocesses responsible for **2** and **3** is clearly occurring near 0 °C. Regardless of the reason for this interesting temperature effect, the cage-escape product **3** cannot be avoided simply by changing temperature (or solvent).

Photodecarboxylation of 2,4,6-Trimethylphenyl *trans*-4-Methylcyclohexanecarboxylate (4**).** The photodecarboxylation of *trans*-**4** has been examined on a preparative scale in purified acetonitrile at 25 °C (Scheme 2). After 3-h irradiation under

argon, decarboxylation product **5** (23% yield; 32% based on consumption of **4**) and 2,4,6-trimethylphenol (13%) were isolated after purification on silica gel column chromatography. The product **5** was determined to be only the *trans*-isomer by ¹H NMR spectroscopy: the coupling constant of the triple-triplet at δ 2.90, J = 12.4 and 3.7 Hz, corresponding to the proton adjacent to the aromatic moiety is indicative of axial–axial and axial–equatorial proton couplings (see Supporting Information for details). This assignment is consistent with our previous conclusions that photodecarboxylation is concerted and proceeds with retention of configuration.³⁵

The influence of temperature on irradiations of **4** was also examined using a Z/E mixture of esters in methylcyclohexane (Table 2). The trends are very similar to those mentioned above for the photolysis of **1**. At low temperature, −80 °C, the reaction proceeded very slowly, and the best yield of photodecarboxylation product was obtained at −25 °C. The relative yield of **5** decreased at either higher or lower temperatures; the “critical temperature” of **4** is slightly lower than that for **1**. Again, a plot of the relative yields of **5** versus the inverse of temperature could be fitted to two linear segments (Figure 4); similar mechanistic changes must be occurring in **1** and **4**.

Interestingly, the Z/E ratios of recovered **4** were always slightly lower than the initial value, 1.79, because the reaction of the Z-isomer, which is sterically more constrained,^{63–65} was slightly more efficient than that of the E-isomer. However, the differences were so small that Z/E ratios of the decarboxylation photoproduct were essentially the same as the initial ratio of the ester at all temperatures examined.

Photolyses of 3,4,5,6-Tetrahydro-2H-1-benzoxocin-2-one (6**).** Photodecarboxylation of some lactones has been reported but only for a limited set of compounds.^{66,67} The more common photochemical course for benzolactones with five-, six- (such as 2,3-dihydrocoumarin), or seven-member rings is transesterification in the presence of an excess of alcohol.⁶⁸ Here, we have examined the photochemistry of a benzolactone with an eight-membered ring, 3,4,5,6-tetrahydro-2H-1-benzoxocin-2-one **6**, expecting that its favored conformations might be more amenable to concerted decarboxylation.

Irradiation of **6** gave the corresponding decarboxylation product, tetrahydronaphthalene **7**, in good yields despite the

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Table 3. Temperature Dependence of the Photochemistry of **6** in Methylcyclohexane^a

T (°C)	irradiation time (min)	conversion ^b (%)	yield of 7 (%)	material balance (%)
−80	24 h	41.0 ± 3.0	19.5 ± 10.8	20
−45	10.0	27.9 ± 0.9	30.7 ± 0.8	31
−25	10.0	41.6 ± 2.1	42.5 ± 1.4	43
−10	5.0	33.2 ± 1.6	45.5 ± 5.0	46
+25	5.0	29.1 ± 0.9	51.3 ± 2.3	51
+60	5.0	27.0 ± 1.7	55.8 ± 4.6	56
+95	5.0	17.2 ± 0.8	72.4 ± 7.3	72

^a Initial concentration of **6** was 3.7 mM. For irradiation conditions, see footnote a in Table 1. ^b All reactions were repeated at least 3 times, and the results were averaged.

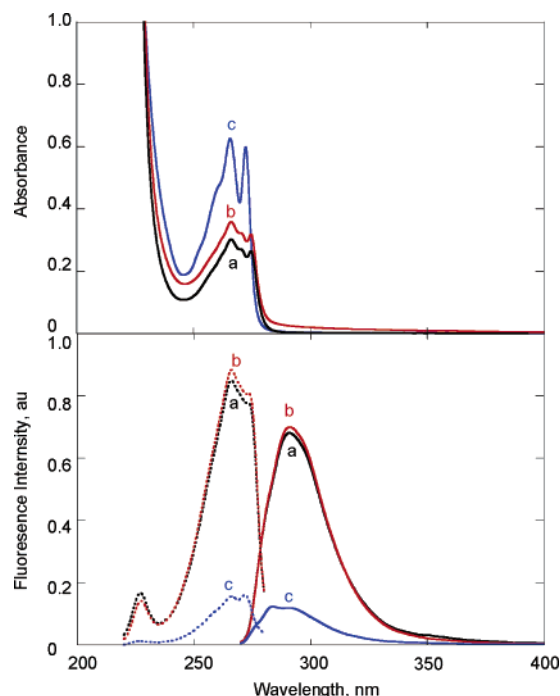


Figure 5. UV-vis absorption (top) and excitation and fluorescence (bottom) spectra of (a) **1**, (b) **4**, and (c) **6** (1 mM) in acetonitrile at 25 °C. Excitation and emission wavelengths were 266 and 290 nm, respectively.

availability of the *ortho* and *para* positions of the benzo ring for photo-Fries type rearrangements (Table 3). The other (unidentified) products are probably derived from ketene intermediates. Qualitatively, conversion of **6** was more efficient than that of **1** or **4**: after 5-min irradiation in methylcyclohexane at 25 °C, 33% of **6** was converted to products; under the same experimental conditions, 16% of **1** and 15% of **4** were converted. In contrast to the sluggish photoreactivity of **1** and **4** at low temperatures, decarboxylation of lactone **6** occurred even at −80 °C, albeit slowly, and 41% conversion was achieved after 24 h.

Absorption and Fluorescence Spectra of 1, 4, and 6. The absorption and fluorescence spectra of **1** were measured in methylcyclohexane and compared with those obtained in the more polar solvent acetonitrile (Table 4 and Figure 5). The UV-vis spectra of **1** were almost the same in both solvent, but the ¹L_b band was slightly blue-shifted in acetonitrile, suggesting partial n,π* nature of the transition. Absorption maxima at ca. 275 nm were vibrationally structured to some extent. The corresponding fluorescence spectra were measured in the same solvents, and the quantum yield of fluorescence Φ_{FL} = 0.027

was evaluated at λ_{ex} = 260 nm by comparison with the value for mesitylene in hexane (Φ_{FL} = 0.088).⁶⁹

The spectra of aryl esters **1**, **4**, and **6** were also compared in acetonitrile. Their absorption spectra are quite similar in shape, but some differences in vibrational structures are apparent. Molar extinction coefficients of **6** were almost twice as large as those of **1** and **4**. The fluorescence wavelength maxima of **1** and **4** were virtually the same, but that of lactone **6** was blue-shifted somewhat, suggesting that its relaxed excited-state and ground-state structures are more similar than those of the conformationally more labile **1** and **4**. As mentioned above, the most favored ground-state conformation of **6** is close to the structure necessary for excited-state decarboxylation. Because the fluorescence spectra were structureless, the singlet energies of **1**, **4**, and **6**, 423, 423, and 431 kJ mol^{−1}, respectively, were estimated from the midpoint of the maxima of the lowest energy absorption and fluorescence band.

Fluorescence lifetimes were obtained by the time-correlated single-photon counting technique (see Figure S-1 in Supporting Information for details). The decay constants of **1** in acetonitrile and methylcyclohexane were indistinguishable, but Φ_{FL} was much higher in methylcyclohexane. The quantum yield for consumption of **1** in acetonitrile at 254 nm excitation was determined to be ~0.02. The fluorescence lifetime and quantum yield of **1** and **4** are similar and larger than those of **6**, as expected from the richer n,π* nature and/or the lactone's higher reactivity.

Temperature Dependence of the Fluorescence of 1. In hopes of understanding better the interesting dependence of the photoproduct distribution from **1** on temperature, we investigated its fluorescence in (liquid) methylcyclohexane between −120 and +100 °C as well (Table 5 and Figure 6). As expected, the overall emission intensity decreased with increasing temperature due to increases in the rates of nonradiative processes.^{70–72} A linear correlation between fluorescence intensity and reciprocal temperature was observed in a temperature range of −120 to 0 °C. Above 0 °C, a somewhat stronger emission intensity than the expected (extrapolated) values were observed and another linear correlation is obtained (Figure 6).

Fluorescence maxima shifted from 288 nm at −120 °C to 295 nm at +100 °C (Δλ = 7 nm). These wavelength shifts suggest that the emission at higher temperatures occurs from a more relaxed excited singlet state and/or to a less relaxed ground state than at lower temperatures. One attractive hypothesis is that the *s-cis* conformation, which is a local minimum in the ground state but not the global energy minimum, fluoresces at relatively longer wavelengths than the *s-trans* and contributes to a greater extent at higher temperatures. The calculated distribution of ground-state conformers in the “gas phase” suggests that the population of *s-cis* conformer is essentially negligible (~0.01%) at room temperature. The energy differences of the *s-trans* and *s-cis* conformers are sufficiently large to preclude a significant population being present in the ground states. Each ground-state conformer would find it difficult to convert to another conformer within the short lifetime of the

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Table 4. Photophysical Data of Esters **1**, **4**, and **6**^a

ester	solvent	additive (amount)	absorption				fluorescence			E_s^b (kJ mol ⁻¹)
			$\lambda_{\max}$ (nm)	log ϵ	$\lambda_{\max}$ (nm)	log ϵ	$\lambda_{\max}$ (nm)	quantum yield, Φ_{FL}	τ_s (ns)	
(S)- 1	methyl- cyclohexane acetonitrile water	β -CD (10 mM)	275.2	2.48	266.6	2.52	291.2	0.027	1.6	423
			274.6	2.42	266.0	2.48	291.0	0.017	1.7	423
	water	γ -CD (10 mM)	274.0		265.8		288.2	0.005	0.2	426
			273.8		265.6		293.4	0.006	0.2	422
<i>trans</i> - 4 6	acetonitrile		274.6	2.50	266.0	2.55	291.0	0.013	1.8	423
	acetonitrile		272.4	2.78	265.6	2.80	283.6	0.0014	0.3	431

^a At 25 °C for 1 mM ester under air. ^b Estimated from midpoint of absorption and fluorescence maxima.

Table 5. Temperature Dependence of Fluorescence Spectra of (S)-**1**^a

T (°C)	$\lambda_{\max}(\text{emission})$, nm	I_{rel}^b	$\lambda_{\max}(\text{excitation 1})$, nm	$\lambda_{\max}(\text{excitation 2})$, nm	$I(\lambda_1/\lambda_2)^c$
-120	287.8	5.63	265.0	273.8	1.046
-100	288.2	4.71	265.2	274.0	1.042
-80	289.0	3.86	265.4	274.2	1.039
-60	289.2	3.03	265.8	274.4	1.038
-40	290.0	2.37	266.0	274.6	1.038
-20	290.4	1.80	266.2	274.6	1.041
0	291.6	1.34	266.4	274.8	1.045
+20	292.0	≡ 1	266.8	274.8	1.065
+40	292.8	0.772	267.0	274.4	1.088
+60	293.4	0.587	267.4	274.4	1.095
+80	294.0	0.444	267.6	274.2	1.098
+100	294.6	0.358	267.6	274.0	1.109

^a In methylcyclohexane for 1 mM solutions under air. ^b Relative fluorescence intensities obtained from integrated areas of spectra. ^c Ratio of intensities at 266 and 274 nm in excitation spectra.

singlet excited states; on this basis, we conclude that the observed fluorescence spectrum is mainly from the *s-trans* conformer. As the temperature is increased, the population of the less stable *s-cis* conformer in the excited state increases (vide infra). We believe an overall bathochromic shift in fluorescence maxima at higher temperature is derived from the partial contribution from excited *s-cis* conformers.

The positions of peaks in the excitation spectrum of **1** also shifted slightly to the red with increasing temperature. More pronounced changes were apparent in the ratios of the peak intensities at ca. 266 and 274 nm (Table 5); they increased from 1.04 at -100 °C to 1.11 at +100 °C. Because no analogous changes in the absorption spectrum could be detected, we conclude that more than one ground-state conformer is being excited and that equilibration among them is incomplete during the excited-state lifetime.

The temperature dependencies of the fluorescence quantum yields (Φ_{FL}), excitation spectra, and product distributions suggest that a different mix of excited species is present at lower and higher temperatures. We choose to interpret these species as predominantly the *s-cis* and *s-trans* conformers, with the content of the more energetic *s-cis* increasing at higher temperatures.

Photolysis of **1 in Solutions of Cyclodextrins.** Although their range of cavity sizes and shapes is rather limited (in contrast to the cavities available in the family of zeolites^{73–77}), cyclodextrins are very useful prototypes for supramolecular complexation and

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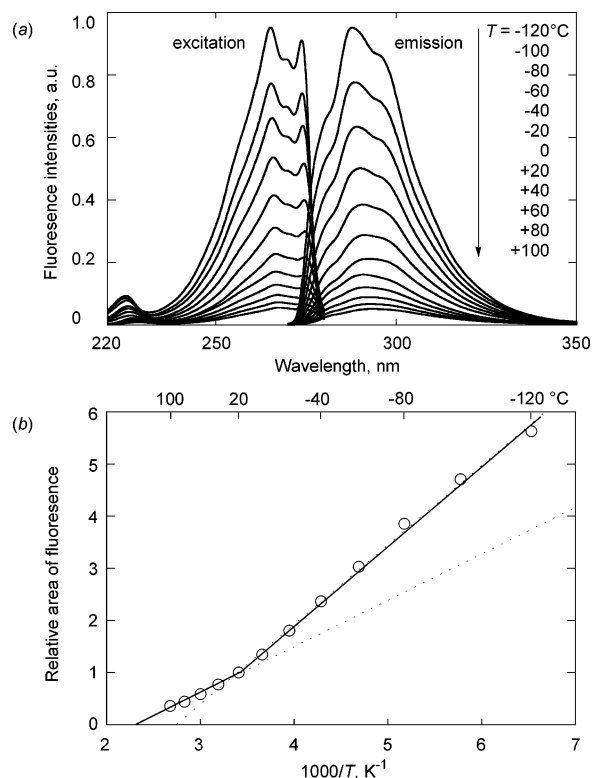


Figure 6. Temperature dependence of excitation and fluorescence spectral intensities of **1** (1 mM) in methylcyclohexane (a). Excitation and emission wavelengths were 266 and 290 nm, respectively. Plot of the integrated fluorescence intensities versus reciprocal temperature (b). The intersection of the two linear segments is at ca. 10 °C.

photochemical studies because they are readily available, easily used, transparent into the UV region, and chiral.^{78–84} A few photodecarboxylations of aryl esters have been reported in other supramolecular hosts, including polyethylene films,^{85,86} SDS micelles,⁸⁷ and cation-exchanged faujasites.⁸⁸

In view of the demonstrated sensitivity of the photoproduct distribution from **1** to its environment, we have irradiated

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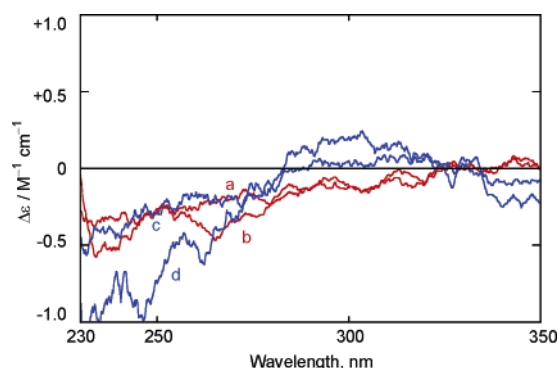
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Table 6. Irradiations of Racemic **1** in Aqueous and Aqueous Methanol Solutions of β - and γ -Cyclodextrins^a

host	solvent	irradiation time (min)	conversion (%)	combined yield of products (%)	2/3 ratio	ee of 2 ^b (%)	MB ^c
β -cyclodextrin	H ₂ O	20	43	6	1.8	2.0 (R)	63
		40	62	9	2.3	0.8 (R)	47
		60	80	11	2.3	0.4 (S)	31
		60	97	9	2.5	14.1 (R)	12
γ -cyclodextrin	H ₂ O	20	77	0	nd ^d	nd ^d	23
	H ₂ O/MeOH (1:1)	20	70	4	<0.05 ^e	nd ^d	34

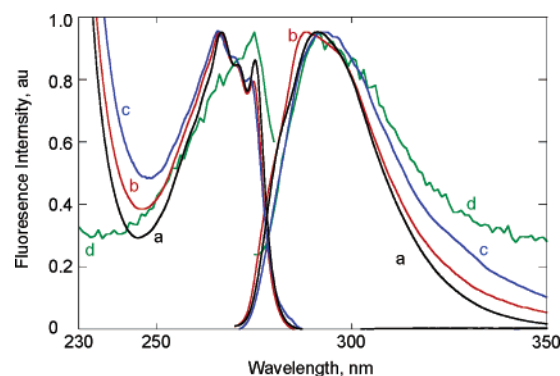
^a Initial concentrations of racemic substrate and β - or γ -cyclodextrin were 0.5 and 2.5 mM, respectively. Reactions at 25 °C under argon. For details, see footnote a in Table 1 and Experimental Section in the Supporting Information. ^b Percentage of ee determined by chiral GC. Error = $\pm 1.0\%$. ^c Material balance (%). ^d Not determined. ^e Photodecarboxylation product **2** was not detected by GC.

**Figure 7.** Induced CD spectra of racemic **1** (1 mM in H₂O) in the presence of (a) 5 mM and (b) 10 mM β -cyclodextrin and in the presence of (c) 5 mM and (d) 10 mM γ -cyclodextrin.

racemic **1** in cyclodextrin cavities. No chiral induction should be observed in **2** after partial conversion of **1** if the photodecarboxylation process is concerted *unless one of the enantiomers of 1 is more photoreactive in cyclodextrin complexes or is complexed to a different extent than the other.*

Initially, the induced CD spectra of **1** were examined spectroscopically in aqueous solutions of β - and γ -cyclodextrins (Figure 7). As the cyclodextrin concentration was increased from 1 to 10 mM, a weak, but appreciable, negative Cotton effect was induced in the 230–280 nm region, where the aryl ester absorbs the light. This indicates that the aryl ester **1** forms complexes with these cyclodextrins and the chromophoric moiety of **1** is included in the cyclodextrin cavity at least to some extent. Unfortunately, due to the weakness of the signals and the low solubility of **1** in water, it was not possible to evaluate the association constant *K* or to assess the exact alignment of the ester and cyclodextrins by applying the empirical Harata⁸⁹ and Kodaka rules.^{90,91}

The inclusion of **1** in cyclodextrin cavities has been investigated also by absorption and fluorescence spectroscopies (Table 4 and Figure 8). The low solubility of **1** precluded our measurement of its fluorescence decay or its absorption and fluorescence spectra in water alone; comparisons of spectral shifts here are based on values in methylcyclohexane. Absorption spectra of **1** are hypsochromically shifted by ~ 1 nm in

**Figure 8.** Normalized fluorescence spectra of **1** (1 mM) at 25 °C. Excitation and emission wavelengths were 266 and 290 nm, respectively. (a) In methylcyclohexane. (b) In 10 mM aqueous β -cyclodextrin. (c) In 10 mM aqueous γ -cyclodextrin. (d) In amorphous **PE0** film (ca. 50 mmol/kg·film). Note that the emission and excitation spectra in **PE0** are somewhat distorted by self-absorption phenomena.

aqueous solutions of β - and γ -cyclodextrins; very small changes were detected in the excitation spectra. In the presence of excess β -cyclodextrin, a 3-nm hypsochromic shift was observed in the emission spectrum, suggesting that the ester portion of **1** is in a relatively polar environment (i.e., outside or at the surface of the cavity). The emission maximum was shifted ca. 2 nm to the red upon complexation by γ -cyclodextrin, indicating that the chromophore is inside the cavity. In both types of cyclodextrins, the fluorescence decay constants of **1** in water (1 mM) in the presence of cyclodextrins (10 mM), ca. 0.2 ns, were significantly smaller than the 1.6–1.7-ns values observed in methylcyclohexane.

Results from photolyses of racemic **1** in aqueous β - and γ -cyclodextrin solutions at 25 °C are summarized in Table 6. Low (6–11%) combined yields of **2** and **3** and in much lower **2/3** ratios than those in organic solvents were obtained in β -cyclodextrin solutions of water or water/methanol, and the detectable unidentified byproducts were also observed in smaller amounts. Apparently, **1** undergoes photoreactions more efficiently with cyclodextrin than it does intramolecularly. Similar low yields have been reported for irradiations in aqueous β -cyclodextrin solutions of other aryl esters for which decarboxylation is a very minor reaction pathway.^{92–95} The preferences for β -bond scission and formation of **3** were expected

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Table 7. Irradiations of (S)-**1** in Polyethylene Films^a

film ^b	cryst ^c (%)	V _{PE} ^c (Å ³)	[1], mmol (kg film) ⁻¹	thickness (μm)	T (°C)	irrad time (min)	conversion (%)	yields (%) ^d		2/3 ratio	ee of 2 (%)	mass balance (%)
								2	3			
PE0 (u)	0	177	2.0	1.2 × 10 ³	23	60	28 ± 6	59 ± 7	13 ± 2	4.5	>98	92
PE46 (u)	46	139	2.7	82	2	90	23 ± 1	32 ± 4	10 ± 1	8.7	>98	89
					23	40	13 ± 1	18 ± 3	7 ± 1	3.1	>98	93
					60	48 ± 10	45 ± 20	5 ± 2	2.5	>98	64	
					65	20	26 ± 3	18 ± 7	19 ± 7	0.96	>98	83
					23	40	11 ± 2	42 ± 23	31 ± 17	1.4	>98	97
PE46 (s)	47	121	2.7	34	23	60	31 ± 5	19 ± 7	10 ± 4	1.9	>98	78
PE50 (u)	50	144	5.0	25	23	40	14 ± 2	3 ± 1	5 ± 2	0.62	>98	87
PE50 (s)	58	141	5.0	16	23	40	28 ± 5	2 ± 1	4 ± 1	0.59	>98	74
PE68 (u)	68	124	19	21	23	60	17 ± 3	44 ± 5	1 ± 1	82	>98	90
PE68 (s)	84	113	19	12	23	60	31 ± 5	51 ± 8	11 ± 2	4.8	>95	88
PE74 (u)	74	129	12	17	23	60	19 ± 2	32 ± 4	1 ± 1	82	>98	88
PE74 (s)	70	120	12	13	23	60	20 ± 3	38 ± 13	10 ± 3	4.0	>98	90

^a Irradiated with a low-pressure Hg lamp (ethanol filter, $\lambda = 254$ nm); samples under vacuum unless stated otherwise. Each datum is the average of at least 9 separate analyses of 3 films. ^c Crystallinities and calculated mean hole free volumes from positron annihilation studies. Gu, W.; Hill, A. J.; Wang, X.; Cui, C.; Weiss, R. G. *Macromolecules* **2000**, 33, 7801–7811. ^d Absolute yields based on consumed **1**.

based on the mode of complexation mentioned above (enhanced population to the extended conformation). When the aryl portion is not inside the cyclodextrin torus, the *s-cis* conformation required for photodecarboxylation is difficult to attain; the more extended *s-trans* conformation that favors **3** should be even more preferred than in organic solvents.

A small enantiomeric enrichment in the (*R*)-isomer of **2** from irradiation of racemic **1** in aqueous β -cyclodextrin was observed at low conversions; the enantioselectivity at high conversions was negligible. In aqueous methanol solutions of β -cyclodextrin, 14% ee of **2**, enriched in the (*R*)-enantiomer, was found at 97% conversion. Given the preponderance of evidence for the concertedness and retention of configuration of the photodecarboxylation, these results strongly suggest that one of the enantiomers of **1** reacts more rapidly than the other and that the reaction pathways of complexed and uncomplexed **1** differ. In an aqueous or aqueous methanol solution of γ -cyclodextrin, **1** was consumed upon irradiation, but no **2** was detected. No other low-mass products were observed (GC–MS analysis) in the aqueous medium, and only a 4% yield of **3** was found in the aqueous methanolic mixture. It appears that **1** reacts preferentially with the γ -cyclodextrin to which it is bound; the CD spectroscopic results above indicate that the aryl portion of **1**, at least, is within the torus, and spectroscopic analyses of the cyclodextrins after irradiation indicate that aromatic groups are covalently attached.

Photolysis of 1 in Polyethylene Films. In all of the experiments above, varying solvent and temperature, cleavage of **1** leading to **3** could not be eliminated. Thus, we investigated a different strategy, involving polyethylene (**PE**) films as the reaction medium, to improve the relative yields of **2** and to suppress the appearance of byproducts such as those found in cyclodextrin solutions. The **PE** films apply “passive” pressure to guest molecules^{96–98} that can influence ground-state conformations and rates of diffusion of pairs of species within one reaction cavity. Both are capable of directing the reactions of molecules in their excited states. The films employed here span a wide range of morphologies. One of their most important

properties, the percent of crystallinity, is indicated in each as a suffix to their **PE** acronyms, and “u” or “s” in parentheses refers to unstretched or cold-stretched films (see Experimental Section in Supporting Information for details); other physical parameters of these films have been reported elsewhere.⁹⁹

There are reasons to believe that **PE** films may be more amenable to directing the photochemistry of **1** than the other media examined above. Some conformational control of decarboxylation upon irradiation of 1-naphthyl esters in **PE** films and at various temperatures has been reported.¹⁰⁰ In addition, the fates of the prochiral radical pair intermediates from decarbonylation of the initial acyl/1-naphthoxy radical pairs, generated during irradiation of 1-naphthyl (*R*)-2-phenylpropanoate, have been used as a diagnostic of the motional freedom within cavities of **PE** films.¹⁰¹ These radical pair recombinations occur with significant stereoselectivity, *but they are not stereospecific*.

Results from the irradiations are summarized in Table 7. The material balances were quite high at <30% conversion (where most of the irradiations were analyzed to avoid secondary reactions) in all cases. The only photoproducts detected were **2** and **3**, and the enantiomeric excess of **2** was >98%, as in other media (above the detection limit; no other enantiomer was detected). In completely amorphous **PE0**, which lacks interfacial sites,⁹⁹ the 2/3 ratio was quite similar to that in methylcyclohexane solution at a comparable temperature. The large differences between the 2/3 ratios from **PE46**(u) and **PE50**(u), films of nearly the same crystallinity, indicate that the similarity between the ratios in methylcyclohexane and **PE0** is fortuitous. There is no clear trend between **PE** crystallinity or any other single physical property of the films we can identify and the relative yields of **2** (Table 7). The natures of the reaction cavities of each film, as well as the effect that they have on the conformations of **1**, must be determined by a combination of the properties. However, the two unstretched high density **PE** films, **PE68**(u) and **PE74**(u), afforded **2** (ee was above detection limit: >98%) almost exclusively (>98%); only trace amounts of **3** were detected. The reaction cavities of the two high-density **PE** films either force all of the molecules of **1** to adopt *s-cis*

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conformations or prohibit the radical pairs from the alternative reaction pathway leading eventually to **3**. We would discard the latter possibility to force the reformation of **1**, because the overall rate of the reaction in films was almost the same to (or slightly faster than) those observed in isotropic solutions, although the absolute rates were not obtained because of technical problems.

Stretching films affects leads to lower 2/3 ratios in all of the films employed. Film stretching of partially crystalline **PE** films redistributes microcrystallites more evenly within the amorphous domains, decreases mean hole free volumes, increases the area of the interfacial region and, thus, the fraction of guest molecules in interfacial cavities.⁹⁹ Stretching films also affect the shapes of the reaction cavities in each film, making them presumably more extended than in unstretched films. Distortion of the cavity shapes may be responsible for the increased relative yields of **3** in the stretched films because it should favor the more extended *s-trans* conformers. Despite these perturbations, the formation of **2** remains stereospecific; a radical mechanism must not be involved, even in the confining reaction cavities of the various unstretched and stretched **PE** films.

We were unable to obtain reliable fluorescence spectra of **1** in all of the **PE** films except **PE0** at a high doping concentration, ~50 mmol (kg film)⁻¹ (Figure 8). The shapes of the emission and the excitation spectra of **1** are almost identical to those in methylcyclohexane, although there appears to be some self-absorption in the **PE** films that distorts the blue edge of the emission and the red edge of the excitation. However, the fluorescence decay histograms in **PE0** are biexponential; the best fits have decay constants of 2.9 ns (37%) and 4.8 ns (63%). One explanation of these decays is that **1** is distributed in two different site types in **PE0** films, perhaps near and far from regions of high chain branching. Regardless, the much larger decay constants in **PE0** than in solution suggest that the esters are conformationally dissimilar in the films and in solution.

The influence of temperature between 2 and 65 °C on the photodecarboxylation of **1** in **PE46(u)** films has been compared with results from irradiations in methylcyclohexane (Figure 4). An Arrhenius-type plot of the relative yield of **2** (or the 2/3 ratio) is linear in **PE46(u)** but is clearly nonlinear in methylcyclohexane. The linearity of the plot in the polyethylene film is consistent with very minor conformational changes of **1** during its short excited singlet lifetime and, therefore, maintenance of the ground-state *s-cis/s-trans* equilibrium ratio. Substantial constraints to motions of **1** are imposed by the reaction cavities of the **PE46(u)**.

These constraints, coupled with cavities that either cause the *s-cis/s-trans* ratio to be very large or force initially formed radical pairs from incipient photo-Fries lyses of *s-trans* conformers to reform **1**, explain why reaction can be channeled to yield almost exclusively **2** in the unstretched high-density **PE** films. Such selectivity is synthetically useful because it is a two-step, high-yield synthesis of enantiopure alkylmesitylenes. Currently available methods for syntheses of similar molecules, but in lower optical purity, involve sophisticated transition metal catalyzed hydrogenations.^{102–104}

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Table 8. Effect of Pressure on the Photochemistry of **1**^a

pressure (MPa)	conversion (%)	yields ^b (%)		2/3 ratio	ee of 2 ^c (%)	MB ^d
		2	3			
0.1	23	43.5	8.7	5.0	>99	89
200	40	35.8	3.0	12	>99	76
350	n.d. ^e	8.8 ^f	<0.1	>50	>99	n.d. ^e
400	26	29.2	<0.1	>50	>99	82

^a Irradiation with an ultrahigh-pressure Hg lamp in a quartz cuvette installed in a high-pressure vessel for 1.8 mM of **1** in MeCN for 20 h under argon at 25 °C. See Supporting Information for details. ^b Absolute yields based on consumed **1**. ^c %ee determined by chiral GC. Error = ±0.5%.

^d Material balance (%). ^e Not determined. ^f Based on amount of substrate used.

Effects of Pressure on the Photochemistry of 1. Pressure effects on (asymmetric) photochemical reactions have been discussed in some depth recently.^{105–108} Pressure-induced changes in activation parameters¹⁰⁹ may be of use to mediate photoproduct selectivities of **1** in acetonitrile, and experiments at pressures up to 400 MPa have been conducted (using procedures described previously^{105,107}) to determine the magnitude of such effects (Table 9). At 350–400 MPa, the 2/3 ratios were >50 (i.e., no **3** was detectable) and the ee of **2** remained >99%.

Because the relative molecular volume calculated at the PM3 level for the *s-cis* conformer of **1**, the putative precursor of **2**, is much smaller than that of the *s-trans* conformer, the putative precursor of **3** (Table 8), the equilibrium between the two favors the *s-cis* as pressure is increased and free volume is decreased. In addition, high pressure would retard the separation of radical pairs from photo-Fries type processes (should they be formed from *s-trans* conformers), thereby attenuating the yield of **3** and accelerating the reformation of **1**. Although more experiments should be conducted in the future to quantify and analyze more deeply the pressure–volume relationship, the results in hand again indicate that the photoselectivity of **1** can be mediated by altering the *s-cis/s-trans* ground-state equilibrium. Whereas polyethylene films rely on “passive” pressure to effect (what may be) the equilibrium changes, these experiments demonstrate that “active” pressure can do the same.

Conformational Study of Aryl Ester 1. (i) By DFT Calculation of Conformational Energies. In order for photodecarboxylation to be concerted and proceed with retention of configuration, reaction must occur from the *s-cis* conformation of the excited singlet state of **1**. At least in “gas phase” calculations, the *s-trans* conformation is much more stable than the *s-cis* in both the ground and excited singlet states. Given that the quantum yields for decarboxylation are much larger than the fraction of **1** calculated to be *s-cis* in the ground state, a large fraction of the excited singlet *s-trans* species must change to the *s-cis* before reacting, and the *s-cis* must then react more rapidly than its return to the *s-trans* in order that photodecarboxylation may be a major pathway. These conditions must be

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Table 9. DFT Calculated Properties of the Four Conformers of **1** at Local Minima^a

conformation	optimized SCF energy (hartree)	zero-point correction (hartree/particle)	Gibbs free energy with thermal correction (hartree)	ΔG (25 °C) (kJ mol ⁻¹)	population (%)	μ (debye)	V^o (Å ³)
for 1							
<i>s-trans-anti</i>	-696.228 774 9	0.264 057	-695.969 893 4	≡0	90.3	1.52	269
<i>s-trans-syn</i>	-696.227 067 6	0.264 463	-695.967 788	+5.52	9.7	1.77	333
<i>s-cis-anti</i>	-696.218 470 5	0.264 25	-695.959 399 8	+27.5	0.01	4.02	236
<i>s-cis-syn</i>	-696.209 203 9	0.264 615	-695.949 775 4	+52.7	~0	4.12	330
for 6							
<i>s-trans</i>	-577.026 457 1	0.173 215	-576.856 637 1	≡0	99.8	2.33	221
<i>s-cis</i>	-577.020 743 9	0.173 428	-576.850 715 1	+15.5	0.2	4.13	215

^a At B3LYP/6-311G+(2d,p)/B3LYP/6-31G(d) level. Zero-point energies were scaled by 0.9804 and corrected. See also Figures 9 and 10 for the calculated conformations. 1 Hartree = 2625.5 kJ mol⁻¹. ^b van der Waals volumes calculated by the PM3 method for the DFT optimized conformations.

met because a large part of the photoreactions of **1** does go through the photodecarboxylation route under almost all of the experimental conditions we have explored.

Structural modifications that stabilize *s-cis* conformers at the expense of *s-trans* ones of aryl amides and aryl esters are known.^{110–112} For instance, although acetanilide exists almost completely in the *s-trans* form, introduction of alkyl groups in the *ortho* positions of the phenyl ring leads to detectable amounts of the *s-cis* form.^{113,114} Recently, *s-cis/s-trans* conformers of the triplet state of alkyl phenylglyoxylates were observed by means of time-resolved FTIR spectroscopy.¹¹⁵ Both conformations are known to exhibit similar (but appreciably different) reactivities in intermolecular hydrogen abstractions, but only the *s-cis* undergoes Norrish Type II photoelimination reactions. Although the short-lived excited singlet state of **1** cannot be detected by this technique, we believe that similar fast equilibration of conformers is operative. Therefore, DFT and CIS calculations¹¹⁶ of the conformers of **1** in the excited singlet state have been conducted.

Initially, ground-state geometries were optimized at the B3LYP/6-31G(d) level for the *s-cis* and *s-trans* conformations of **1**. They afforded four conformational energy minima (Table 9 and Figure 9). Among them, the two *s-cis* conformers are potential immediate precursors of the spiro-lactonic transition state required for concerted decarboxylation. All of the conformers have significantly larger molecular volumes than the mean free void volumes of the **PE** films (113–177 Å³),^{101,117} and thus, their reaction cavities are expected to impose some

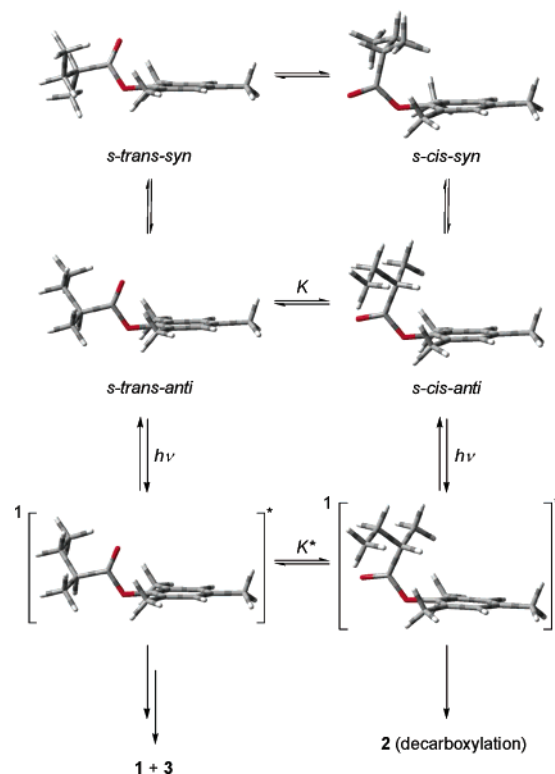


Figure 9. Possible conformations in the ground and singlet excited states of **1**. Optimized structures of *s-cis* and *s-trans* conformations were calculated at the B3LYP/6-31G(d) level for the ground states at the CIS(Nstates = 8)/6-31+G(d) level for the excited state.

constraints on shape changes of **1**. The optimized geometries at B3LYP/6-31G(d) level were further subjected higher-level (B3LYP/6-311+(2d,p)) single-point energy calculations that were corrected for their zero-point energies by applying an empirical factor of 0.98. The calculated (gas phase) distributions of the conformers using these energies predict only ca. 0.01% equilibrium population of *s-cis* at 25 °C. The quantum yield for decarboxylation of **1** in methylcyclohexane at 0 °C, ~0.2%, is much larger than the calculated ground-state population, suggesting (as noted above) that some *s-trans/s-cis* equilibration in the excited singlet state is occurring. Although the calculated (gas phase) and methylcyclohexane equilibria probably differ to some extent, the quantum yield value is the lower limit of the actual *s-cis* content in the excited state because not all of the excited singlets that attain the appropriate conformation may undergo decarboxylation.

Energies of the singlet excited-state conformers of **1** were also calculated at the CIS/6-31+G(d) level with Nstate = 8

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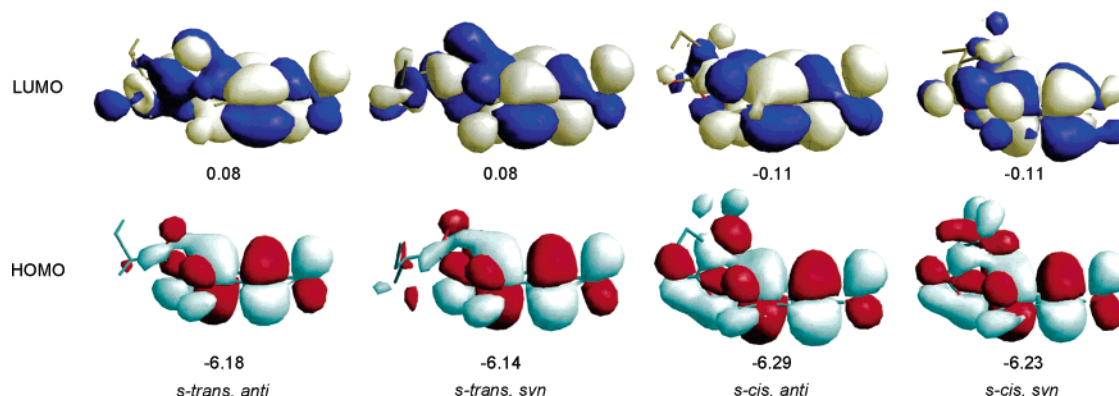


Figure 10. Calculated HOMO and LUMO (corresponding to the 60th and 61st molecular orbitals) of energy-minimized conformers of ground-state **1** calculated at the B3LYP/6-31G(d) level. Numbers under figures are calculated energies of the levels in eV.

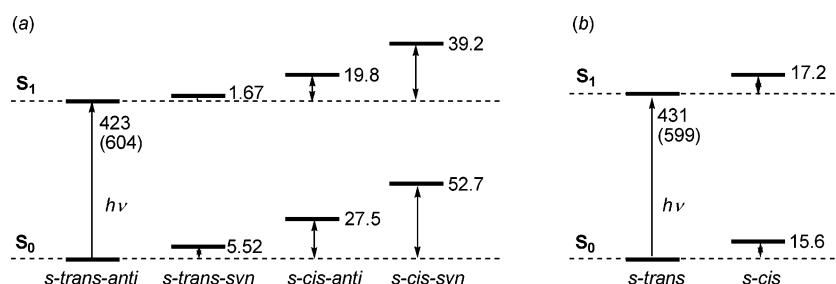


Figure 11. Energy diagrams in the ground- and excited-state conformers of (a) aryl ester **1** and (b) lactone **6**. A relative energetic difference calculated by DFT method is shown in kJ mol⁻¹. Singlet excitation energies shown are experimental and calculated (in parentheses) values.

(Figure 9). Although the *s-trans* conformer is energetically favored again in the excited singlet state, each of the ground-state *s-cis* and *s-trans* conformations had a local minimum in the excited singlet state at a comparable geometry. In the *s-cis* conformation, the distance between the *ipso* carbon on the aromatic ring and the carbon atom α to the carbonyl of the ester (i.e., the two atoms that make a σ -bond in **2**) moves from 2.929 Å in the ground state to a shorter distance, 2.913 Å, in the excited singlet state. The shorter distance facilitates concerted extrusion of CO₂. Appreciable interaction between the σ (CO–C)-orbital and the π -orbital of the aromatic ring prior to electronic excitation of the *s-cis-anti* conformation also supports the cheletropic concerted decarboxylation mechanism.

Molecular orbital calculations have been also performed on the four conformers of **1** at the B3LYP/6-31G(d) level (Figure 10). HOMO–LUMO energy gaps were calculated to be 6.26, 6.22, 6.18, and 6.12 eV for the *s-trans-anti*, *s-trans-syn*, *s-cis-anti*, and *s-cis-syn* conformations, respectively. Energy differences between the four conformers in their excited singlet states have been estimated from these HOMO–LUMO energy gaps and calculated gas-phase ground-state energies (Figure 11). In the excited state, the Boltzmann distribution at room temperature indicates 0.2% of the *s-cis* conformer assuming that complete equilibrium is attained. The value is small but much larger than the calculated population in the ground state. Therefore, the excited-state potential energy surface is predicted to facilitate formation of the *s-cis* conformer.

The *s-cis* conformers are also predicted to have much lower excitation energies and, thus, absorb selectively at longer wavelengths than the *s-trans* conformers (Figure 11). In the context of these calculations, the aforementioned shifts of excitation maxima in fluorescence measurements upon changing the temperature can be explained on the basis of changing

populations of *s-cis* and *s-trans* conformers in the ground state. The relative contribution from the *s-cis* (and presumably *anti*, as judged from the energy calculations) conformer is increased at higher temperatures.

Rotation of the methyl groups at the 2- and 6-positions of the aromatic ring of **2** is predicted to be slightly hampered at room temperature according to molecular dynamics calculations (using the MM2 force field). To test these calculations, line shape analyses of the ¹H NMR peaks of **2** and **5** in chloroform-*d* were made over a range of temperatures. They reveal that rotations of the *ortho*-methyl groups are somewhat restricted in both compounds: from Eyring-type plots, $\Delta H^\ddagger = 53.1$ kJ mol⁻¹ and $\Delta S^\ddagger = -25$ J mol⁻¹ K⁻¹ ($T_c = 11$ °C) for **2** (Figure S-2 in the Supporting Information) and $\Delta H^\ddagger = 57.3$ kJ mol⁻¹ and $\Delta S^\ddagger = -23$ J mol⁻¹ K⁻¹ ($T_c = 37$ °C) for **5**. These results help to explain the origin of the slope changes detected in plots a and b of Figure 4: photodecarboxylation may be facilitated at lower temperatures due, at least partially, to the restricted movement of the methyl groups; at elevated temperatures, their rotation may hamper the approach of the carbon α to the carbonyl to the *ipso* carbon of the aromatic ring in the *s-cis* conformations.

The *s-cis* conformation is probably much easier to achieve in lactone **6** than in either **1** or **4**. However, our calculations of the energies of the various conformations of **6** indicate that its preferred conformation is not completely appropriate to effect photodecarboxylation and that small conformational changes are required to attain the correct atomic orientations (Figure 12). The temperature dependence on the efficiency of formation of **7** is consistent with the energy barrier to the necessary conformation being small. Indeed, the highest yield of **7**, 72%, was achieved in methylcyclohexane at 95 °C. This result is rather amazing because the efficiency of β -bond cleavage, the

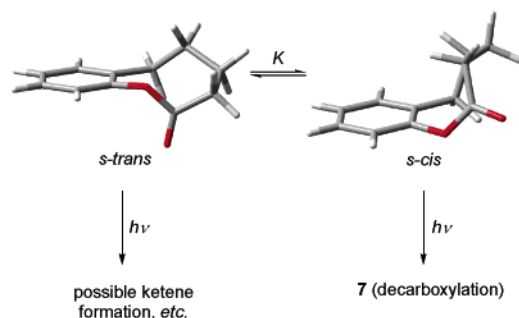


Figure 12. Possible conformations involved in the photoreactions of **6** optimized at the B3LYP/6-31G(d) level.

initial step in photo-Fries reactions, also increases drastically with increasing temperature. However, this amazement should be tempered by the probable increase in the rate of recombination of the (intramolecular) radical pair to reform **7** at higher temperatures. The exact cause of the high yields of **7** from irradiations of **6** at high temperatures deserves further scrutiny.

Two minimum energy conformations of lactone **6** have been calculated at the B3LYP/6-31G(d) level (Figure 12). Single-point calculations at the B3LYP/6-311G+(2d,p) level with zero-point energies were then performed. The energy difference, 15.5 kJ mol⁻¹, corresponds to a 0.2% equilibrium population of the more energetic *s-cis* conformer at 25 °C. In the singlet excited state, the calculated distribution of the *s-cis* is slightly lower than that in the ground state, but it is much higher than for **1**. In the *s-cis* conformation, the distance between the *ipso* carbon of the aromatic ring and the carbon α to the carbonyl of **6**, 2.885 Å, is significantly shorter than that in the *s-cis* conformation of **1**, 2.929 Å. Both the higher content of the *s-cis* conformer of **6** and its more favorable distance facilitate photodecarboxylation. A principal reason the eight-membered lactone **6** underwent facile photodecarboxylation and the analogous five-, six-, and seven-membered lactones do not is that the latter cannot form *s-cis* conformers easily.

(ii) By VCD Spectroscopy. Recently, information about conformations of chiral molecules, including esters,^{118–121} in solution have been deduced by analyses of vibrational circular dichroic (VCD) spectra combined with DFT calculations.^{122–127} This approach has been applied to the conformational analysis of **1**. The VCD spectrum of **1** in dichloromethane-*d*₂ was compared with simulated spectra from the four conformations identified above (Figure 13). Relative contributions from each conformer were estimated as a Boltzmann distribution based on the gas-phase calculations at the B3LYP/6-311G+(2d,p) level with zero-point energy corrections (Table 9). As expected, the main contributor in the simulated VCD spectrum that best

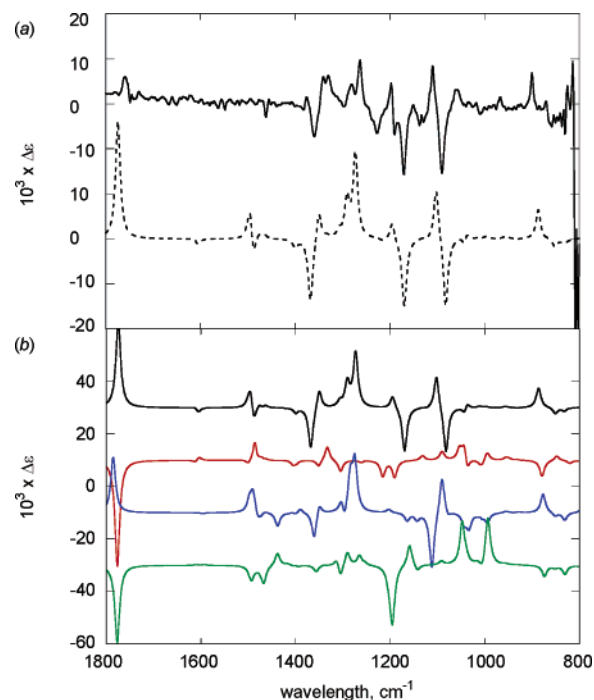
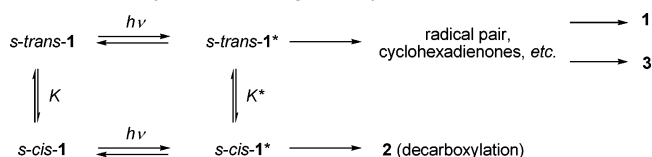


Figure 13. (a) Experimental VCD spectrum of (*S*)-**1** in dichloromethane-*d*₂ at ambient temperature (solid line) and the B3LYP/6-31G(d) calculated VCD spectrum of (*S*)-**1** (dashed line). The calculated spectrum is based on the fractional contribution from ground-state energies of the calculated VCD spectrum of each conformation as shown in part b. Black: *s-trans-anti*. Red: *s-trans-syn*. Blue: *s-cis-anti*. Green: *s-cis-syn*.

Scheme 4. Proposed Conformational Control of Photodecarboxylation and Cage-Escape Process



approximates the experimental data is from the *s-trans-anti* form. However, some of the peaks observed require the inclusion of contributions from the other conformers. For example, a weak, positive Cotton effect observed at 1770 cm⁻¹ cannot be reproduced by the calculated signals of the *s-trans-anti* form alone; it could be reproduced only by including contributions from *syn* conformers.

Concluding Remarks

A proposed photodecarboxylation mechanism that accounts for the body of the results presented here is illustrated in Scheme 4. A spiro-lactonic transition state, which presumably forms from a singlet excited-state *s-cis* conformer and loses a molecule of carbon dioxide in a concerted manner, predicts products with complete retention of stereochemistry. The decarboxylation process has many of the characteristics of symmetry-allowed suprafacial [1,3]sigmatropic rearrangements. The results indicate that no radical intermediates are involved in decarboxylation, but they are in the competing photo-Fries type cleavage that occurs from the *s-trans* conformers of the excited singlet state. The *s-trans* conformers are thermodynamically more stable than the *s-cis* in the ground and excited states. Despite this, experimental conditions can be found for which photodecarboxylation occurs to the near exclusion of the photo-Fries

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cleavage products. The reason for this may be conformational control imposed by the media or forced recombination of radical pairs to yield starting ester. Where both photoproducts are observed, the relative amounts of photodecarboxylation product increase with increasing temperature. One important contributing reason for this observation is the greater importance of the *s-cis* conformer, especially in the excited state, at higher temperatures. In several of the media where both products are obtained, the rates at which the *s-trans* undergoes cleavage and then the radical pair separates must increase with temperature. The fact that the relative yields of photodecarboxylation products increase even under these conditions strongly suggests the increased importance of *s-cis* conformations.

The photochemistry of chiral ester **1** has been studied in detail. Under a wide range of experimental conditions, including changes in temperature, solvent, and pressure and in the presence of radical trapping reagents, the decarboxylation product is formed with complete retention of chirality. Only an *s-cis* conformation is reasonable as the immediate precursor of the product-forming transition state which, again, is most easily assigned to a spiro-lactonic structure. DFT and CIS calculations reveal that the *s-cis* conformations are higher in energy than the more stable *s-trans* conformers, but the energy differences are compatible with involvement by the *s-cis* in the reactions. The presence of some *s-cis* conformers is further indicated by VCD spectroscopic measurements. The importance of conformational equilibria in the ground (and probably excited singlet) states in most of the media investigated is also indicated by the efficient photodecarboxylation of the eight-membered ring lactone **6**, especially at elevated temperatures. The constraints imposed by reaction cavities of polyethylene films, especially those of higher crystallinity, may well be too large to allow significant equilibration of conformers within the short excited singlet state lifetimes of the aryl esters.

From a synthetic standpoint, the stereospecific conversion of a readily available chiral acid to an ester and then transformation of the ester to an enantiopure arylalkane is a much simpler and

much more efficient reaction sequence than other currently available routes for the syntheses of the same molecules. Especially, our irradiations of **1** in unstretched high-density **PE** films or in acetonitrile under high pressure provide very high yields of the photodecarboxylation product **2** and almost none of the competing cleavage product **3**; in the **PE** films, **2** was isolated in >98% yield (based on consumed **1**) and >98% ee. As such, each of these drastically attenuates “side reactions”, allowing easy isolation of **2**, and, we believe, many other products similar to it from reactions of appropriate precursor aryl esters by a simple irradiation of the doped films. The results presented here demonstrate that seemingly slight changes of the reaction conditions can lead to large changes in the conformational contents of the aryl esters and the division between their competing photoreaction pathways. Conformational control via confining media as a tool in synthetic organic photochemistry should be exploited much more in the future than it has been to date.

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Supporting Information Available: Details of experimental procedures, figures of exponential fittings of fluorescence decay profiles to time-correlated single photon counting measurements, and B3LYP/6-31G(d) or CIS/6-31G(d) optimized geometries of conformers of aryl ester **1** (Z-matrix) in their ground and excited states, and optimized ground-state geometries of lactone **6**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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