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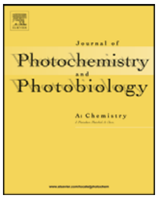

The effect of fluorine as leaving group in the photolysis of 2-fluoro-1,2-diphenylethanone: Preparative and mechanistic investigation

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ABSTRACT

Photolysis of 2-fluoro-1,2-diphenylethanone (**1**) in MeCN or MeOH produces mainly 2-phenylbenzofuran. In MeOH some traces of solvent addition to the benzoyl radical formed by α-cleavage were detected. In trifluoroethanol several products are due to direct α-cleavage. Only 3% of 2-phenylbenzofuran and 13% of the α-ketocation solvent adduct are formed. The triplet state of **1** observed in nanosecond experiment at low temperature has been confirmed in femtosecond experiment. The triplet is formed quite fast at 370 nm (rise time 4.5 ps in acetonitrile and 22 ps in trifluoroethanol) and is stable up to 1.9 ns (a lifetime of 20 ns has been determined by quenching experiments with naphthalene).

1. Introduction

Benzoins are important representatives of “caged compounds”, which are inert in the dark but, upon exposure to light, are converted to active species that are able to participate in a chemical or biochemical process. Benzoins are an attractive alternative to the widely used 2-nitrobenzyl caging groups for a number of reasons. First of all, the syntheses of benzoin-caged derivatives are accomplished in good yield by easy procedures. Benzoin properties fulfill most of the criteria required for the design of a good photoremovable protecting group. The main advantages of benzoins are the high quantum yields and rates of release. The photochemical by-product accompanying the released reagent is an inert benzofuran.

The first study about the photolysis of benzoin compounds was made by Sheehan and Wilson in 1964 [1]. They observed that benzoin acetate undergo photolytic cyclization to form 2-phenylbenzofuran. They also studied the photolysis of many derivatives for which they determined the reaction yield. They used a high-pressure mercury-vapour lamp with a Pyrex filter and isolated 2-phenylbenzofuran as the major product. Factors which should influence the cyclization reaction were investigated. The benzofuran chemical yields are to a small extent solvent dependent (from 15% in benzene to 8 and 10% in dioxane and propan-2-ol, respectively). Another important discovery is the effect of the leaving group. By replacing acetate by chloride as a leaving group, a reduction from 15 to 1% of the chemical yield is observed in benzene.

Givens et al. [2] studied benzoin phosphate. Benzoin-caged phosphates are capable of rapid release of nucleotides and other biologically active phosphates, which are used to study the kinetics of muscle action by ATP, or calcium channel activation by GTP, for example. Photolysis at 350 nm of solutions of γ-*o*-desyl glutamate and *o*-desyl GABA in 1:1 H_2O:acetonitrile releases glutamate and GABA, respectively, with rate constants of ca. $10^7\ s^{-1}$ to give 2-phenylbenzofuran as the only by-product.

Wirz et al. [3] have studied the kinetics and the mechanism of diethyl phosphate photorelease from the benzoin ester by ns and ps laser flash photolysis. Steady-state irradiation of benzoin diethylphosphate gives 2-phenylbenzofuran as a main product with a quantum yield of 0.26 in benzene. In trifluoroethanol, only 25% of 2-phenylbenzofuran was formed, the major product being a solvent adduct.

Nanosecond laser flash photolysis of benzoin diethyl phosphate in degassed acetonitrile at 248, 308 or 351 nm gave a permanent absorbance around 300 nm that was formed in less than 25 ns (laser pulse width). In water or trifluoroethanol, a second absorption band was observed at $\lambda = 570$ nm, that was also formed within the duration of the laser pulse and decayed with a rate constant of $k = (2.3 \pm 0.2) \times 10^6\ s^{-1}$ in degassed aqueous solution. Addition of sodium azide accelerates the decay rate of the 570 nm transient with a quenching coefficient $k_q = (9.9 \pm 0.4) \times 10^9\ M^{-1}\ s^{-1}$ and reduced the amplitude of the signal.

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In acetonitrile, dichloromethane, chloroform, tetrahydrofuran, diethyl ether, methanol, ethanol, propan-2-ol and ethyl acetate no transient was observed at 570 nm. The permanent product observed at 300 nm was identified as 2-phenylbenzofuran by comparison of its fluorescence with that of an authentic sample. The lifetime of the triplet state of the diethyl phosphate benzoin was determined by energy transfer experiments with naphthalene ($\tau = (24 \pm 2)$ ns in trifluoroethanol).

Picosecond laser flash photolysis in acetonitrile at room temperature gave a large transient at 340 nm with a rise time of 2–4 ps and a lifetime of at least 5 ns.

The triplet of the starting molecule was assigned as the reactive excited state, the lifetime of which has been estimated to be between 10 and 25 ns, depending on the solvent.

Quenching experiments have allowed Wirz et al. to prove that the triplet-excited state of benzoin diethyl phosphate is the common precursor of 2-phenylbenzofuran and the transient at 570 nm. Radicals and carbenes were ruled out as candidates to describe this intermediate because of their incompatible reactivity, solvent dependency and absorption spectra. Wirz et al. also gave arguments to explain the role of the solvent. In principle a polar solvent should favour heterolytic dissociation, but no cation transient has been observed in the case of acetonitrile. The difference of conformation in the different solvents may explain the different reactivity.

The photolysis of many benzoin derivatives shows that the nature of leaving group being bonded at C2 position has substantial effect on the transient kinetics. To determine what is more important: bond energy between carbon atom and leaving group or nucleofugacity of leaving group, we chose 2-fluoro-1,2-diphenylethanone as substrate from several reasons:

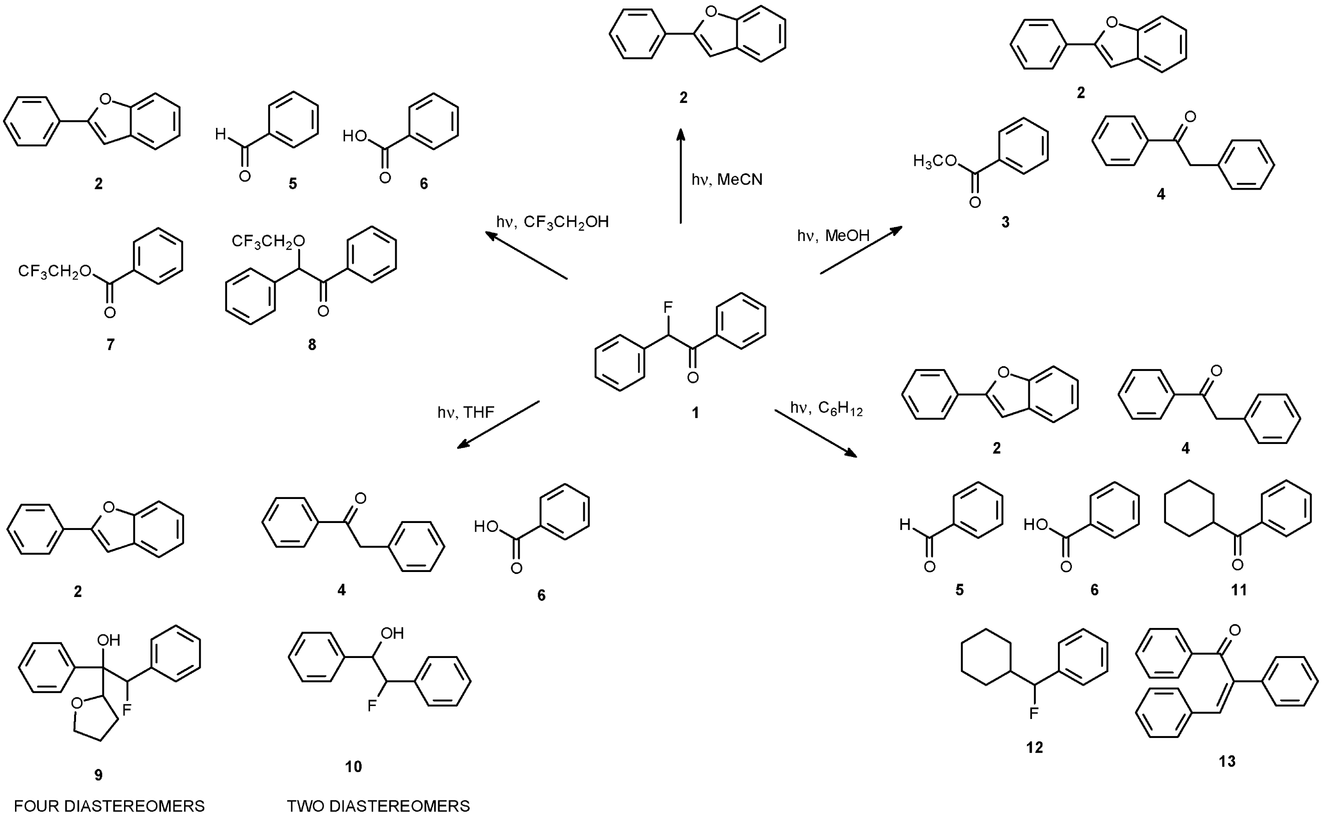
- C—F bond is the strongest single bond and homolysis under the conditions used in photolytic experiments is not possible;
- acidity constant of HF ($pK_a = 3.17$) is very close to diethylphosphate ($pK_a = 1.39$) and acetic acid ($pK_a = 4.76$), quite different to that of HCl ($pK_a = -7$);
- fluorine atom stabilized the intermediates in many cases;
- fluorine atom can serve as a marker in different reactions.

2. Experimental

The photochemical reactions were performed in PhotoReactors Ltd MLU 18, equipped with light source of 350 nm. The reaction mixture were analyzed by GC Hewlett Packard HP 6890 equipped with flame ionization detector using 30 m capillary column HP5 and HP1 and temperature program: $T_{\text{start}} = 150\,^{\circ}\text{C}$ (3 min); rise 20 °C/min; $T_{\text{end}} = 280\,^{\circ}\text{C}$ (10 min). The NMR spectra were recorded in $CDCl_3$ at 302 K with Bruker Avance DPX 300 spectrophotometer. Chemical shifts are given on the δ scale (ppm) and are referenced to internal TMS for ^1H and ^{13}C spectra and to CCl_3F for ^{19}F spectra. IR spectra were determined on a PerkinElmer 1310 spectrometer. Melting points were measured on Kofler microscope and are uncorrected. The reaction mixtures were analyzed by GC and GC/MS and by comparison of the spectral data of products to those of the authentic samples: 2-phenylbenzofuran (**2**), methyl benzoate (**3**), deoxybenzoin (**4**), benzaldehyde (**5**), benzoic acid (**6**), 2,2,2-trifluoroethyl benzoate (**7**) [4], 2-(2,2,2-trifluoroethoxy)-1,2-diphenylethanone (**8**) [3], 2-fluoro-1,2-diphenylethanol (**10**) [5], cyclohexyl phenyl ketone (**11**), 1,2,3-triphenylprop-2-en-1-one (**13**) [6].

2.1. *1,2-Diphenyl-2-fluoroethanone (**1**) [7]*

To dichloromethane (20 mL) solution of 4.03 g (19 mmol) of benzoin at room temperature was dropwise added 2.5 mL (19 mmol) of (diethylamino)sulfur trifluoride (DAST). Stirring was continued for



Scheme 1. Products formed in photolysis of 2-fluorobenzoin (**1**) in different solvents.

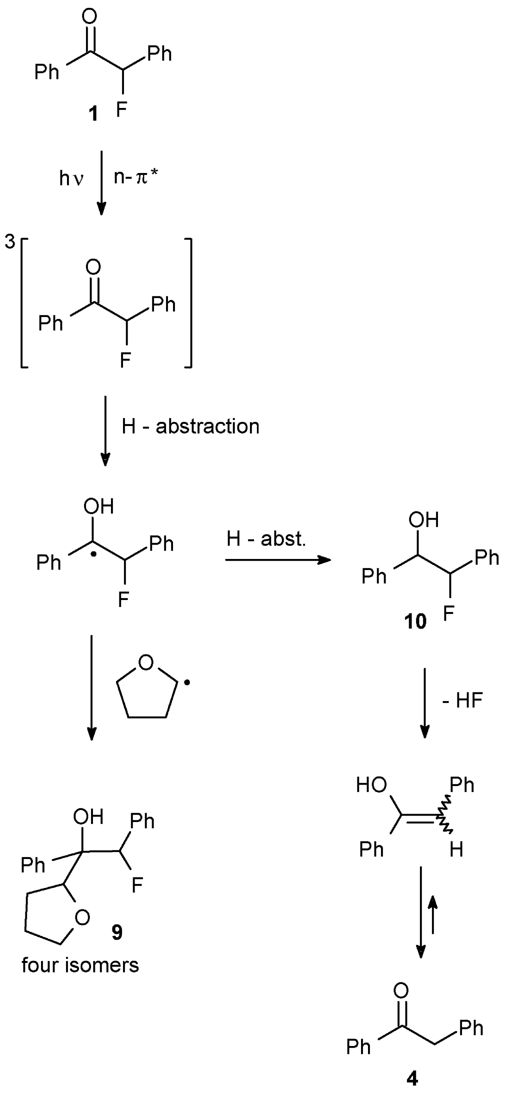
Table 1
Product distribution[a] in photolysis[b] of **1** in different solvents

Solvent	Conversion	Product distribution												
		1	2	3	4	5	6	7	8	9	10	11	12	13
MeCN	99	1	99											
MeOH	86	14	83	1	2									
CF_3CH_2OH	40	60	3			10	8	6	13					
THF	94	6	14		9		13			54	4			
C_6H_{12}	75	25	10		23	10	3					6	6	17

[a] Relative yields in % by GC/MS.

[b] Irradiation time 2 h, λ = 350 nm, concentration of substrate = 0.01 M.

additional 1 h, the reaction mixture was poured into 20 mL of water. Organic and water phases were separated, organic phase washed with 20 mL of saturated aqueous $NaHCO_3$ and 20 mL of water, dried over anhydrous Na_2SO_4, filtered and evaporated to dryness. The crude product was purified by column chromatography (silica gel) with dichloromethane–hexane 2:1 as eluent and obtained 2.38 g (57%) of pale yellow product with melting point 53–55 °C (T_{lit} [7] = 49–51 °C). ^1H NMR ($CDCl_3$) δ 7.94 (m, 2H), 7.54–7.37 (m, 8H), 6.50 (d, $^2J_{HF}$ = 47.5 Hz, 1H). ^{19}F NMR ($CDCl_3$) δ −176.20 (d, $^2J_{HF}$ = 47.5 Hz).



Scheme 2.

2.2. General procedure for photolysis

0.05 mmol of substrate **1** was dissolved in 5 mL of solvent, and the reaction mixture was irradiated at 350 nm for 2 h. The reaction mixtures were analyzed by GC and GC/MS.

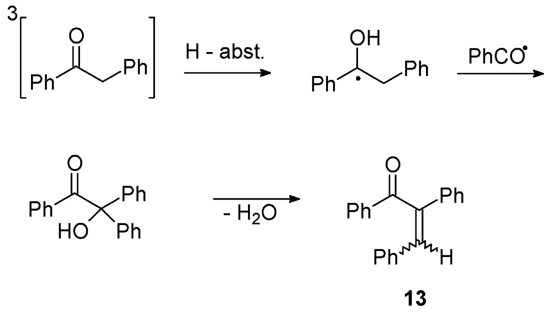
2.3. 2-Fluoro-1-(2-tetrahydrofuryl)-1,2-diphenylethanol (**9**)

Two hundred and twelve milligram (1.0 mmol) of 1,2-diphenyl-2-fluoroethanone (**1**) was dissolved in 20 mL of THF and argon was bubbled through solution for 15 min. The solution was then irradiated for 7 h at 350 nm. After the end of irradiation the solvent was evaporated in vacuum and the crude reaction mixture was separated by preparative TLC (silica gel, CH_2Cl_2 as mobile phase). Four isomers of compound **9** were isolated, two in pure form and one fraction as a mixture of two isomers in the ratio of 1:1.

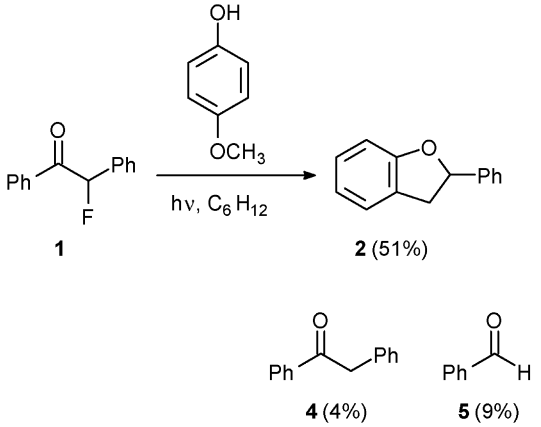
Isomer **A** (**9a**) (R_f = 0.3). ^1H NMR ($CDCl_3$) δ 7.43–6.98 (m, 10H), 6.09 (d, $^2J_{HF}$ = 44.9 Hz, 1H), 4.52 (dt, J = 7.1, 1.1 Hz, 1H), 3.79 (dt, J = 6.7, 1.0 Hz, 2H), 2.27 (s, 1H), 2.10–1.35 (m, 4H). ^{19}F NMR ($CDCl_3$) δ −189.48 (d, $^2J_{HF}$ = 45 Hz). MS m/z (%): 266 (M^+−HF, 1), 196 (35), 177 (10), 165 (15), 131 (9), 105 (22), 71 (100). HR EIMS calcd. for fragment $C_{18}H_{18}O_2$: 266.1307; found: 266.1304.

Isomer **B** (**9b**) (R_f = 0.4). ^1H NMR ($CDCl_3$) δ 7.42–6.97 (m, 10H), 5.80 (d, $^2J_{HF}$ = 46.2 Hz, 1H), 4.41 (t, J = 7.7 Hz, 1H), 4.06–3.93 (m, 2H), 3.14 (s, 1H), 2.10–1.72 (m, 4H). ^{19}F NMR ($CDCl_3$) δ −190.53 (d, $^2J_{HF}$ = 46 Hz). MS m/z (%): 266 (M^+−HF, 1), 196 (37), 177 (46), 165 (16), 131 (26), 105 (35), 71 (100). HR EIMS calcd for fragment $C_{18}H_{18}O_2$: 266.1307; found: 266.1309.

Isomers **C** and **D** (**9c**, **9d** 1:1) (R_f = 0.2). ^1H NMR ($CDCl_3$) δ 7.46–6.88 (m, 20H), 5.88 (d, $^2J_{HF}$ = 44.8 Hz, 1H, **D**), 5.68 (d, $^2J_{HF}$ = 45.1 Hz, 1H, **C**), 4.81 (dt, J = 7.8, 2.5 Hz, 1H, **C**), 4.26 (t, J = 7.3 Hz, 1H, **D**), 4.10–3.94 (m, 2H, **C**), 3.82–3.69 (m, 2H, **D**), 2.89 (s, 1H, **C**), 2.49 (s, 1H, **D**), 2.10–1.57 (m, 8H). ^{19}F NMR ($CDCl_3$) δ −183.47 (d, $^2J_{HF}$ = 45 Hz, **C**), −191.82 (d, $^2J_{HF}$ = 45 Hz, **D**). MS m/z (%): 266 (M^+−HF, 2), 196 (10), 177 (2), 165 (17), 131 (1), 105 (6), 71 (100). HR EIMS calcd. for fragment $C_{18}H_{18}O_2$: 266.1307; found: 266.1302.



Scheme 3.



Scheme 4.

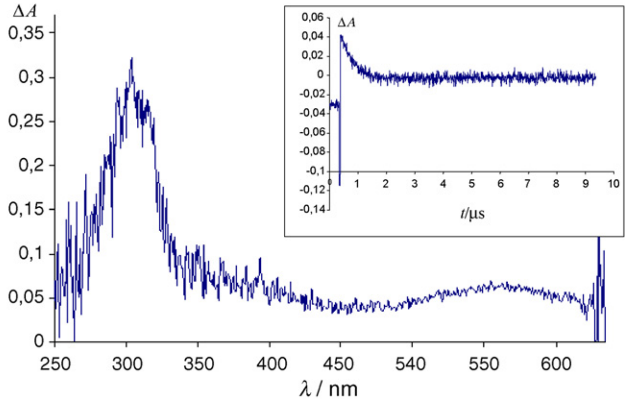


Fig. 1. UV spectra of the transients 10 ns after the laser excitation of **1** in aqueous solution containing 4% of MeCN. Inset: kinetic trace of the absorbance at 570 nm.

2.4. Nanosecond laser flash photolysis

Laser flash photolysis experiments were carried out by exciting the sample solutions (absorbances of <0.5 cm^{-1} at the excitation wavelength) with 20-ns, ca. 100-mJ pulses of an excimer laser (248 nm, KrF; 308 nm, XeCl; 351 nm, XeF; Lambda Physik Compex 205). A pulsed Xenon arc was used as the monitoring light source (cell path length 4.5 cm, orthogonal to the excitation pulse). The detection system allowed monitoring of either the kinetics at a single wavelength using a transient digitizer, or the whole transient spectrum, with a gated diode array [8]. Measurements were made with fresh solutions, which were replaced after each flash.

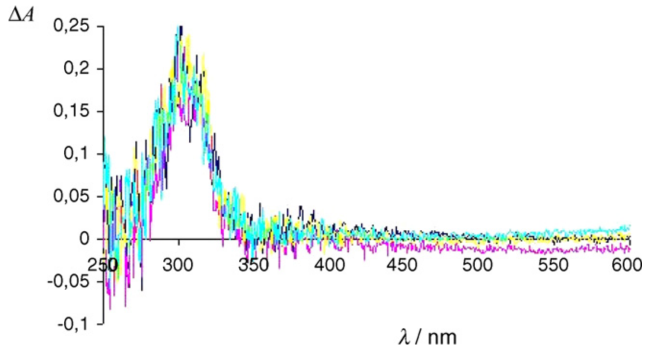


Fig. 2. UV spectra of the transients 20 ns (blue), 200 ns (pink), 1 µs (yellow) and 4 µs (cyan) after the laser excitation of **1** in air saturated MeCN.

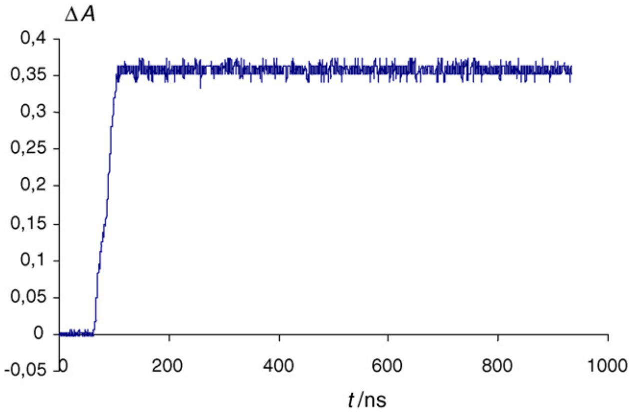


Fig. 3. Kinetic traces of **1** in air-saturated MeCN observed at 301 nm (growth, formation of 2-phenylbenzofuran).

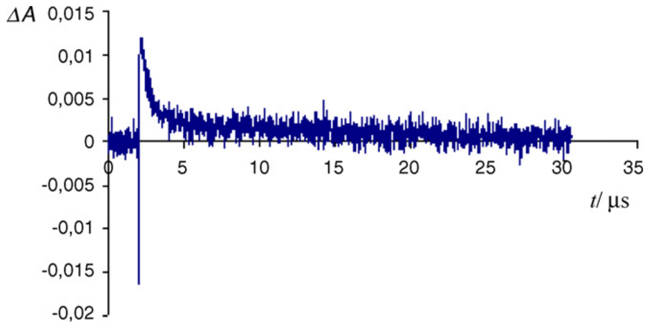


Fig. 4. **1** in degassed EtOH at −110 °C, kinetic trace of the absorbance at 370 nm.

2.5. Femtosecond laser flash photolysis

Pump-probe spectroscopy was used to investigate processes on the subnanosecond time-scale. The measurements were done with solutions in acetonitrile and trifluoroethanol. Experiments were carried out by exciting of the sample solutions with the 150–200-fs pump pulse (at 263 nm, CPA-2001 Laser System manufactured by Clark-MXR Inc.) of a titanium:sapphire amplified laser system. The remainder of the laser output was used to generate a white light continuum in a thick piece of calcium fluoride and used as probe beam. Transient spectra were collected within the wavelength range from 300 to 600 nm. A more detailed description can be found elsewhere [8].

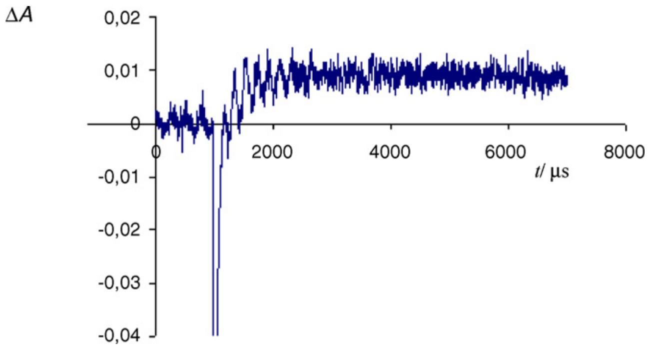


Fig. 5. Kinetic trace of the absorbance of **1** at 300 nm.

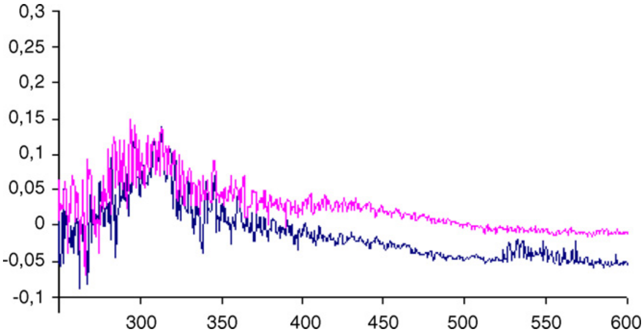


Fig. 6. UV spectra of the transients 20 ns (blue), 500 ns (pink), after the laser excitation of **1** in degassed hexane.

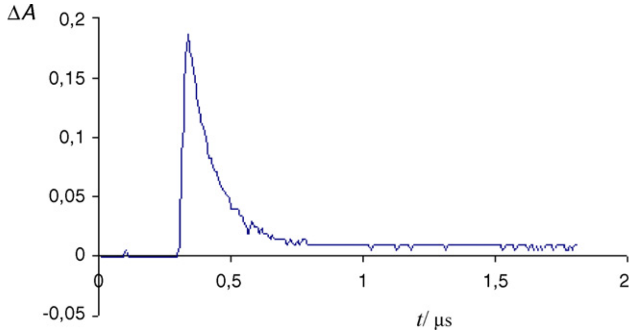


Fig. 9. Kinetic trace of **4** in air saturated hexane observed at 310 nm.

2.6. Calculations

SPECFIT 32 and origin 7.0 were used for global analysis and kinetics fitting, respectively. CIS and DFT calculation were carried out with the GAUSSIAN 03 package.

3. Results

3.1. Preparative photolysis

Compound **1** (0.01 M) was photolysed at 350 nm for 2 h in various solvents: MeCN, MeOH, THF, CF_3CH_2OH and C_6H_{12}. Crude reaction mixtures were analyzed by GC and GC/MS and product distribution was calculated from the ratios of area of signals in GC chromatograms using the relative response factors (Scheme 1, Table 1). A mixture of equal weights of compound **1** and products were prepared and chromatographed. The results of peak areas were used to calculate relative response factors using compound **1** as the standard. The product structures were determined by comparison of the retention times with those of authentic reference compounds, by comparison of mass spectra and in some cases the products were isolated and their structure deduced from spectroscopic data.

Photolysis of **1** in MeCN led after 2 h of irradiation to 99% conversion with 2-phenylbenzofuran (**2**) as the only product. On the other hand, photolysis in MeOH under the same reaction conditions resulted in 86% conversion and beside cyclic product **2** also a small amount of methyl benzoate (**3**) was formed, as a result of α-cleavage, and 2-deoxybenzoin (**4**). The latter is a product of photoreduction of carbonyl group, yielding at first 2-fluoro-1,2-diphenylethanol (**10**), followed by elimination of HF, leading to the enol form of **4** (Scheme 2). To confirm this statement we prepared by independent synthesis 2-fluoro-1,2-diphenylethanol [5] and photolysed it in methanol in the presence of small amount of HF. Compound **10** is converted to 2-deoxybenzoin (**4**).

In 2,2,2-trifluoroethanol the conversion of starting compound **1** was lower (40%) and several products (benzaldehyde (**5**), benzoic acid (**6**), trifluoroethyl benzoate (**7**)) are formed by direct

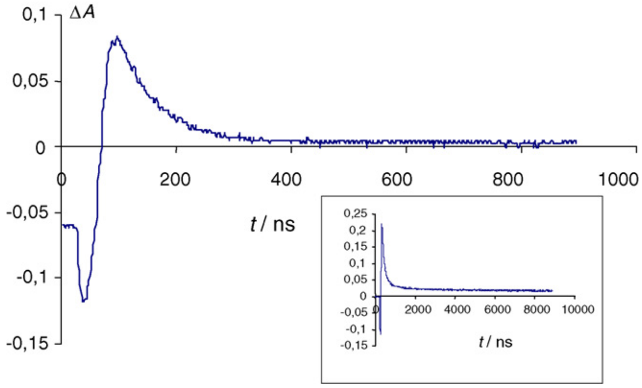


Fig. 7. Kinetic traces of **1** in degassed (air saturated in the inset) hexane observed at 310 nm.

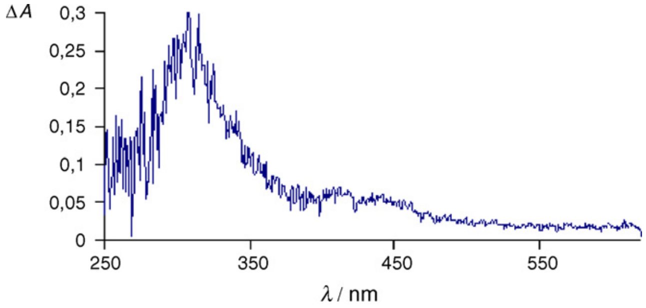


Fig. 8. UV spectra of the transients 20 ns after the laser excitation of **4** in degassed hexane.

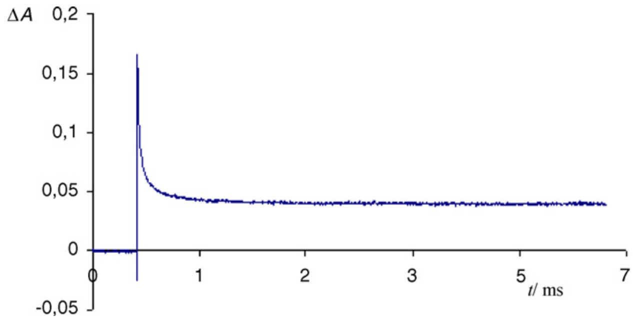


Fig. 10. Kinetic trace of **4** in degassed hexane observed at 310 nm.

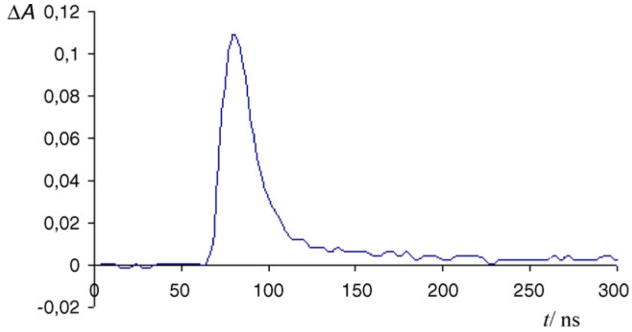
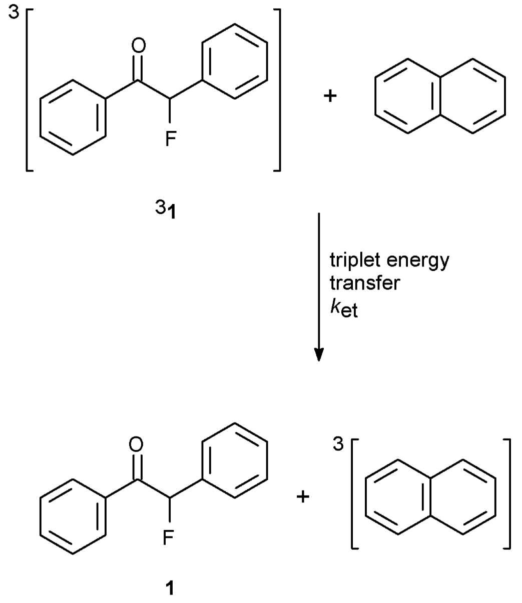


Fig. 11. Kinetic trace of **4** in oxygen-saturated hexane observed at 310 nm.



Scheme 5. Mechanism of photoinduced energy transfer between **1** and naphthalene.

α-cleavage. Only 3% of 2-phenylbenzofuran (**2**) and 13% of 1,2-diphenyl-2-(2,2,2-trifluoroethyl)ethanone (**8**) were obtained.

Photolysis of **1** in THF under the same reaction conditions gave a 94% conversion, yielding besides cyclic product **2** and benzaldehyde (**5**) also 2-deoxybenzoin (**4**), 2-fluoro-1-(2-tetrahydrofuryl)-1,2-diphenylethanol (**9**, 54%) and 2-fluoro-1,2-diphenylethanol (**10**). The reaction products **4**, **9** and **10** resulted from *n*–π* excited state of carbonyl group, which has the ability to abstract a hydrogen atom from solvent and resulting radical can further react with tetrahydrofuryl radical (Scheme 2). After evaporation of solvent, the crude reaction mixture was separated by preparative TLC. Three fractions were isolated, containing the products **9** (compound **9** have three stereogenic centres thus should consist of four diastereomers). Two of them corresponded to pure isomers of **9** (**9a** and **9b**), while the third was a mixture of isomers **9c** and **9d**. Structures of these products were determined from ^{1}H NMR, ^{19}F NMR, COSY and mass spectra. In all cases tetrahydrofuryl group is bonded at C2 position, which is evident from chemical shifts and coupling constants for protons on C2 of tetrahydrofuryl group (δ = 4.52 ppm, dt, 1H; 4.41 ppm, t, 1H; 4.81 ppm, dt, 1H; 4.26 ppm, t, 1H) (see Section 2).

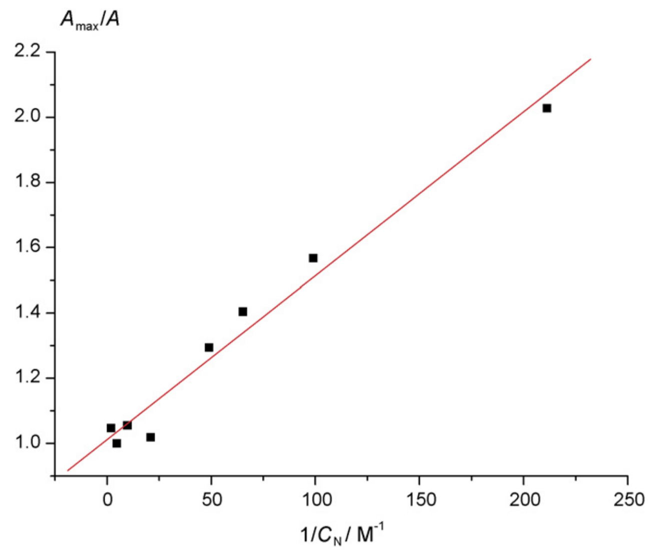
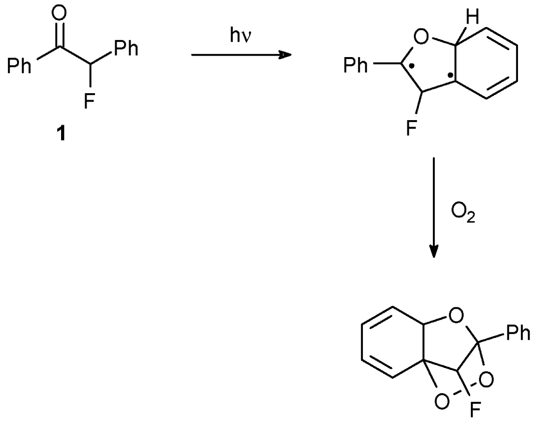
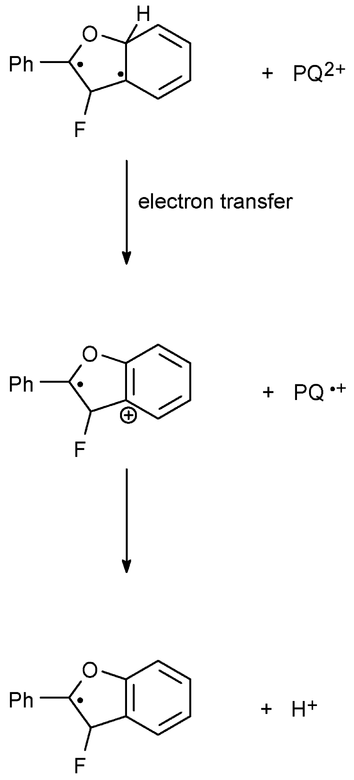


Fig. 12. Data treatment of the quenching experiment of ^{3}**1** by energy transfer reaction with naphthalene.



Scheme 6. Mechanism of diradical (from **1** photolysis) trapping with O$_2$.

In apolar solvents, such as cyclohexane, at 75% conversion only 10% of cyclic benzofuran (**2**) was formed. The main products formed by photolysis of **1** in cyclohexane are due to H-abstraction or recombination after α-cleavage of the starting compound (benzaldehyde (**5**), benzoic acid (**6**), cyclohexyl phenyl keton (**11**) and cyclohexyl-phenyl-fluoromethane (**12**)). Beside these products 2-deoxybezoin (**4**) and 1,2,3-triphenylprop-2-en-1-one (**13**) were also detected. The product **13** was formed by H-abstraction of the excited carbonyl group of 2-deoxybenzoin (**4**), followed by recombination of the resulting radical with acyl radicals (Scheme 3). Another possible route to the formation of **13** would be an aldol



Scheme 7. The electron transfer reaction between intermediate issue of **1** and paraquat dication.

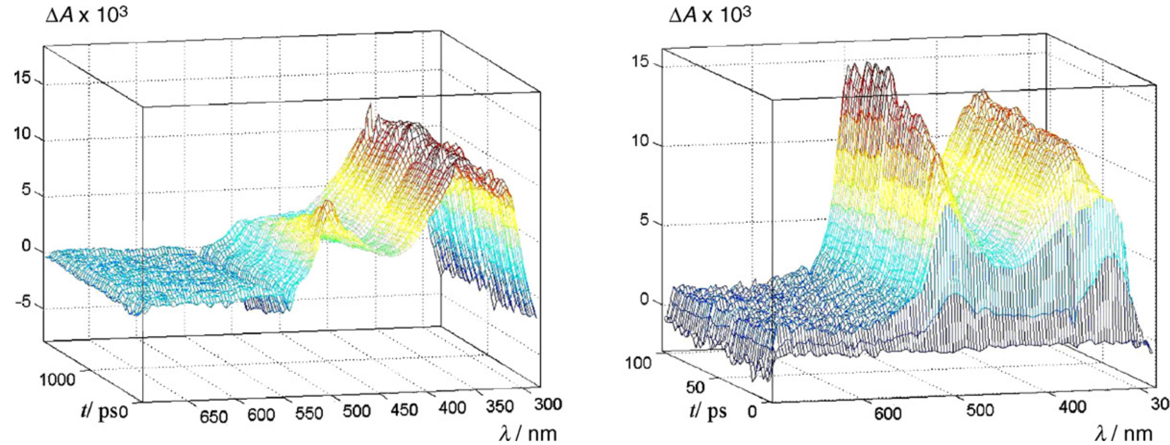


Fig. 13. Femtosecond pump-probe spectra of **1** in acetonitrile solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 1.9 ns (left), and 0–120 ps (right). The transient absorbing around 497 nm is due to reexcitation of 2-phenylbenzofuran (**2**).

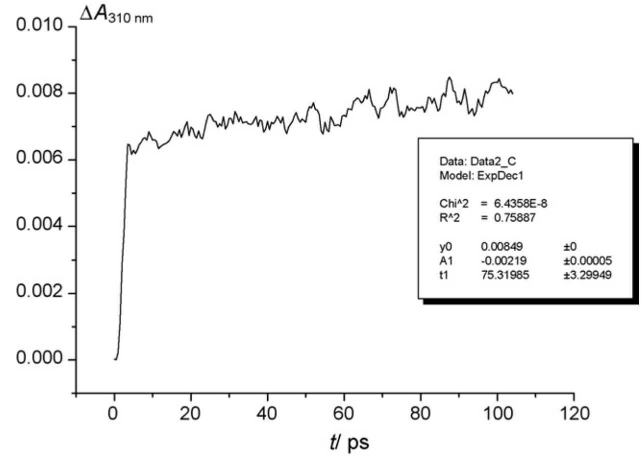


Fig. 14. Kinetic trace of the absorbance at 310 nm extracted from femtosecond pump-probe spectra of **1** in acetonitrile solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 120 ps.

condensation between benzaldehyde and 2-deoksybenzoin catalyze by HF which is present in the reaction mixture. Compound **13** shows in its mass spectrum a molecular signal at $m/z = 284$ and basic signal at $m/z = 180$ corresponding to $[\text{Ph–CH=CH–Ph}]^+$ ion formed by benzoyl radical elimination from $M^{\bullet +}$.

*3.2. Photolysis of **1** in cyclohexane in the presence of p-methoxyphenol (pMP)*

0.01 M cyclohexane solution of **1** was irradiated at 350 nm in the presence of radical inhibitor *p*-methoxyphenol for 2 h. The crude reaction mixture was analyzed by GC/MS and determined that conversion of starting compound is lower then in photolyses of **1** without adding pMP (75% and 64%). The products **6**, **11**, **12** and **13** disappeared while the percentage of phenylbenzofuran increase (from 10 to 51%) (Scheme 4).

*3.3. Quantum yield for **1** in MeCN*

Quantum yield was determined for compounds **1** in MeCN (0.01 M at 25 °C, $\lambda_{\text{irradiation}} = 350$ nm, $I_{\text{lamp}} = 1.65 \times 10^{16}$ quanta/mL s). Actinometry was done with ferrioxalate. The solution was irradiated for 5, 10, 14 and 20 min. The conversion was determined by GC using naphthalene as an internal standard. The quantum yield of disappearance was found to be 0.74.

3.4. Quenching experiment

To 0.01 M solution of compound **1**, 4 mol excess of naphthalene was added and the solution was irradiated for 2 h with wavelength at 350 nm. The conversion was reduced from 98% obtained by direct photolysis of **1** to 43%, while in the case when 20 mol

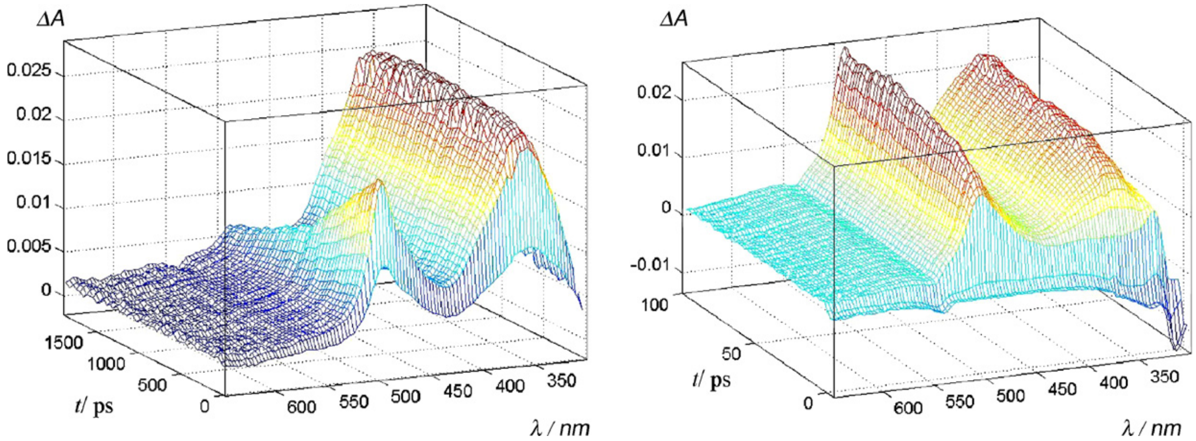


Fig. 15. Femtosecond pump-probe spectra of **1** in trifluoroethanol solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 1.9 ns (left), and 0 and 120 ps (right). Transient absorbing at 490 nm is due to reexcitation of 2-phenylbenzofuran (**2**).

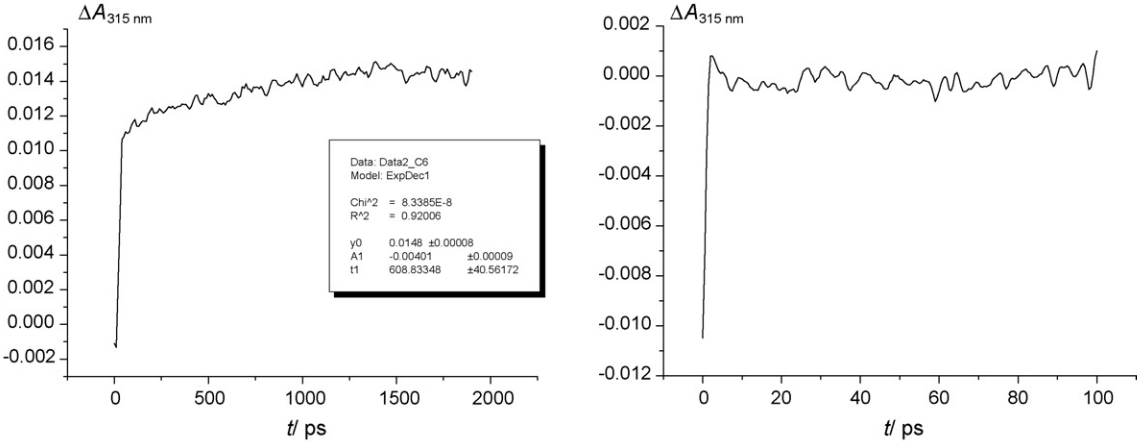


Fig. 16. Kinetic traces of the absorbance at 310 nm extracted from the femtosecond pump-probe spectra of **1** in trifluoroethanol solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 1.9 ns (left) and 0 and 120 ps (right).

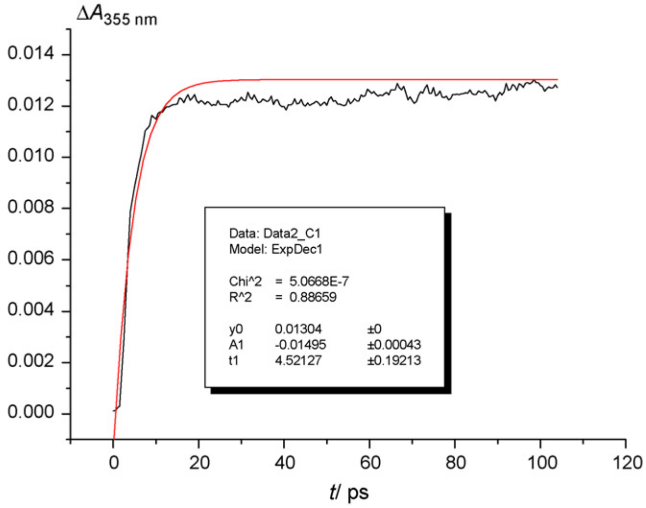


Fig. 17. Kinetic traces of the absorbance at 355 nm extracted from the femtosecond pump-probe spectra of **1** in acetonitrile solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 120 ps.

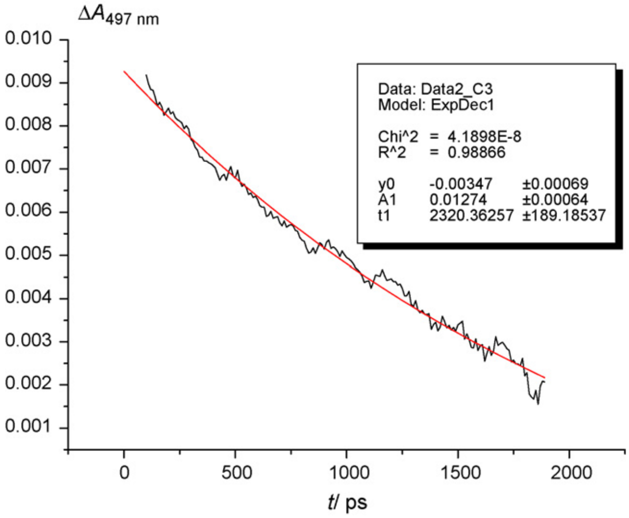


Fig. 19. Kinetic traces of the absorbance at 497 nm extracted from the femtosecond pump-probe spectra of **1** in acetonitrile solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 1.9 ns.

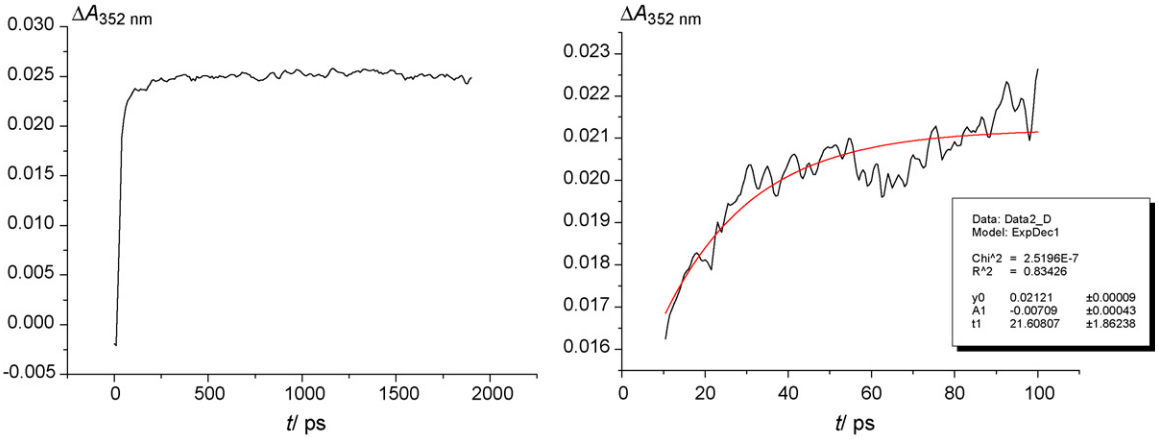


Fig. 18. Kinetic traces of the absorbance at 352 nm extracted from the femtosecond pump-probe spectra of **1** in trifluoroethanol solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 1.9 ns (left) and 0 and 120 ps (right).

excess of naphthalene was added the reaction was completely inhibited.

3.5. Mechanistic investigation: nanosecond LFP of **1** in MeCN and in water

Solutions of **1** with an absorbance of 0.25–0.2 per cm were excited at 248 nm (100 mJ) to observe UV–vis spectra and kinetics of the transients. In pure MeCN, a band at 300 nm is formed immediately after the first flash (no decay was observed in either degassed or in air saturated solution), which can be attributed to formation of the end product. A second band at 400 nm (decay observed: $k_1 = (3.61 \pm 0.14) \times 10^4\ \mathrm{s}^{-1}$, $k_2 = (1.16 \pm 0.01) \times 10^4\ \mathrm{s}^{-1}$), seen only on second excitation, may be due to reexcitation of 2-phenylbenzofuran. In an aqueous solution containing 4% of MeCN, absorption spectra taken shortly after the laser pulse exhibit an additional absorption maximum between 500 and 600 nm (at 570 nm; decay rate constant $k = (2.58 \pm 0.09) \times 10^6\ \mathrm{s}^{-1}$ in degassed solution) (Fig. 1).

A solution of **1** in air-saturated MeCN was studied (observation 20 ns, 200 ns, 1 μs and 4 μs after the laser pulse; Figs. 2 and 3). We can see a band centred around 300 nm (observed 20 ns after the laser excitation), which represents the absorbance of the final product (2-phenylbenzofuran).

3.6. In ethanol at low temperature

The goal of an experiment at low temperature was to resolve the formation and/or decay of an intermediate of short lifetime, not visible at room temperature. From quenching experiments of related compounds [3], we suspected that the triplet of **1** has a lifetime of less than 20 ns at room temperature. LFP of **1** in EtOH ($A_{248\mathrm{nm}} = 0.97$ per cm) at −110 °C produced a transient absorbing at 370 nm with an $A_{\max} = 0.012$. This signal is attributed to the triplet of **1** (Fig. 4). It decayed with a rate constant of about $(1.80 \pm 0.02) \times 10^6\ \mathrm{s}^{-1}$ to form the final product (2-phenylbenzofuran). Wirz et al. [3] have assumed that the rate-determining step of this transformation is the cyclization of the triplet to the biradical. At low temperature the formation of this triplet seems to be accomplished within the laser pulse, because the growth preceding the decay at 370 nm cannot be resolved.

At 300 nm, a growth with a rate constant of $(1.7 \pm 0.8) \times 10^6\ \mathrm{s}^{-1}$ is observed (Fig. 5). Strong fluorescence from the photoproduct made kinetic analysis at 300 nm difficult. This result confirms an observation made by Wirz et al. [3]; if another intermediate is involved, it must be shorter-lived than the triplet state, because the rate of formation of the final product is equal to the decay rate of the **1** triplet.

3.7. In hexane

The low polarity of the solvent should disfavour any heterolytic release of the leaving group. Solutions of **1** in hexane were degassed and flashed with an excimer laser 248 nm (120 mJ). UV–vis spectra were recorded 20 and 500 ns after the laser excitation (Fig. 6). Just after the laser, a strong and a large band is observed with a maximum around 310 nm. Longer delays show the same band structure with a lower intensity. Kinetic analysis at 310 nm indicates that the species is formed in less than 25 ns and has a lifetime in degassed solution of (75 ± 5) ns. It is a second order decay ($k = (1.95 \pm 0.03) \times 10^8\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$) in air-saturated hexane (Fig. 7). In oxygen saturated hexane: $k_1 = (8.28 \pm 0.09) \times 10^6\ \mathrm{s}^{-1}$, $k_2 = (7.22 \pm 1.06) \times 10^5\ \mathrm{s}^{-1}$. The longer lifetime in the presence of oxygen may be explained by O_2 trapping of radicals. A study of deoxybenzoin should help to understand these signals.

3.8. Nanosecond LFP of deoxybenzoin in hexane

LFP experiments were done with a solution of deoxybenzoin (**4**) in hexane ($A_{248} = 0.35$ per cm). The transient spectrum (20 ns after the laser) shows two bands, one centred at 310 nm and another one at 430 nm (Fig. 8). The 310 and 430 nm absorptions are due to formation of ketyl, benzoyl and benzyl radicals. Kinetic measurement at 310 nm gave a monoexponential decay ($k_1 = (9.93 \pm 0.09) \times 10^6\ \mathrm{s}^{-1}$) in air saturated solution (Fig. 9), a second order decay in degassed hexane $k = (1.98 \pm 0.02) \times 10^5\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$ (Fig. 10). In oxygen saturated solution $k = (6.50 \pm 0.14) \times 10^7\ \mathrm{s}^{-1}$ (Fig. 11).

3.9. 2-Fluoro-1,2-diphenylethanone triplet lifetime determination

Quenching of the triplet state of **1** by naphthalene was used to determine its lifetime. A solution of **1** in MeCN was excited by 351-nm laser pulses in the presence of naphthalene, and the amount of energy transfer was monitored by the triplet absorbance of naphthalene at 413 nm at the end of the laser pulse (Scheme 5).

The lifetime of $^3\mathbf{1}$ can be defined as follows:

$$\tau_{^3\mathbf{1}} = \frac{1}{k_0 + k_{\mathrm{et}} + c_{\mathrm{N}}} \tag{1}$$

c_{N} is the naphthalene concentration (M), k_{et} the energy transfer reaction rate constant (s^{-1}) and k_0 is the decay rate constant of triplet excited state naphthalene to its ground state (s^{-1})

$$A(^3\mathrm{N}) = \varepsilon_{^3\mathrm{N}} \times l \times c_{^3\mathrm{N}_{t=0}} \tag{2}$$

$$c_{^3\mathrm{N}_{t=0}} = c_{^3\mathrm{N}} \times \frac{k_{\mathrm{et}} \times c_{\mathrm{N}}}{k_0 + k_{\mathrm{et}} + c_{\mathrm{N}}} \tag{3}$$

$A_{\max}$ is the triplet absorbance at high concentration of naphthalene, k_0 the rate constant for the triplet decay of **1** in the absence of naphthalene, and k_{et} is the rate constant for energy transfer (bimolecular).

$$\frac{A_{\max(^3\mathrm{N})}}{A_{(^3\mathrm{N})}} = \frac{\varepsilon_{^3\mathrm{N}} \times l \times c_{^3\mathrm{N}}}{\varepsilon_{^3\mathrm{N}} \times l \times (c_{^3\mathrm{N}} \times k_{\mathrm{et}} \times c_{\mathrm{N}})/(k_0 + k_{\mathrm{et}} + c_{\mathrm{N}}))} \tag{4}$$

This expression can be simplified:

$$\frac{A_{\max(^3\mathrm{N})}}{A_{(^3\mathrm{N})}} = \frac{k_0 + k_{\mathrm{et}} \times c_{\mathrm{N}}}{k_{\mathrm{et}} \times c_{\mathrm{N}}} = 1 + \frac{k_0}{k_{\mathrm{et}} \times c_{\mathrm{N}}} \tag{5}$$

Linear regression of $A_{\max(^3\mathrm{N})}/A_{(^3\mathrm{N})}$ versus $1/c_{\mathrm{N}}$ gave a slope of $k_0/k_{\mathrm{et}} = (5.02 \pm 0.33) \times 10^{-3}$ M (Fig. 12).

A rate constant for triplet–triplet energy transfer between benzophenon or acetophenon and naphthalene (in benzene and isooctane, respectively) of $k_{\mathrm{et}} = 1.0 \times 10^{10}\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$ has been determined by Porter and Wilkinson [9]. By assuming this value, the triplet lifetime of **1** is then 20 ns in MeCN. This triplet lifetime is in the same order of magnitude as the one found for diethyl phosphate benzoin by Rajesh et al. [3] (24 ± 2 ns in trifluoroethanol).

3.10. Diradical trapping experiments

The main intermediate expected for photolysis of **1** in MeCN is a biradical. We tried, without success, two different techniques to trap it (Scheme 6). The first one is based on the use of oxygen to react with the biradical to form the dioxo adduct. In oxygen saturated CD_3CN at −40 °C, **1** was irradiated with an Hg lamp during 30 min. No change was observed in the NMR spectra. A new, oxygen saturated solution at −40 °C was flashed 120 times with 248 nm

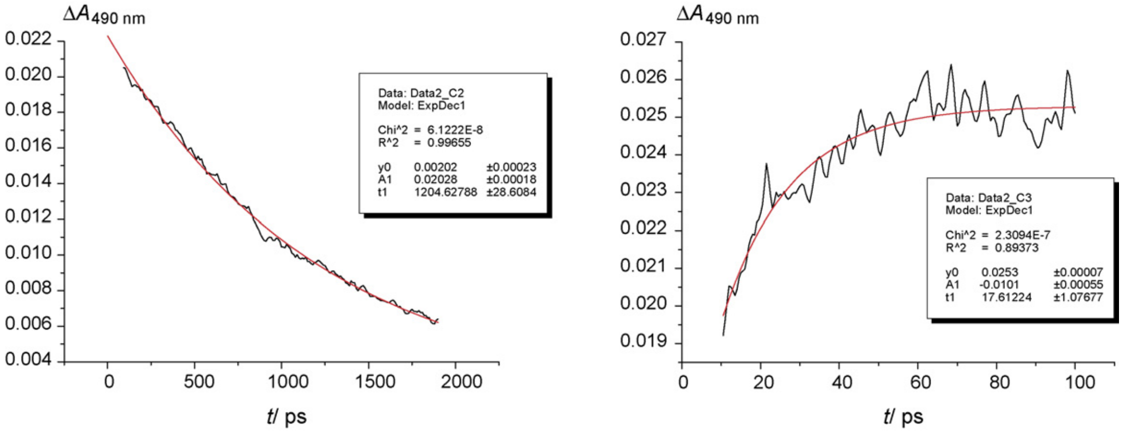


Fig. 20. Kinetic traces of the absorbance at 490 nm extracted from the femtosecond pump-probe spectra of **1** in trifluoroethanol solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 1.9 ns (left), and 0 and 120 ps (right).

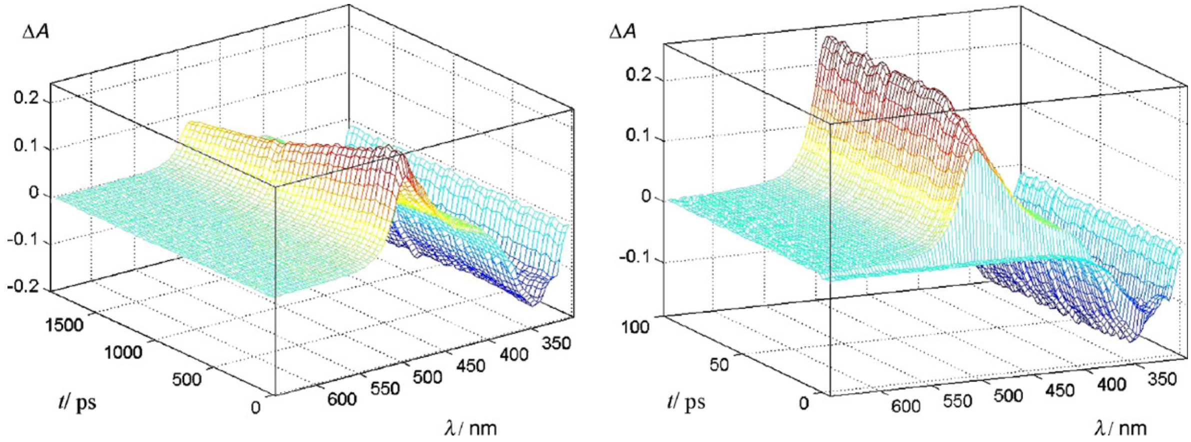


Fig. 21. Femtosecond pump-probe spectra of 2-phenylbenzofuran in trifluoroethanol solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 1.9 ns (left), and 0 and 100 ps (right).

laser (100 mJ) with no success, only formation of benzofuran was observed. The same solution was then irradiated with 1800 flashes at ambient temperature but still only formation of benzofuran was observed.

A biradical intermediate can be investigated by laser flash photolysis using the paraquat dication (1,1′-4,4′-bipyridinium, PQ^{2+}) as an electron transfer trapping agent (Scheme 7). When an electron transfer occurs between PQ^{2+} and the biradical, we should observe a transient at 603 nm, due to $PQ^{\bullet +}$ absorption. Only weak signals have been observed. Two explanations are possible. First the biradical formed may be a poor electron donor. The other explanation could be that the lifetime of the biradical is too short for interception.

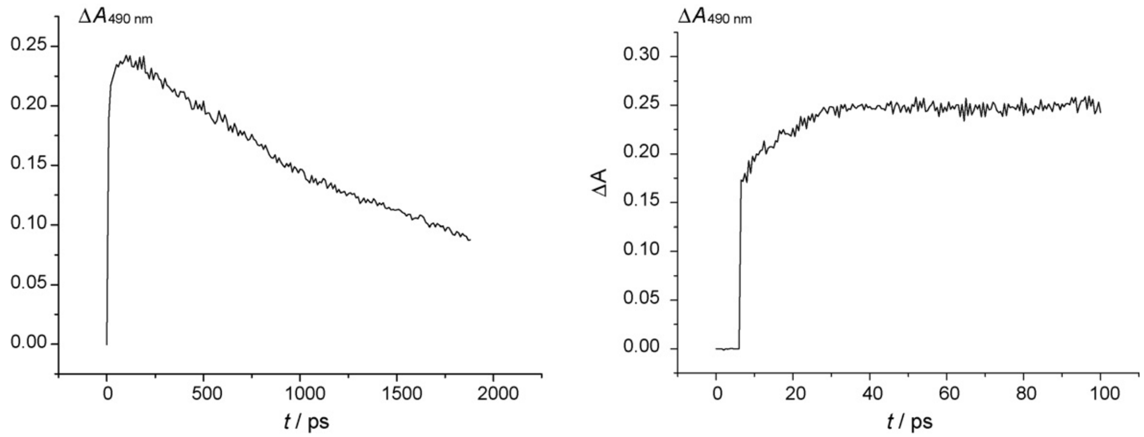


Fig. 22. Kinetic traces of the absorbance at 490 nm extracted from the femtosecond pump-probe spectra of 2-phenylbenzofuran in trifluoroethanol solution (excitation with a subpicosecond flash at 263 nm) with delays between 0 and 1.9 ns (left), and 0 and 120 ps (right).

*3.11. Femtosecond LFP of **1** in MeCN and in trifluoroethanol*

Femtosecond experiments were carried out using solutions of **1** in acetonitrile and trifluoroethanol. Pump-probe spectra, covering a time range from 0 to 1.9 ns, and from 0 to 100 ps to resolve the formation of the transients, were done and shown before their factor analysis in the different figures. On excitation by a subpicosecond pulse at 263 nm, all solutions showed a broad transient absorption in the near-UV, λ_{max} = 310 nm in MeCN (Figs. 13 and 14) and λ_{max} = 315 nm in CF_3CH_2OH (Figs. 15 and 16).

This transient (310 nm) is formed within the first measurement step and observable up to 1.9 ns, hence its lifetime must be at least 2 ns. The data were accumulated through 500 pulses and the final spectrum is an average of three experiments. The transient at 310 nm is attributed to the superposition of the singlet absorbance to the triplet absorbance of **1** (growth of the triplet and decay of the singlet).

The pump-probe spectra of **1** in acetonitrile and trifluoroethanol showed a second absorbance band around 355 nm (Figs. 13 and 15). This band is attributed to the triplet of **1**, because it was still observable after 1.9 ns and corresponds to the signal around 360 nm observed in nanosecond laser flash photolysis at low temperature. Another argument for the triplet assignment is the similarity of the chromophore of **1** with acetophenone. Triplet acetophenone is known to absorb around 330 nm [4], which is relatively close to the triplet band observed for **1**. This transient is formed in 4.5 ps in acetonitrile, and 22 ps in trifluoroethanol (Figs. 17 and 18).

In addition, a short-lived transient absorbing around 497 nm in acetonitrile (490 nm in trifluoroethanol) was observed (lifetime: 2.3 and 1.2 ns in acetonitrile and trifluoroethanol, respectively, and formation in 21 and 18 ps in acetonitrile and trifluoroethanol, respectively) (Figs. 19 and 20). This transient may be due to the presence of another intermediate formed from the singlet in competition with the triplet, or it could be due to accumulation and reexcitation of the photoproduct (2-phenylbenzofuran) in the recycled solution of the flow cell.

To check if the transient observed at 490 nm is due to reexcitation of 2-phenylbenzofuran, we did femtosecond LFP of 2-phenylbenzofuran in CF_3CH_2OH. We can see a transient at 490 nm (lifetime of 1.6 ns in trifluoroethanol, rise time of 10 ps), due to the singlet excited state of 2-phenylbenzofuran (Figs. 21 and 22). The shape of the band and kinetics are similar to the one observed for **1** in the same solvent. A higher intensity maximum has been observed when the spectra have been recorded from 1.9 to 0 ns delay, compare to the spectra recorded from 0 to 1.9 ns delay. This means that photoproduct accumulates (due to prolonged exposure) during the measurements and the signal observed at 490 nm is due to its reexcitation.

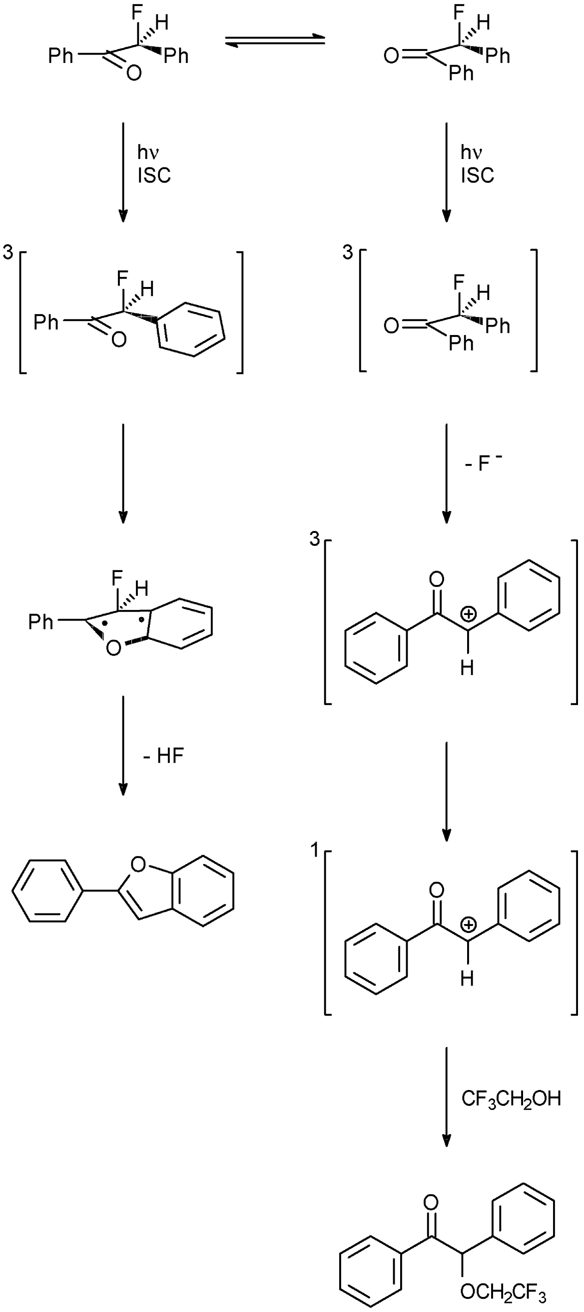
Global analysis of the three dimensional absorption spectra for the two different solvents, using factor analysis, indicated two main factors. A model including two coloured species was then applied to do the global kinetic fits.

$$S \xrightarrow{k_{isc},\ 20\ \mathrm{ps}} T$$

Following this model, the software is able to fit the different parts of the three-dimensional curves and give an accurate rate constant of ^{1}**1** decay in acetonitrile $(3.45 \pm 0.15) \times 10^{11}\ s^{-1}$ and in trifluoroethanol $(7.68 \pm 0.30) \times 10^{11}\ s^{-1}$.

4. Discussion

The observations with **1** (2-fluoro-1,2-diphenylethanone) are quite similar as those reported [3] for benzoin diethyl phosphate. We observed the triplet of **1** at 370 nm with a lifetime of 550 ns at −110 °C in EtOH and the formation of the 2-phenylbenzofuran (**2**) at 310 nm. Observation of the assumed biradical intermediate was not possible, in spite of a lot of effort. One of the possible explanations is that the final product 2-phenylbenzofuran (**2**) is formed from the triplet to a biradical which eliminates HF faster than it is possible to observe (Scheme 8). Fast release of β-leaving groups from related biradical intermediates is also well substantiated [10].



Scheme 8. Proposed mechanism for LFP of **1**.

Two main conformers of **1** can exist. One in which carbonyl group and phenyl ring on α-position is in *syn* orientation and another with *anti*-orientation of these two groups. Recent calculations indicate that the fast concerted elimination of diethyl phosphoric acid occurs from a *syn*-configuration of benzoin diethylphosphate [3] and [11]. We proposed that such fast concerted reaction leading to the final benzofuran also occurred in the case of 2-fluorobenzoin (**1**). This process appears like a one step reaction following the observation done in ethanol at low temperature. The decay rate constant of the triplet corresponds exactly to the growth of the 2-phenylbenzofuran (**2**). Recently, the primary intermediate, $\lambda_{max} = 355$ nm, which is formed within 50 ps from n–π^* excited singlet state of 2-acetoxy or 2-fluoro-3′,5′-dimethoxybenzoin is assigned to the prebenzofuran biradical intermediate [12]. A triplet α-ketocation was observed at 570 nm with a lifetime of 400 ns by LFP of **1** in water (4% MeCN). Product analysis indicates that 2-phenylbenzofuran (**2**) is mainly formed in MeCN, and that solvent addition on α-ketocation occurs in trifluoroethanol and water. On the other hand, photolysis of **1** in THF, good hydrogen donor of nucleophilic character, led to the formation of a complex reaction mixture and beside cyclic product **2**, the main products derived from hydrogen atom and tetrahydrofuryl radical from the solvent abstraction. In nonpolar cyclohexane as a solvent, α-cleavage is the main process. Banerjee and Falvey determined [13] that excited triplet state of phenacyl phenyl acetate abstracts a H-atom form various donors to form the ketyl radical. H-atom donors cause formation of a new longer-lived transient species having a maximum near 310 nm and a much weaker tail extending to 425 nm. We observed that such an absorption spectrum is also characteristic of ketyl radical formed from 2-deoxybenzoin in hexane. Compound **1** shows the same transients in hexane as 2-deoxybenzoin, and chemical analysis of the photolysis products show a large distribution of products issued from homolysis.

We propose the following mechanism for the photolysis of **1** in MeCN and trifluoroethanol (Scheme 8). The triplet state of **1** observed in nanosecond experiment at low temperature has been confirmed in femtosecond experiments. ^{3}**1**, which was identified by transient absorption at 370 nm (rise time: 4.5 ps in acetonitrile, and 22 ps in trifluoroethanol), is stable up to 1.9 ns (a lifetime of 20 ns has been determined by quenching experiments with naphthalene) and has the similarities with acetophenone triplet (330 nm). Triplet of diethylphosphate benzoin has also been observed in the past by Wirz et al. [3]. This study has shown that replacement of diethyl phosphate by fluorine as a leaving group does not affect the mechanism of photocyclization and does not slow the reaction, compare to diethylphosphate benzoin [3]. It is possible to explain this observation by the similar acidity constants of HF ($pK_a = 3.17$) and diethylphosphate ($pK_a = 1.39$).

Acknowledgments

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