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2-Hydroxyphenacyl ester: A new photoremovable protecting group

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Abstract

2-Hydroxyphenacyl moiety absorbing below 370 nm is proposed as a new photoremovable protecting group for carboxylates and sulfonates. Laser flash photolysis and steady-state sensitization studies showed that the leaving group is released from a short-lived triplet state. In addition, DFT-based quantum chemical calculations were performed to determine the key reaction steps. We found that triplet excited state intramolecular proton transfer represents a major deactivation channel. Minor productive pathways involving the triplet anion and quinoid triplet enol intermediates have also been identified.

Introduction

The 4-hydroxyphenacyl (**1**, pHP) photoremovable protecting group (PPG)^{1,2} has received considerable attention due to its fast and efficient substrate release along with the major byproduct, 4-hydroxyphenylacetic acid (Scheme 1).^{3–6} A recent study has shown that various substituents on the pHP chromophore affect only slightly the overall efficiency and the release rates.⁷ The presence of water is essential for this reaction; the photorearrangement is completely suppressed at low water concentrations.^{8,9} The pHP derivatives have been utilized as PPGs in a variety of fields, such as neurobiology, enzyme catalysis, or biochemistry.¹⁰ Release of the protected substrate from the pHP chromophore (Scheme 1) is believed to occur via a water-assisted adiabatic triplet biradical extrusion followed by formation of a putative ground state spirodienedione (**2**), reminiscent of the Favorskii rearrangement intermediate.

We have recently demonstrated that benzofuranones are formed by irradiation of the substituted 2-hydroxyphenacyl (oHP) benzoate **3** in the presence of water (Scheme 2).⁹ It

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Dedicated to Professor Jakob Wirz on the occasion of his 70th birthday.

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was suggested that the products are formed via the photo-Favorskii-type rearrangement through a putative spirodienedione intermediate.

The 2-hydroxyphenyl ketones are known to undergo a very fast (hundreds of fs) and efficient singlet excited-state intramolecular proton transfer (ESIPT) between the two neighboring oxygen atoms in the gas phase.^{11–16} Fluorescence and phosphorescence spectroscopy of oHP derivatives confirmed that the singlet ESIPT occurs in non-polar solvents while hydrogen bonding of the 2-hydroxy moiety with protic solvent molecules prevents the singlet ESIPT and subsequently leads to the triplet state.¹⁵ However, time-resolved EPR study of 2-hydroxyacetophenone (oHA) in ethanol suggested that singlet ESIPT precedes ISC to the triplet state.¹⁴

In this work, we report on the synthesis of oHP derivatives and their photochemical behavior. A series of laser flash photolysis experiments and DFT-based quantum chemical calculations were performed to determine the key reaction steps. We show that the oHP chromophore has interesting properties as a photoremovable protecting group for carboxylic and sulfonic acids.

Results

Synthesis

2-Hydroxyphenacyl esters (**3a–c**) were synthesized in a two-step procedure by bromination of 2-hydroxyacetophenone **4** to give **5** and subsequent nucleophilic displacement of the bromine atom by benzoate, acetate or methanesulfonate (Scheme 3). 2-Methoxyphenacyl acetate (**6**) was prepared using the same reaction sequence from 2-methoxyacetophenone (**7**) and subsequently the bromide **8**. The overall chemical yields were approximately 50% (Supporting Information).

Absorption spectra

Figure 1 shows the absorption spectra of 2-hydroxyacetophenone (**4**; $\lambda_{\text{max}} = 248$ and 325 nm), the corresponding anion **4**[−] ($\lambda_{\text{max}} = 222$, 255, and 360 nm) and the protonated form **4**⁺ ($\lambda_{\text{max}} = 283$ and 372 nm). The ground state pK_a (**4** $\rightarrow$ **4**[−]; H₂O/CH₃CN (98:2, v/v); 10 mM phosphate buffer) = 10.3 ± 0.3 was determined by a spectrophotometric titration using a global fit to the data.

The absorption spectra of **3b** in H₂O/CH₃CN (95:5, v/v) ($\lambda_{\text{max}} = 210$, 254, and 325 nm) and **3b**[−] in aq solution of sodium hydroxide (1 mM; $\lambda_{\text{max}} = 240$, 260, and 365 nm) are shown in Figure 2. The ground state pK_a (**3b**, H₂O/CH₃CN (98:2, v/v); 10 mM phosphate buffer) = 10.2 ± 0.3 was determined using the same method as that used for **4**. The carboxylates **3a,b** were found to be stable for over 24 h in buffered (pH = 7.4; $c = 1$ mM) and non-buffered aqueous (pH = 10; $c = 3$ mM) solutions in the dark; they hydrolyzed at pH = 11. The hydrolysis products were also detected after 48 h in both buffered and non-buffered solutions. **3c** decomposed in the solutions of pH = 8, which prevented the determination of its pK_a . The maximum aqueous solubility of **4**, **3b** and **3c** was determined to be approximately 3×10^{-3} M.

Photochemistry

Solutions of the phenacyl ester (**3a–c**; $c \sim 10$ mM) in various solvents or solvent mixtures were irradiated until more than 95% of the starting material had disappeared. All esters released the corresponding acids (HX) in very high yields (Scheme 4; Table 1). The 2-hydroxyphenacyl moiety was transformed into two photoproducts, benzofuran-3(2*H*)-one

(**9**) and minor amounts of benzofuran-2(3*H*)-one (**10**). The disappearance quantum yields of **3a–c** in H₂O/CH₃CN (1:1 or 7:3, v/v) were determined (Table 2).

The dihydrobenzofuran **11** was formed by irradiation of 2-methoxyphenacyl acetate **6** (~10 mM) in dry CH₃CN through a Pyrex filter ($\lambda = 280$ nm); the acetate group was not released (Scheme 5). The reaction efficiency (Φ) was below 0.01.

The role of dissolved oxygen was evaluated by obtaining the ratios of the disappearance quantum efficiencies of **3b, c** in samples purged with either gaseous oxygen (Φ_{O_2}) or nitrogen (Φ_{N_2}) (Table 3). One sample Student's *t*-tests indicated that the means of the ratios measured were significantly different from unity at the 0.95-confidence level, signifying the importance of oxygen presence on the phototransformation efficiency. Also, a two-sample *t*-test showed a statistically significant difference between the means given in entries 1 and 2 of Table 3 at the 0.95-confidence level.

Irradiation ($\lambda_{exc} = 366$ nm) of **3b** in the presence of 2-naphthalene sulfonate (0.2 M; triplet quencher, $E_T < 61$ kcal mol⁻¹; this value is estimated with respect to $E_T = 61$ kcal/mol for naphthalene¹⁹ which does not absorb at 366 nm) in D₂O/CD₃CN (1:1, v/v) led to the formation of both **9** and **10** with approximately the same efficiency as that obtained in the absence of a quencher (see Table 2).

Triplet sensitization of **3c** with xanthenone (0.1 M) in D₂O/CD₃CN (1:1, v/v) ($\lambda_{exc} = 366$ nm; $\epsilon(\text{xanthenone}) / \epsilon(\text{3c})$ was 5 : 1 at this wavelength) led to the same distribution of photoproducts as that shown in Table 1.

Isotope labeling

The incorporation of oxygen from water as a solvent to the products **9** and **10** during irradiation of **3a** (Scheme 4) was studied. Irradiation of **3a** in D₂¹⁸O/CD₃CN (1:4, v/v) gave the same photoproduct distribution (**9/10**) as that found in D₂¹⁶O/CD₃CN (1:4, v/v); no ¹⁸O incorporation was observed according to the HRMS analyses. However, the –CH₂– group protons in both **9** and **10** can be exchanged by deuterons in D₂O solutions. This process has a half-life in the order of hours.

In contrast, irradiation of 4-hydroxyphenacyl (**1**, pHP) benzoate (~10 mM) in D₂¹⁸O/CD₃CN (1:4, v/v) to 90% conversion gave, along with the release of benzoic acid, two photoproducts, 4-hydroxyphenacylacetic acid (**2**, 80%) and 4-(hydroxymethyl)phenol (8%), which had one ¹⁸O atom incorporated (Scheme 6). This result is in accord with the current knowledge about the photo-Favorskii reaction mechanism (Scheme 1).

Nanosecond laser flash photolysis: 2-Hydroxyacetophenone

Laser flash photolysis (LFP) of **4** in various solvent systems was carried out using the fourth harmonic of a Nd:YAG laser at 266 nm for excitation. Analogous to our work on the triplet state tautomerization of 4-hydroxyacetophenone,²⁰ we hypothesized that four excited triplet forms of **4** or **3a–c** may persist under various conditions (Chart 1; q = quinoid enol). The assignments of the transient suggested in this section are explained in the Discussion.

LFP of **4** in acetonitrile and *n*-hexane provided a transient absorption with $\lambda_{max} = 415$ nm, which was assigned to the quinoid triplet enol ³q4* (Chart 1, Figure 3). Excitation of the ground state anion **4**[–] (Figure 1) in 1 mM NaOH in acetonitrile at 266 nm gave a broad transient absorption band with $\lambda_{max} \sim 490$ nm (Figure 3), assigned to the triplet anion ³4*[–].

Transient absorption spectra with a maximum at $\lambda_{max} = 420$ nm and a shoulder at 380 nm were observed in aqueous non-buffered solutions of **4** (pH = 6.2, measured with a glass

electrode; Figure 4). The common decay rate constants at both 420 nm and 380 nm were $k_d \sim 1 \times 10^6$ and $4 \times 10^4 \text{ s}^{-1}$ in aerated and degassed solutions, respectively. The transient was assigned to $^3\mathbf{q4}^*$ (Chart 1; vide infra). After the $^3\mathbf{q4}^*$ signal disappeared, a weak band with $\lambda_{\text{max}} = 380 \text{ nm}$ and $k_d = (7.2 \pm 0.3) \times 10^3 \text{ s}^{-1}$ was observed. It was assigned to the ground state anion $\mathbf{4}^-$ (Figure 1). The tail of the absorption band of $\mathbf{4}^-$, perturbed by ground state $\mathbf{4}$ bleaching, was observed in the given spectral window. The transient spectra in acetate buffer solutions (pH = 3.3, $I = 0.1 \text{ M}$) were similar to those of aqueous solutions showing $^3\mathbf{q4}^*$. The spectra with $\lambda_{\text{max}} = 460 \text{ nm}$ obtained in NaOH (1 mM)/CH₃CN 95:5 (v/v) solutions were assigned to $^3\mathbf{4}^{*-}$; those observed in 70% aqueous HClO₄ solutions to $^3\mathbf{4}^{+*}$ ($\lambda_{\text{max}} = 430 \text{ nm}$) (Figure 5).

We found that $\mathbf{4}$ in CH₃CN quenches the triplet state of xanthenone giving rise to the absorption band at $\lambda_{\text{max}} = 415 \text{ nm}$ which is assigned to $^3\mathbf{q4}^*$ (Figure 6).

Nanosecond laser flash photolysis: 2-Hydroxyphenacyl esters

LFP studies ($\lambda_{\text{exc}} = 266 \text{ nm}$) of $\mathbf{3b}$ and $\mathbf{3c}$ solutions in various solvent systems were also carried out. Compounds $\mathbf{3b}$ and $\mathbf{3c}$ in pure acetonitrile or *n*-hexane gave transient absorption spectra with maxima at $\sim 420 \text{ nm}$ (Figure S5) which were assigned to the quinoid triplet enols $^3\mathbf{q3b}^*$ and $^3\mathbf{q3c}^*$, respectively, analogous to the transients formed from $\mathbf{4}$ (Chart 1).

Flash photolysis of $\mathbf{3b}$ in unbuffered H₂O/CH₃CN (95:5, v/v) and in the same solvent system with pH adjusted to 2 (0.01 M HClO₄) provided transient absorption spectra with maxima at 425 nm (and a shoulder at 380 nm; Figures S6a and S8) which were assigned to $^3\mathbf{q3b}^*$. Excitation of $\mathbf{3b}$ in 1 mM NaOH in H₂O/CH₃CN (95:5, v/v, pH = 11.2) gave a transient spectrum with a maximum at 460 nm (Figure S7) assigned to the triplet anion $^3\mathbf{3b}^{*-}$.

LFP of $\mathbf{3c}$ in H₂O/CH₃CN (95:5, v/v) provided transient absorption spectra with a maximum at 460 nm (Figure S6b) assigned to $^3\mathbf{3c}^{*-}$. In weakly acidic solutions (acetate buffer, pH = 5.5, $I = 0.01 \text{ M}$), $\mathbf{3c}$ provided an absorption band at 460 nm assigned to $^3\mathbf{3c}^{*-}$ (Figure S9); an absorption with $\lambda_{\text{max}} = 425 \text{ nm}$ observed at pH = 1 (aq HClO₄) was assigned to $^3\mathbf{q3c}^*$. The kinetic traces of the transients formed by LFP of $\mathbf{4}$, $\mathbf{3b}$ and $\mathbf{3c}$ were measured in unbuffered 2% acetonitrile aqueous solution and were fitted by monoexponential functions. The corresponding rate constants (k_d) are summarized in Table 4. In addition, we found that quenching of $^3\mathbf{3c}^{*-}$ ($\lambda_{\text{exc}} = 355 \text{ nm}$) in water by potassium sorbate was nearly diffusion-controlled (Figure S1), and that both $\mathbf{3b}$ and $\mathbf{3c}$ were sensitized by energy transfer from xanthenone triplet in water/acetonitrile 1:1 (v/v) (Figures S2 and S3).

Quantum chemical calculations

The relative energies of various conformers of $\mathbf{4}$ and $\mathbf{q4}$ in their singlet ground and lowest triplet states are summarized in Figure S11. The solvation effects were modeled within a polarizable continuum model (PCM) to account for long range solvent effects or a hybrid approach, combining the PCM with explicit solvation by a small number of water molecules to include specific interactions. Two water molecules were used in the case of a hybrid approach, each connecting an oxygen atom of $\mathbf{4}$, $\mathbf{q4}$ or $\mathbf{4}^-$ to hydrogen atom in the water molecule via a hydrogen bond or connecting the proton on the oxygen atom of $\mathbf{4}$ or $\mathbf{q4}$ via a hydrogen bond with the oxygen atom of the water molecule.

No minimum was found for a conformer possessing an intramolecular hydrogen bond (Figure S11) of $\mathbf{q4}$ in the ground state; proton transfer to $\mathbf{4}$ thus occurred spontaneously during the optimization procedure suggesting on a very small barrier for this process. The same behavior was observed for a $^3\mathbf{4}^*$ conformer possessing an intramolecular hydrogen

bond in the triplet state which leads to the formation of a corresponding $^3\mathbf{q4}^*$ conformer. The triplet-triplet absorption spectra calculated for the most stable conformers of $^3\mathbf{4}^*$, $^3\mathbf{q4}^*$ and $^3\mathbf{4}^{*-}$ in PCM employing the linearized harmonic reflection principle²⁰ are shown in Figure 7. The two major vertical electronic transitions in the spectrum of $^3\mathbf{q4}^*$ with two explicit water molecules within a simple TD-DFT model are shown as blue bars. Obviously, there are two important transitions which broaden the signal observed for the spectrum of $^3\mathbf{q4}^*$.

Discussion

The major advantages of the *p*-hydroxyphenacyl (**1**, pHP) photoremovable protecting group (PPG) is the solubility of their cages in aqueous solutions and ultrafast release rates with high efficiencies of decaging forming chemically and biologically benign byproducts. Thus, pHP proved to be superior among a variety of known PPGs in neurobiology, enzyme catalysis, and other biochemical applications.¹⁰ A major disadvantage of the pHP chromophore is the necessity to use rather short-wavelength UV light for irradiation, which can be destructive to biological material. Excitation of derivatives of **1** is followed by ultrafast intersystem crossing (ISC) to the triplet state (~3 ps)⁸ and a subsequent cascade of intermediates formed in steps, in which water plays a crucial role. The reaction, termed the photo-Favorskii rearrangement due to its obvious similarity with the base-catalyzed transformation of α -haloketones,²¹ finally gives *p*-hydroxyphenylacetic acid as the major rearrangement product (Scheme 1).

Recently, we reported that benzofuranones are formed in high yields upon irradiation of 2-hydroxy-4,6-dimethylphenacyl esters (**3**) in solvents containing an appreciable amount of water (>10%; Scheme 2).⁹ This phototransformation, which led to the concomitant release of a carboxylic acid, appears to parallel the photo-Favorskii pathway of the pHP chromophore. In contrast to the photorearrangement of **1**, the decarbonylation product (benzyl alcohol) was not formed by the photolysis of **3**. In this work, we decided to explore the photochemical behavior of *o*-hydroxyphenacyl derivatives (**3**, oHP) as a novel PPG.

The UV spectrum of the parent chromophore of compounds **3**, 2-hydroxyacetophenone (**4**, oHA), is significantly red-shifted with appreciable absorption above 350 nm (Figure 1) compared to *p*-hydroxyacetophenone.²⁰ We determined the pK_a of **4** by spectrophotometric titration to be 10.3 ± 0.3 , which is shifted by more than two orders of magnitude compared to that of *p*-hydroxyacetophenone ($pK_a = 7.9 \pm 0.1$ ²⁰). It is well known that the conjugate bases of pHP derivatives display a significant decrease in their quantum yields of the leaving group release at pH above their pK_a s.⁷ Thus the pK_a of **4** suggests that derivatives of **3** may not suffer from this drawback. The conjugate acid of **4**, **4**⁺, requires very acidic conditions to exist in appreciable amounts.

The synthesis of the oHP esters **3a–c** was straightforward and parallels a well-known synthetic approach to derivatives of **1**. Thermal stability of **3a,b** (at pH <10) and **3c** (at pH <8) in aqueous solutions holds promise for their application at physiological conditions. Irradiation of **3** in water-containing solvents led to the formation of the two benzofuranones **9** and **10**, accompanied by release of the corresponding acids in high chemical yields (Table 1). This photoreaction was suppressed when dry solvents were used, which is also known from the photochemistry of **1**.^{9,22} However, water obviously does not trap any reactive intermediates, which was demonstrated for **3a** by isotopic labeling experiments (Scheme 6 and the related text in the Results).

The *o*-hydroxy group is essential for the observed transformation. A different although inefficient reaction channel opens when the hydroxy group is replaced by a methoxy group

in **6**. The dihydrobenzofuran **11**, formed as the sole product, retains the acetate group (Scheme 5). Such photoinduced δ -hydrogen abstraction reactions have been studied before^{23–25} and were recently applied in the synthesis of cyclophanes.²⁶

The quantum yields of **3a–c** degradation were lower by a factor of 2 than those of the corresponding PHP esters **1**.^{7,10} The product formation was only slightly reduced by the presence of a triplet quencher (2-naphthalene sulfonate). The triplet energy (E_T) of **4**, estimated from our DFT calculations, was ~ 72 kcal mol⁻¹. The triplet energy of *p*-hydroxyacetophenone is approximately 70.5 kcal mol⁻¹.²⁷ We found that triplet-excited xanthenone ($E_T = 74$ kcal mol⁻¹ ²⁸) sensitized the reaction of **3c** resulting in the formation of both **9** and **10**. As a result, the triplet state of **3**, **³3***, is most likely the reactive state responsible for the release of the leaving group. Provided that energy transfer from **³3*** to 2-naphthalene sulfonate in 95% water/acetonitrile (v/v) is a diffusion controlled process ($k_{\text{diff}} \sim 4 \times 10^9$ M⁻¹ s⁻¹),²⁹ the lifetime of **³3*** must be on the order of 1 ns or less, comparable to those of PHP carboxylates.^{10,22}

The *o*-hydroxyaryl compounds, such as oHP, are known to undergo ultrafast and very efficient excited state intramolecular proton transfer (ESIPT).^{30–32} Although the ISC rate of **¹3*** can be comparable to that of **¹1*** (~ 3 ps),⁸ the singlet ESIPT can effectively compete (600 fs in molecular beam)¹¹ provided that the rate constants do not differ in gas phase and aqueous solutions. We cannot unambiguously claim at the moment that **³3*** is obtained by direct irradiation of **3** followed by subsequent ISC of **¹3***. ESIPT that leads to the formation of **¹q4*** would be feasible if the intramolecular hydrogen bond between the *o*-hydroxy group and the carbonyl oxygen assuring an ideal ESIPT geometry is achieved. It has been reported that polar protic solvents such as methanol or ethanol prevent the intramolecular hydrogen bond to be established in the ground state and, consequently, diminish the efficiency of the singlet ESIPT. This enabled Nagaoka and coworkers to measure the phosphorescence spectra of the triplet intermediates.¹⁵ Hoshimoto and co-workers used time-resolved EPR to study ESIPT in oHA in ethanol and concluded that the formation of **³q4*** is consistent with the singlet state ESIPT followed by ISC to give the triplet excited state.¹⁴

In this work, we performed nanosecond LFP supported by quantum chemical calculations based on the DFT to find whether the triplet excited oHP intermediates are responsible for the group's release and to reveal the subtleties of the triplet ESIPT. Analogous to our recent study of triplet state tautomerization processes of a related system, the *p*-hydroxyacetophenone,²⁰ four species were anticipated to co-exist in the triplet manifold of **4** (Chart 1). DFT calculations on these species predicted that a minimum which would correspond to conformer of **³4*** retaining an intramolecular hydrogen bond does not exist. The hydroxy group proton was spontaneously transferred to the carbonyl oxygen to give **³q4*** during the optimization process. This suggests that there is very little, if any, barrier for the formation of **³q4*** except for rotational barriers of the hydroxy or acetyl groups. Any conformer of **³4*** is destabilized compared to the most stable conformer of **³q4*** by more than 24 kcal mol⁻¹ (Figure S11). Thus the equilibrium constant of **³4*** $\rightleftharpoons$ **³q4*** is $pK_E < -17$. The equilibrium is markedly shifted toward **³q4***, which should be formed rapidly from **³4***. For comparison, the equilibrium constant pK_E for *p*-hydroxyacetophenone equals only to -2.1 .²⁰

LFP of **4** provided a band at ~ 400 nm in all solvents used at neutral pH. The rise of this band was not resolved within the time resolution of our LFP setup (~ 5 ns). Its lifetime was prolonged ~ 20 -times upon degassing which confirms a triplet nature of the transient. Adjusting pH to 3.3 did not influence its shape or lifetime. Thus, we assigned this band to **³q4*** with the help of our TD-DFT calculations (Figure 7). A new band with a maximum at ~ 450 nm appeared for all derivatives **3** and **4** in the presence of a base (Figures S7 and

Figure 5) and, according to the kinetics observed for aerated and degassed solutions and quantum chemical calculations, it was assigned to the triplet conjugate bases $^3\mathbf{3c}^-*$ and $^3\mathbf{4}^-*$. In highly acidic solutions, a band with a maximum at 425 nm was attributed to $^3\mathbf{4}^{+*}$. No signal, which would correspond to $^3\mathbf{4}^*$ (a calculated spectrum in Figure 7), was observed under any experimental condition within the response time of our apparatus. These results are summarized in Scheme 7.

The most striking observation came from a comparison of the decay rate constant changes found for $^3\mathbf{q3b}^*$ and $^3\mathbf{q4}^*$ in aerated and degassed solutions (Table 4). The rate constants measured for $^3\mathbf{q4}^*$ in degassed solutions were nearly an order of magnitude smaller than those of $^3\mathbf{q3b}^*$, while they did not differ (within the experimental error) in the presence of oxygen. This led us to anticipate that $^3\mathbf{q3b}^*$ may partially be responsible for the acetate release.

Leaving group release from the quinoid triplet enol $^3\mathbf{q1}^*$ (Scheme 8) of pHP cages is a matter of considerable debate.^{20,33,34} It has been suggested that it is the low triplet energy of $^3\mathbf{q1}^*$ (for $^3\mathbf{q1}^*$ (X = H): $E_T \sim 48 \text{ kcal mol}^{-1}$)²⁰ that prevents the release. Because the calculated equilibrium constant for $^3\mathbf{4}^* \rightleftharpoons ^3\mathbf{q4}^*$ is $pK_E < -17$, a decrease in the triplet energy of $^3\mathbf{q4}^*$ can be expected. The DFT calculations found that the triplet energy of $^3\mathbf{q4}^*$ is $E_T \sim 41 \text{ kcal mol}^{-1}$ and that $^3\mathbf{q4}^*$ should not be quenched by typical triplet quenchers such as naphthalenes or sorbate. As a result, the release of acetate from $^3\mathbf{q3b}^*$ was experimentally confirmed by measuring the relative quantum efficiencies of a series of nitrogen- and oxygen-saturated solutions of **3b** under the same conditions at which appreciable amounts of $^3\mathbf{q3b}^*$ are formed upon excitation. The triplet $^3\mathbf{3b}^*$ cannot be effectively quenched by oxygen due to its short lifetime ($\tau = 1 \text{ ns}$). We were able to observe a statistically significant (at 95% confidence level, Table 3) decrease of the quantum yield in the oxygen-saturated solutions in all samples in which only $^3\mathbf{q3}^*$ is present (Figure S8; Table 3, entries 2 and 3). In addition, we found an even greater, statistically significant, decrease in the quantum yield in oxygen-saturated solutions at neutral pH (Table 3, entry 1) where both $^3\mathbf{3b}^-*$ and $^3\mathbf{q3b}^*$ were present (Figure S6a). This suggests that the acetate release took place from both $^3\mathbf{3b}^-*$ and $^3\mathbf{q3b}^*$ regardless of a very low triplet energy of the latter species. The release rate constant from $^3\mathbf{q3b}^*$ was estimated from our LFP measurements to be $\sim 2 \times 10^5 \text{ s}^{-1}$ provided that the ISC rate constants of $^3\mathbf{q3b}^*$ and $^3\mathbf{q4}^*$ are comparable. The oxygen concentration in non-degassed water/acetonitrile solutions amounts to $\sim 10^{-3} \text{ M}$,³⁵ sufficiently high to interfere with the release step. Inability to unambiguously confirm that $^3\mathbf{q1}^*$ is not responsible for the leaving group release originates from the ISC rate $k_{\text{ISC}} = 5 \times 10^6 \text{ s}^{-1}$ found in degassed aqueous solutions for $^3\mathbf{q1}^*$ (X = H),²⁰ which is higher than that of $^3\mathbf{q4}^*$ by two orders of magnitude (Table 4). Therefore, it is not its low triplet energy but the release step itself that, provided its rate constant equals to that calculated for $^3\mathbf{q3b}^*$, cannot efficiently compete with ISC.

These results show that the adiabatic tautomerization to $^3\mathbf{q3b}^*$ overwhelms any attempt of photorelease from $^3\mathbf{3b}^*$, while $^3\mathbf{q3b}^*$ is not capable of efficient releasing of the leaving group. The quantum yields of the photoreaction of **3b**, **c** are half of those reported for the pHP derivatives **1**. The steady-state sensitization experiment clearly showed that triplet energy transfer to **3** leads to the photoproducts. It must be $^3\mathbf{3}^*$ that is populated by the energy transfer because none of the diastereomers of **q3** is populated in the ground state (Figure S11). However, the LFP spectra measured upon excitation of xanthenone followed by diffusion-controlled triplet energy transfer ($\sim 3.8 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, Supporting Information) do not contain any traces of $^3\mathbf{3}^*$. Therefore, triplet ESIPT has occurred fully within 20 ns (Figure 6). In addition, $^3\mathbf{q4}^*$ (and not $^3\mathbf{4}^*$) is detected within the response time of our apparatus (5 ns) upon direct irradiation of **4**. This, together with the results of our quantum

chemical calculations, suggests that the decrease in the quantum yields, compared to pHP cages, is a consequence of very fast ESIPT, which is under investigation in our laboratories at the moment. The proposal of the photo-Favorskii-like reaction mechanism of oHP derivatives is presented in Scheme 9.

Conclusions

In conclusion, the oHP group can be utilized as a photoremovable protecting group for mediocre and good leaving groups. The major advantages are its simple synthesis, ground state $pK_a > 8$, and bathochromically shifted absorption spectrum with appreciable molar absorption coefficients above 350 nm compared to pHP derivatives. The deprotection quantum yield is most probably lowered by competing, nonproductive adiabatic tautomerization reactions, in which the ESIPT represents a dominant energy wasting pathway. We found that the leaving group is released predominately from a short-lived triplet state ($^3\mathbf{3}^*$) but inefficiently also from both the $^3\mathbf{3}^*$ and $^3\mathbf{q3}^*$ intermediates.

Experimental

Quantum yields measurements

The quantum yield measurements were performed on an optical bench consisting of a 40-W medium pressure mercury lamp equipped with a 313 nm band-path filter. The concentration of the sample solutions was in the interval of 5×10^{-4} and 1×10^{-3} M. Hexadecane and ethyl benzoate (1×10^{-3} M) were used as GC and HPLC internal standards, respectively. A sealed capillary containing TMS in CD_3CN was used as an internal standard for NMR measurements. 2-Nitrobenzaldehyde in acetonitrile¹⁷ and valerophenone in cyclohexane¹⁸ were used as the actinometers. The reaction conversions were always kept below 15% to avoid the interference of photoproducts. The relative standard deviations of the mean for multiple (at least three) samples were found below 10% in all analyses.

Laser Flash Photolysis

The nanosecond laser flash photolysis setup was operated in a right angle arrangement of the pump and probe beams. Laser pulses of 700 ps duration at 355 nm (120–200 mJ) or 266 nm (30–80 mJ) were obtained from a Nd:YAG laser and were dispersed over the 4-cm optical path of a quartz cell by a cylindrical concave lens. The absorbance of the sample solution was adjusted to 0.3–0.5 per cm at the wavelength of excitation. A pulsed 75-W xenon lamp was used as the source of probe white light. Kinetic (photomultiplier) and spectrographic detection (ICCD camera) of the transient absorption were available. Measurements were performed at ambient temperature (20 ± 2 °C). Oxygen was removed from the sample solutions by repeated freeze-thaw cycles under reduced pressure (5 Pa).

Synthesis

2-(2-Hydroxyphenyl)-2-oxoethyl benzoate (3a)—2-Bromo-*o*-hydroxyacetophenone (**5**, 2.56 g, 11.9 mmol; Supporting Information) in acetone (5 mL) and TEA (1.6 mL, 11.9 mmol) were added to a solution of benzoic acid (1.45 g, 11.9 mmol) in acetone (30 mL) at 20 °C. The reaction mixture was then refluxed. When the conversion reached >98% (GC; ~ 2 h), the mixture was cooled to 20 °C, filtered, and the solvent was removed under reduced pressure. The resulting solid was dissolved in ethyl acetate (20 mL) and water (20 mL) was added. The aqueous layer was separated and washed with ethyl acetate (20 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), dried over MgSO_4 , filtered, and the solvent was removed under reduced pressure to give the crude title product. The compound was purified using flash column chromatography (ethyl acetate/*n*-hexane, 1:4, v/v). Yield: 1.92 g (63%); yellowish crystals; mp 103–105 °C (lit. 104–105

$^{\circ}\text{C}$).³⁶ ^1H NMR (200 MHz, CDCl_3): δ (ppm) 5.65 (s, 2H), 6.90–7.10 (m, 2H), 7.48–7.70 (m, 4H), 7.74 (dd, 1H, $J_1 = 8.0$ Hz, $J_2 = 1.4$ Hz), 8.18 (distorted d, 2H), 11.71 (s, 1H, –OH) (Figure S12). ^{13}C NMR (75.5 MHz, CDCl_3): δ (ppm) 65.5, 117.5, 119.1, 119.5, 128.6, 128.8, 129.4, 130.2, 133.7, 137.3, 162.6, 166.2, 197.5 (Figure S13). MS (EI, 70 eV): $m/z = 256$ (8), 225 (4), 134 (15), 121 (70), 105 (100), 93 (12), 77 (35), 65 (12), 51 (11). FTIR (KBr, cm^{-1}): 3049, 2936, 1730, 1663, 1617, 1583, 1493, 1451, 1415, 1273, 1210, 1123, 1017, 1113, 1017, 968, 860, 798, 755, 712. UV-Vis: ϵ_{313} (2 % (v/v) CH_3CN in H_2O) = $3050 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; ϵ_{366} (2 % (v/v) CH_3CN in H_2O) = $400 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ (Figure S14). Anal. calcd for $\text{C}_{15}\text{H}_{12}\text{O}_4$: C, 70.31; H, 4.72, found C, 70.44; H, 4.74. HRMS (HPLC-APCI-MS): calcd for $\text{C}_{15}\text{H}_{11}\text{O}_4$ ($\text{M} - \text{H}^+$) 255.0657, found 255.0659. This compound has also been characterized elsewhere.³⁷

2-(2-Hydroxyphenyl)-2-oxoethyl acetate (3b)—This compound was synthesized from **5** and acetic acid according to the same procedure as **3a**. Yield: 50%; white crystals; mp 59.0–59.8 $^{\circ}\text{C}$ (lit. 58–59 $^{\circ}\text{C}$).³⁶ ^1H NMR (300 MHz, CDCl_3): δ (ppm) 2.26 (s, 3H), 5.37 (s, 2H), 6.95 (ddd, 1H, $J_1 = 7.0$ Hz, $J_2 = 7.0$ Hz, $J_3 = 1.0$ Hz), 7.03 (dd, 1H, $J_1 = 8.6$ Hz, $J_2 = 1.0$ Hz), 7.53 (ddd, 1H, $J_1 = 7.3$ Hz, $J_2 = 7.3$ Hz, $J_3 = 1.3$ Hz), 7.63 (dd, 1H, $J_1 = 8.3$ Hz, $J_2 = 1.3$ Hz), 11.64 (s, 1H, –OH) (Figure S15). ^{13}C NMR (75.5 MHz, CDCl_3): δ (ppm) 20.0, 64.7, 116.9, 118.4, 119.0, 128.3, 136.7, 161.9, 170.0, 197.4 (Figure S16). MS (EI, 70 eV): $m/z = 194$ (7), 163 (2), 152 (20), 134 (13), 121 (100), 105 (6), 93 (10), 77 (5), 65 (12), 43 (22). FTIR (KBr, cm^{-1}): 3064 (br), 2988, 2940, 1740, 1658, 1613, 1577, 1491, 1426, 1385, 1292, 1279, 1245, 1204, 1158, 1083, 974, 868, 790, 753, 730, 667, 646, 518, 506, 449. UV-Vis: ϵ_{313} (CH_3CN) = $2770 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; ϵ_{366} (CH_3CN) = $250 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; UV-Vis: ϵ_{313} (50 % (v/v) CH_3CN in H_2O) = $2870 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; ϵ_{366} (50 % (v/v) CH_3CN in H_2O) = $240 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; UV-Vis: ϵ_{313} (2.5 % (v/v) CH_3CN in H_2O) = $2660 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; ϵ_{366} (2.5 % (v/v) CH_3CN in H_2O) = $370 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ (Figure S17). HRMS (HPLC-APCI-MS): calcd for $\text{C}_{10}\text{H}_9\text{O}_4$ ($\text{M} - \text{H}^+$) 193.0501, found 193.0500. This compound has also been characterized elsewhere.³⁷

2-(2-Hydroxyphenyl)-2-oxoethyl methanesulfonate (3c)—A suspension of 2-bromo-*o*-hydroxyacetophenone (**5**, 1.45 g, 6.73 mmol), silver (I) oxide (2.34 g, 10.1 mmol) and methanesulfonic acid (0.88 mL, 13.5 mmol) in acetonitrile (150 mL) was vigorously stirred overnight at 60 $^{\circ}\text{C}$. After the starting material disappeared (TLC), the reaction mixture was cooled to 20 $^{\circ}\text{C}$, filtered through a Celite pad, and the solvent was removed under reduced pressure. The compound was purified from the residue using flash column chromatography (ethyl acetate/*n*-hexane, 1:2, v/v). Yield: 0.95 g (62%); white crystals; mp 78.0–80.2 $^{\circ}\text{C}$. ^1H NMR (300 MHz, CDCl_3): δ (ppm) 3.29 (s, 3H), 5.53 (s, 2H), 6.96 (ddd, 1H, $J_1 = 7.3$ Hz, $J_2 = 7.3$ Hz, $J_3 = 1.3$ Hz), 7.09 (dd, 1H, $J_1 = 8.7$ Hz, $J_2 = 1.0$ Hz), 7.56–7.63 (m, 2H), 11.49 (s, 1H, –OH) (Figure S18). ^{13}C NMR (75.5 MHz, CDCl_3): δ (ppm) 39.3, 69.1, 116.8, 119.2, 119.8, 119.9, 128.4, 137.8, 162.6, 196.2 (Figure S19). MS (EI, 70 eV): $m/z = 230$ (6), 214 (<1), 196 (<1), 185 (<1), 151 (10), 134 (20), 121 (100), 105 (16), 93 (14), 77 (10), 65 (16), 50 (4). FTIR (KBr, cm^{-1}): 3433 (br), 3037, 3016, 2952, 1656, 1614, 1488, 1447, 1349, 1291, 1207, 1167, 1056, 975, 957, 782, 753, 714, 523, 504. UV-Vis: ϵ_{313} (CH_3CN) = $4050 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; ϵ_{366} (CH_3CN) <50 $\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; ϵ_{313} ($\text{H}_2\text{O}/\text{CH}_3\text{CN}$, 9:1, (v/v)) = $2900 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$; ϵ_{366} ($\text{H}_2\text{O}/\text{CH}_3\text{CN}$, 9:1, (v/v)) = $420 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ (Figure S20). HRMS (HPLC-APCI-MS): calcd for $\text{C}_9\text{H}_9\text{O}_5\text{S}$ ($\text{M} + \text{H}^+$) 231.0322, found 231.0322.

Photochemical experiments

Irradiation in NMR tubes (a general procedure)—A solution of the corresponding phenacyl derivative (**3a–c**, **6** or **1** ($\text{X} = \text{benzoate}$), ~2 mg) in a deuterated solvent or solvent mixture (0.50–0.75 mL) was irradiated either in a Rayonet reactor at $\lambda = 300 \pm 20$ nm or

with a 40-W medium-pressure mercury lamp equipped with a 313 nm band-pass filter. NMR cuvettes also act as a Pyrex filter ($\lambda_{\text{irr}} = 280 \text{ nm}$). ^1H NMR spectra were measured in the corresponding time intervals to follow the course of the reaction.

Preparative-scale irradiation—Irradiation was done in two different ways. (a) A large test tube containing a sample solution ($c = 0.01\text{--}0.02 \text{ M}$, 70–100 mL) was fitted with a rubber septum and the sample was degassed by bubbling with argon for 10 min. The test tube was then irradiated in an immersion well. (b) For a larger-scale reaction ($c = 0.01\text{--}0.02 \text{ M}$ in 250 mL), photolysis was carried out in an immersion well equipped with a quartz cooling jacket and a condenser. A 450-W medium-pressure mercury arc lamp with a Pyrex filter ($\lambda > 290 \text{ nm}$) was used as a light source.

Characterization of the photoproducts—Identification of the photoproducts was based on NMR analyses and a comparison of their mass spectra (GC-MS) and the GC retention times with those obtained from authentic samples.

Benzofuran-3(2H)-one (9)—The title compound was separated from the irradiated solution of **3a–c** in the corresponding solvent (Table 1) using flash column chromatography (dichloromethane/ethyl acetate/*n*-hexane, 2:1:20, v/v). Orange powder; mp 84–85.5 °C. ^1H NMR (200 MHz, CDCl_3): δ (ppm) 4.67 (s, 2H), 7.09–7.20 (m, 2H), 7.73–7.61 (m, 2H). ^{13}C NMR (50 MHz, CDCl_3): δ (ppm) 74.8, 113.7, 121.3, 122.1, 124.2, 137.9, 174.1, 199.9. MS (EI, 70 eV): $m/z = 134$ (100), 105 (80), 76 (60), 63 (8), 50 (30). FTIR (KBr, cm^{-1}): 3535, 2935, 1725, 1613, 1469, 1405, 1318, 1195, 1155, 1107, 991, 842, 767, 667. HRMS (ESI[−]): calcd for $\text{C}_8\text{H}_5\text{O}_2$ ($\text{M} - \text{H}^+$) 133.0295, found 133.0292. This compound has also been characterized elsewhere.³⁸

Benzofuran-2(3H)-one (10)—The title compound was separated from the irradiated solution of **3a–c** in the given solvent (Table 1) using flash column chromatography (dichloromethane/ethyl acetate/*n*-hexane, 2:1:20, v/v). White crystals; mp 37–40 °C. ^1H NMR (200 MHz, CDCl_3): δ (ppm) 3.78 (s, 2H), 7.12–7.20 (m, 2H), 7.30–7.38 (m, 2H). ^{13}C NMR (50 MHz, CDCl_3): δ (ppm) 33.1, 110.9, 123.1, 124.2, 124.7, 129.0, 154.8, 174.2. MS (EI, 70 eV): $m/z = 134$ (90), 106 (55), 89 (2), 78 (100), 63 (10), 51 (25). FTIR (KBr, cm^{-1}): 3447, 2962, 1803, 1616, 1462, 1386, 1329, 1296, 1230, 1202, 1118, 1057, 961, 891, 822, 761, 673. HRMS (ESI[−]): calcd for $\text{C}_8\text{H}_5\text{O}_2$ ($\text{M} - \text{H}^+$) 133.0295, found 133.0293. This compound has also been characterized elsewhere.³⁹

(±)-3-Hydroxy-2,3-dihydrobenzofuran-3-methylenyl acetate (11)—This product was isolated by flash column chromatography (ethyl acetate/*n*-hexane, 1:3 to 1:1, v/v) from the irradiated solution of 2-(2-methoxyphenyl)-2-oxoethyl acetate **6** in dry CH_3CN to a >90% conversion. Yield: 30%, colorless viscous liquid. ^1H NMR (300 MHz, CDCl_3): δ (ppm) 2.13 (s, 3H), 2.57 (s, 1H, $-\text{OH}$), 4.35–4.55 (m, 4H), 6.89 (d, 1H, $J = 7.9 \text{ Hz}$), 6.97 (dt, 1H, $J_1 = 7.6 \text{ Hz}$, $J_2 = 0.7 \text{ Hz}$), 7.30 (dt, 1H, $J_1 = 7.9 \text{ Hz}$, $J_2 = 1.0 \text{ Hz}$), 7.36 (dd, 1H, $J_1 = 7.6 \text{ Hz}$, $J_2 = 0.7 \text{ Hz}$) (Figure S24). ^{13}C NMR (75.5 MHz, CDCl_3): δ (ppm) 21.0, 68.2, 79.8, 80.6, 111.1, 121.4, 124.1, 128.1, 131.4, 160.7, 170.9 (acetate carboxyl C_q was observed in ^1H – ^{13}C HMBC NMR) (Figures S25 and S26). MS (EI, 70 eV): 208 (10), 190 (2), 148 (8), 135 (100), 119 (1), 107 (30), 91 (6), 79 (35), 77 (25), 63 (4), 51 (5), 43 (25). HRMS (APCI⁺) calcd for $\text{C}_{11}\text{H}_{11}\text{O}_4$ [$\text{M} - \text{H}^+$] 207.0663, found 207.0658.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Ground state absorption spectra of **4** (black, dashed), **4⁻** (red, solid), and **4⁺** (green, dash-dot) obtained in $\text{H}_2\text{O}/\text{CH}_3\text{CN}$ (95:5, v/v), aq NaOH (1 mM, pH = 11)/ CH_3CN (95:5, v/v), and 70% aq HClO_4 , respectively.

Figure 2. Ground state absorption spectra of **3b** (black, dashed) and **3b⁻** (red, solid) obtained in H₂O/CH₃CN (95:5, v/v) and aq NaOH (1 mM, pH = 11)/CH₃CN (95:5, v/v), respectively.

Figure 3.

Normalized triplet-triplet absorption spectra of ${}^3\mathbf{q4}^*$ in acetonitrile (blue) and *n*-hexane (blue empty circles), and ${}^3\mathbf{4}^*$ in aq NaOH (1 mM)/CH₃CN 95:5 (v/v; red). All spectra were recorded 15 ns after excitation of **4** solutions (5×10^{-4} M) with a laser pulse at 266 nm.

Figure 4. Transient absorption spectra recorded 50 ns (blue) and 5 μs (red) after a 266 nm flash in a 50-ns time window in non-buffered $\text{H}_2\text{O}/\text{CH}_3\text{CN}$ (95:5, v/v) solutions of **4** (4×10^{-4} M; pH = 6.2).

Figure 5.

Normalized transient absorption spectra of ${}^3\mathbf{q4}^*$ in aqueous (blue) and acetate buffer (5% CH₃CN; pH = 3.3, $I = 0.1$ M, blue circles) solutions of **4** (5×10^{-4} M), ${}^3\mathbf{4}^{*-}$ in aq NaOH (1 mM, pH = 11)/CH₃CN (95:5, v/v; red) and ${}^3\mathbf{4}^{+*}$ in aq HClO₄ (70%; green) solutions of **4**. All spectra were recorded in a 50-ns time window after a delay of 15 ns following a 266-nm flash.

Figure 6.

Triplet-triplet absorption spectra of pure xanthenone (black circles) and xanthenone in 6.2×10^{-4} M (black), 9.4×10^{-4} M (blue), and 1.6×10^{-3} M (red) CH_3CN solutions of **4**. A spectrum of $3\mathbf{q4}^*$ (red triangles) obtained from the 5×10^{-4} M **4** solution is shown for comparison. The spectra were recorded in a 50-ns time window after a delay of 19 ± 2 ns following the laser flash ($\lambda_{\text{exc}} = 355$ nm). The concentration of xanthenone was $c = 0.37$ mM in all samples except for pure **4**.

Figure 7.

The triplet-triplet absorption spectra employing the linearized harmonic reflection principle calculated for the most stable conformer of the **4** triplet species – neutral ${}^3\mathbf{4}^*$ (black), quinoid enol ${}^3\mathbf{q4}^*$ (blue), and anion ${}^3\mathbf{4}^{*-}$ (red). The blue bars denote the two major electronic transitions of ${}^3\mathbf{q4}^*$.

Scheme 1.
Photochemistry of pHP esters

Scheme 2.
Photochemistry of substituted oHP derivatives

Scheme 4.
Photochemistry of **3a-c**

Scheme 5.
Photochemistry of **6**

Scheme 6.
Photochemistry of **1** in $\text{D}_2^{18}\text{O}/\text{CD}_3\text{CN}$

Scheme 7.
Triplet-state proton transfer equilibria of **4**

Scheme 8.
Release of the leaving group from $^3\text{q1}^*$

Scheme 9.
Proposed reaction mechanism

Chart 1.
Anticipated triplet state transients formed from **3** and **4**

Table 1Photoproducts from irradiation of **3a–c**

compound	solvent ^a	chemical yields / % ^b		
		9	10	HX ^c
3a	benzene	n.r. ^d		
	CH ₃ OH	77 ± 2	14 ± 2	89 ± 2
	CH ₃ CN	n.r. ^d		
	H ₂ O/CH ₃ CN (1:1)	62 ± 3	11 ± 2	71 ± 2
	acetone	n.r. ^d		
	H ₂ O/acetone (1:9)	95 ± 2	traces ^e	96 ± 1
3b	H ₂ O/CH ₃ CN (1:1)	76 ± 4	12 ± 4	88 ± 3
3c	H ₂ O/CH ₃ CN (1:1)	75	15	92 ± 4
	H ₂ O/acetone (1:4)	90	traces ^e	n.d. ^f

^aCommercial perdeuterated solvents were used. The ratios of the solvent mixtures are given as v/v.^bIrradiated at $\lambda_{\text{exc}} = 300$ or 313 nm in non-degassed solutions to >95% conversion; the chemical yields were determined by ¹H NMR; the isolated chemical yields given were lower (by 3–8%) but preserved the same product ratios. The standard deviation is given when at least two independent measurements were carried out.^cHX = HO₂CPh (**3a**), HO₂CCH₃ (**3b**), HOSO₂CH₃ (**3c**).^dNo reaction detected.^ePhotoproducts not detected by ¹H NMR of the reaction mixture.^fNot determined.

Table 2Degradation quantum yields of **3a–c**

compound	solvent	Φ^a
3a	H ₂ O/CH ₃ CN (1:1, v/v)	0.10 ± 0.02
3b	H ₂ O/CH ₃ CN (7:3, v/v)	0.21 ± 0.02
3c	H ₂ O/CH ₃ CN (7:3, v/v)	0.34 ± 0.02

^aIrradiated at $\lambda_{\text{exc}} = 313$ nm in aerated solutions ($c \sim 3$ mM) to <15% conversion. 2-Nitrobenzaldehyde ($\Phi = 0.41 \pm 0.02$ in CH₃CN)¹⁷ and valerophenone ($\Phi = 0.30$ in cyclohexane)¹⁸ were used as the actinometers. HPLC (**3a**) and ¹H NMR (**3b–c**) were used to determine the ester concentrations. The results are based on three independent measurements; the standard deviations of the mean are shown.

Table 3The role of dissolved oxygen in photochemistry of **3b**, **c**

entry	compound	solvent	$\Phi_{O_2}/\Phi_{N_2}^a$
1	3b	H ₂ O/CH ₃ CN (95:5, v/v)	0.796 ± 0.074 (11)
2	3b	aq 1 M malonate, pH = 2.5	0.911 ± 0.043 (6)
3	3c	aq HCl, pH = 1.5	0.911 ± 0.064 (6)

^aThe ratio of the quantum efficiencies of **3b**, **c** (~0.2–0.5 mM) disappearance in the samples purged with O₂ (Φ_{O_2}) and N₂ (Φ_{N_2}) for 15 min.

Irradiated at $\lambda = 313$ nm; the conversions were followed by HPLC using methyl benzoate (2×10^{-4} M) as an internal standard. The 95% confidence interval is given; the number of independent measurements is given in the parentheses for each set of experiments.

Table 4

The observed decay rate constants (k_d) of triplet species formed from **4**, **3b** and **3c** in H₂O/CH₃CN (98:2, v/v) upon excitation at $\lambda_{exc} = 266$ nm

compound (observed transient)	λ_{obs} / nm	k_d (aerated) / 10^6 s^{-1}	k_d (degassed) / s^{-1}
4 ($^3\text{q4}^*$)	380	(1.0 ± 0.3)	$(4.3 \pm 0.2) \times 10^4$
	425	(1.2 ± 0.3)	$(5.3 \pm 0.2) \times 10^4$
	500	(1.6 ± 0.2)	$(3.9 \pm 0.3) \times 10^4$
3b ($^3\text{q3b}^*$)	380	(1.0 ± 0.1)	$(2.4 \pm 0.2) \times 10^5$
	425	(1.3 ± 0.2)	$(2.6 \pm 0.2) \times 10^5$
	500	(1.3 ± 0.4)	$(3.3 \pm 0.2) \times 10^5$
3c ($^3\text{c}^*$)	460	(1.7 ± 0.2)	$(5.0 \pm 0.4) \times 10^5$