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4-Hydroxyphenacyl Ammonium Salts: A Photoremovable Protecting Group for Amines in Aqueous Solutions

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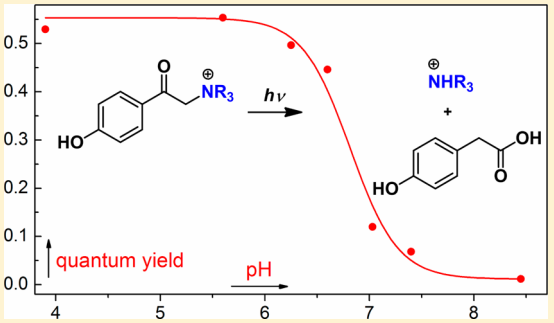
Supporting Information

ABSTRACT: Irradiation of N-protected *p*-hydroxyphenacyl (pHP) ammonium caged derivatives at 313 nm releases primary and secondary amines or ammonia in nearly quantitative yields via the photo-Favorskii reaction when conducted in acidic or neutral aqueous buffered media. The reaction efficiencies are strongly dependent on the pH with the most efficient and highest yields obtained when the pH of the media maintains the ammonium and *p*-hydroxyl groups as their conjugate acids. For example, the overall quantum yields of simple secondary amines release are 0.5 at acidic pH from 3.9 to 6.6 dropping to 0.1 at neutral pH 7.0 and 0.01 at pH 8.4. Speciation studies provide an acid−base profile that helps define the scope and limitations of the reaction. When the pK_a of the ammonium group is lower than that of the phenolic hydroxyl group, as is the case for the α-amino-protected amino acids, the more acidic ammonium ion deprotonates as the media pH is changed from acidic toward neutral or basic, thus diminishing the leaving group ability of the amino group. This, in turn, lowers the propensity for the photo-Favorskii rearrangement reaction to occur and opens the reaction pathway to alternative competing photoreduction process.

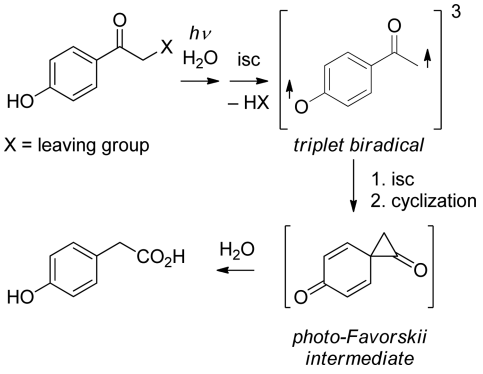


INTRODUCTION

Photoremovable protecting groups (PPGs) are important auxiliary systems for applications that require spatial and temporal control during the release of the molecules of interest.[1,2] A combination of several attractive features makes the 4-hydroxyphenacyl chromophore (pHP) one of the more promising photoremovable protecting groups available today. Fast and efficient substrate release accompanied by the near UV transparency of the major byproduct, 4-hydroxyphenylacetic acid, formed through a photo-Favorskii skeletal rearrangement (Scheme 1).[3−7] A triplet biradical is formed by deprotonation of the phenolic ketone concomitant with departure of the leaving group. Water-based solvents are essential for this rearrangement and, furthermore, are ideal for deployment in biological studies.[6,8] Thus, the pHP protecting group has been successfully employed for the protection of a variety of functional groups, e.g., carboxylates, phosphates, and thiophosphates in neurobiology, enzyme catalysis, biochemistry, and biophysics.[1,9] Modifications of the pHP chromophore itself have had only a modest influence on the overall efficiencies and rates of release from the protecting group.[8,10]

The amino functional group is ubiquitous in nature and very often present in biologically active compounds. They are generally poor leaving groups in heterolytic substitution reactions and, therefore, poor substrates for conventional PPG applications. For example, *o*-nitrobenzyl amines[11] photochemically liberated the amine, but the reaction is accompanied by strongly absorbing, toxic *o*-nitrosobenzaldehyde byproducts. Recently, photorelease of amines from 3-dimethylaminotrityl[12] and *o*-nitroveratryl[13] PPGs in aqueous solutions was reported. Indirect strategies based on release of carbamate-protected amines require two steps, release of the carbamic acid followed by decarboxylation. This approach has been a successful

Scheme 1. General Mechanism of the Photo-Favorskii Rearrangement[a]



[a]isc = intersystem crossing.

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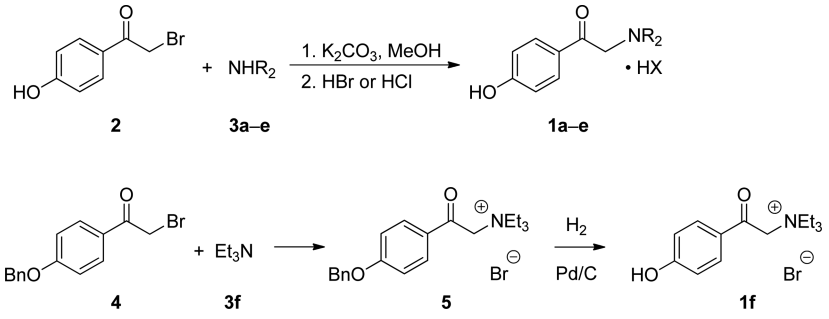
Scheme 2. Synthesis of *p*-Hydroxyphenacyl Ammonium Salts 1a–e



strategy for amine release,[1,9,14−23] but it suffers from the relatively slow, rate-limiting CO_2 elimination ($k_{-CO_2} \sim 10^{-3}$ s^{-1}).

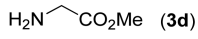
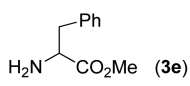
We provide here our detailed investigation of *p*-hydroxyphenacyl as the photoremovable protecting group and discuss its scope and limitations as a PPG for primary, secondary, and tertiary amines and for ammonia as their ammonium salts. Although a recent report by Heckel and co-workers[24,25] used pHP to protect N^3-deoxythymidine which did photochemically release deoxythymidine-containing oligonucleotides, the reported photoreactions were rather inefficient and accompanied by competing [2 + 2] cycloadditions.

In our study, we have established that the pK_a of aliphatic amines in aqueous media is critical for efficient reaction; thus the pH of irradiated solution plays a pivotal role in the selectivity, efficiency, and complexity of the overall photochemical process. Quantum yields, pK_a effects, and mechanistic considerations, including time-resolved (TR) transient absorption measurements are provided for a representative series of the aliphatic amines examined.

RESULTS AND DISCUSSION

Synthesis. The 4-hydroxyphenacyl ammonium salts **1a–e** were prepared by coupling 4-hydroxyphenacyl bromide (**2**) with amines **3a–e** in the presence of base and subsequently acidified with HCl or HBr (Scheme 2, Table 1). Triethylammonium salt **1f** was prepared in two steps by first reacting 4-benzyloxyphenacyl bromide (**4**) with triethylamine (**3f**) followed by removal of the benzyl group with H_2/Pd/C in 70% overall yield. The 4-hydroxyphenacyl methyl (**1g**·HCl) and *n*-butyl ammonium (**1h**·HCl) derivatives were purchased.

Table 1. Synthesis of 1a–f

compound	NHR_2 or NR_3	yield/%[a]
1a•HCl	$HNEt_2$ (**3a**)	53%
1b•HBr	 (**3b**)	43%
1c•HCl	NH_3 (**3c**)	75%
1d•HCl	 (**3d**)	41%
1e•HCl	 (**3e**)	38%
1f	NEt_3 (**3f**)	70%

[a]Isolated chemical yields.

Acid–Base Properties of 1a–f. The pK_a values of the phenolic proton of **1a–f** and the ammonium group of **1a–e** were determined by UV and ^{1}H NMR titration (Table 2). For the UV–vis method, solutions of the compounds (c = 0.1 mmol dm^{-3}) in phosphate buffer ($c \sim 7.0 \times 10^{-2}$ mol dm^{-3}) were titrated with aqueous KOH. The change in the concentration of each acid–base form was followed by changes in the absorption spectra (e.g., for **1a** see Figure S1). Deconvolving of the spectral data provided individual spectra of each protonated form of the amine. Three forms (e.g., the deconvolved spectra for **1a** as depicted in Figure 1) were identified for each of the amines **1a–c**: the ammonium salt (A), zwitterion (B), and phenolate salt (C) with corresponding pK_a of ∼7.3 and 9.3–10.1 for the hydroxyl and ammonium groups, respectively. The values are given in Table 2. A mixture of all three forms, A, B, and C, exists at pH 7. A considerably lower pK_a value of the ammonium group (6.1–7.1) was found for **1d**

Table 2. pK_a Values of 1a–f[a]

compound	pK_a (OH)	pK_a ($^+$NH)
1a	7.2 (7.5)	10.1 (10.2)
1b	7.3 (7.6)	9.6 (9.4)
1c	7.3 (6.9)	9.3 (9.8)
1d	7.9 (7.8)	6.2 (6.2)
1e	8.1 (8.8)	7.1 (7.6)
1f	7.3 (7.6)	–

[a]The pK_a values were obtained by UV and ^{1}H NMR (in parentheses).

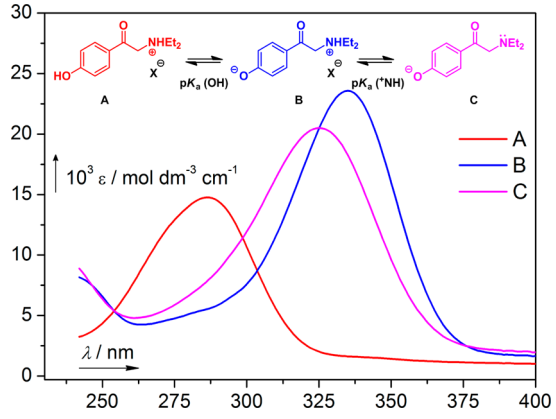


Figure 1. Calculated spectra of the acid–base forms (A: red; B: blue; C: magenta) of **1a** in aqueous buffered solutions for the pH range of 4.0–7.4.

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and **1e**, thus making their hydroxyl pK_a (OH)'s higher than the ammonium pK_a ($^+$NH)'s. This inverts the order of pK_a's for these two amines resulting in a fourth neutral acid−base form D (**1d**: Figure 2). In addition, ^{1}H NMR indicates that

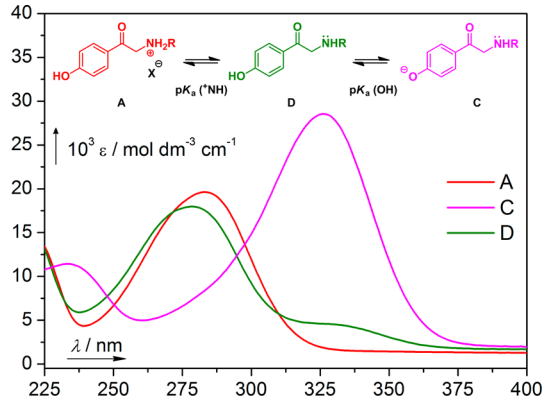

Figure 2. Calculated spectra of the acid−base forms (A: red; C: magenta; D: green) of **1d** (R = CH_2COOMe) in aqueous buffered solutions for the pH range of 4.0−7.4.

enolization occurred at elevated pH for **1d** and **1e** (not shown). The corresponding molar absorptivity coefficients of the band maxima are listed in Table S1.

For NMR measurements, the pHP derivatives ($c \sim 7 \times 10^{-3}$ mol dm^{-3}) dissolved in aqueous Na_2HPO_4 ($c \sim 7.0 \times 10^{-2}$ mol dm^{-3}) were titrated with aqueous DCl or NaOD. The pK_a values were obtained by fitting the dependence of the chemical shifts (δ) of the isolated signals at a given pH using a sigmoidal function at the inflection points. The values were in good agreement with those determined by UV titrations. Figures S2 and S3 show the representative titration curves for **1a** using the signals of C_{Ar}−*H* in the vicinity of OH group and the proton in $COCH_2NR_2$, respectively.

The pK_a values determined in this work (Table 2) are in good agreement with those reported for related compounds. For example, the pK_a values of 4-hydroxyacetophenone derivatives are in the range of 7.9−8.0,[11,26,27] e.g., 4-hydroxyphenacyl-caged γ-aminobutyric acid, diethyl phosphate, or acetate derivatives have pK_a of ∼8.0.[28] The typical pK_a of α-aminoketones and esters is ∼8. For example, the reported pK_a ($^+$NH) of methyl 2-aminoacetate is ∼7.7.[29,30] The pK_a values of the pHP amines **1a**−**c** are about 10, typical of those observed for aliphatic amines and ammonia. The hydroxyl group on the 4-hydroxyphenacyl moiety has a negligible impact on the pK_a of the ammonium group ($^+$NH). A more pronounced effect is observed for the phenacyl group itself on an amine. For example, the pK_a of piperidinium ion (11.1)[31] differs from that of simple *N*-phenacyl piperidinium ion (8.3)[31] due to an inductive effect of the phenacyl group. The same effect may also explain the significant decrease in pK_a of α-amino ketones and esters, as observed for **1d** and **1e**. The electron-withdrawing methoxycarbonylmethylene group on 4-hydroxyphenacyl amine **1d** reduced the pK_a by 2−3 units. A similar decrease is observed for methyl 2-aminoacetate (pK_a = 7.73)[29] when compared to ammonia (pK_a = 9.25).

Photochemistry of 1a−c and 1g,h in Aqueous Solutions as a Function of pH. Compounds **1a**−**c** ($c \sim 7 \times 10^{-3}$ mol dm^{-3}) were irradiated at 313 nm in aqueous (formate, acetate, and phosphate) buffers at pH 4.0−7.4. Through the entire pH range, the secondary amines were released in high chemical yield and accompanied by rearranged chromophore, 4-hydroxyphenylacetic acid (**6**), the only detected side-product[5,32−34] (Scheme 3, Table 3). Chemical

Scheme 3. Photochemistry of the Ammonium Salts of 1a−c,g,h

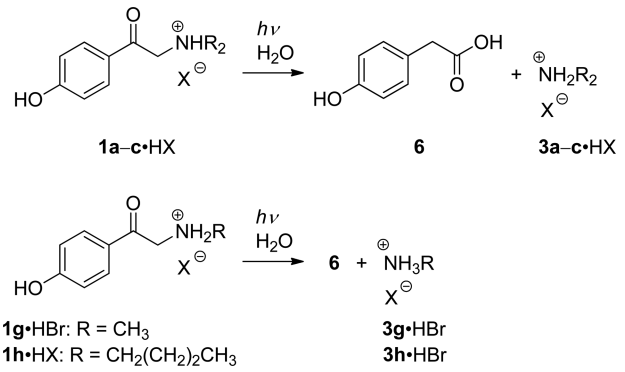

Table 3. Effect on the Photoproduct Yields from 1a When Varying the pH[a]

pH	yield **3a** (%)	yield **6** (%)
4.0[b]	99	99
4.0[c]	99	93
5.6[d]	99	90
7.4[d]	99	96

[a]Buffered solutions, each titrated by DCl, of **1a** ($c \sim 7 \times 10^{-3}$ mol dm^{-3}) were irradiated at λ = 313 nm; the chemical yields were determined by ^{1}H NMR; the reaction conversions were 83−88%. [b]Formate buffer ($c = 8.6 \times 10^{-2}$ mol dm^{-3}). [c]Acetate buffer ($c = 4.3 \times 10^{-2}$ mol dm^{-3}). [d]Phosphate buffer ($c = 5.6 \times 10^{-2}$ mol dm^{-3}).

yields were only marginally affected by buffer composition or pH and were independent of the reaction conversion. A correlation between product yields and conversion of the starting material for **1a** at pH 4.0 and different buffer conditions is shown in Figures S4−S7.

The quantum yields (Φ) of **1a** disappearance in the pH range of 3.9−8.4 were obtained using ^{1}H NMR (Table 4). The highest quantum yields (∼0.5) were obtained at the lowest pH, and decreased to 0.01 at pH = 8.4. Figure 3 shows the dependence of **1a** disappearance (Φ) as a function of changes

Table 4. Disappearance Quantum Yields (Φ) for 1a over a pH Range of 3.9−8.4[a]

pH	Φ
3.9[b]	0.53 ± 0.09
5.6[b]	0.55 ± 0.04
6.3[c]	0.50 ± 0.02
6.6[c]	0.45 ± 0.02
7.0[c]	0.12 ± 0.01
7.4[c]	0.07 ± 0.01
8.4[c]	0.010 ± 0.002

[a]Buffered solutions of **1a** (∼7×10^{-3} mol dm^{-3}) were irradiated at λ = 313 nm; the quantum yields (Φ) were calculated from solution absorbance and NMR data using valerophenone as the actinometer.[35] The reaction conversions were kept below 20%. [b]Acetate buffer ($c = 4.3 \times 10^{-2}$ mol dm^{-3}) was titrated by DCl. [c]Phosphate buffer ($c = 5.6 \times 10^{-2}$ mol dm^{-3}) was titrated by DCl.

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in the equilibrium concentrations of the corresponding acid–base forms of A–C vs pH.

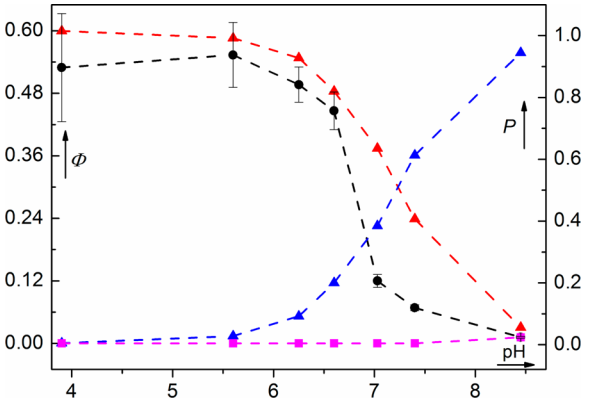

Figure 3. Disappearance quantum yields Φ of **1a** (black circle, left ordinate) and the population *P* (in percent, right ordinate) of the acid–base forms A (red triangle), B (blue triangle), and C (magenta square) (see Figure 1) at different pH's. The standard deviations for Φ were calculated using at least 8 measurements. The dashed lines are provided for the reader's guidance.

Analogous to the photochemistry of **1a**, irradiation of **1b** (also secondary amine release) as well as **1g,h** (both primary amine release) ($c \sim 7 \times 10^{-3}$ mol dm^{-3}) at 313 nm at pH 5.6 and 7.4 gave the photo-Favorskii product **6** and the corresponding amines (**3**) in high chemical yields (Scheme 3, Table 5). In some cases (**1g** and **1h**), **6** along with unidentified photoproducts precipitated from the buffer solution, especially at higher concentrations of **1**. In the case of **1c**, the yield of released ammonia was not determined (Table 5). Neither the nature of the counterion (Cl^- or Br^-) nor added H atom donors, e.g., propan-2-ol, changed the yields of the photoproducts. The disappearance quantum yields of **1b** and **1g** at pH 5.6, similar to that of **1a**, were all three an order of magnitude larger than that of **1c** (Table 6).

Table 5. Photochemistry of 1b,c,g,h over a pH Range of 5.6–7.4[a]

compound	pH	yield **3** (%)	yield **6** (%)
1b	5.6[b]	99	99
1b	5.6[c]	99	99
1b	5.6[c,d]	99	96
1b	7.4[c]	97	94
1c	5.6[b]	n.d.	99
1c	7.4[c]	n.d.	99
1g	5.6[e]	>95	>95
1g	7.4[c]	>95	45[f]
1h	5.6[e]	>95	40[f]
1h	7.4[c]	>95	25[f]

[a]Buffered D_2O solutions, prepared by titration of the corresponding salts (CD_3COONa and Na_3PO_4) with DCl (c = 0.6 mol dm^{-3}), of **1b,c** ($\sim 7 \times 10^{-3}$ mol dm^{-3}) and **1g,h** ($\sim 6 \times 10^{-4}$ mol dm^{-3}; precipitation of the photoproduct(s) occurred at a higher **1g,h** concentration) were irradiated at 313 nm; the yields were determined by ^{1}H NMR; the reaction conversions were 77–85%. [b]Formate buffer ($c = 8.6 \times 10^{-2}$ mol dm^{-3}). [c]Phosphate buffer ($c = 5.6 \times 10^{-2}$ mol dm^{-3}). [d]Propan-2-ol ($c = 5.6 \times 10^{-2}$ mol dm^{-3}) added to the solution. [e]Acetate buffer ($c = 4.3 \times 10^{-2}$ mol dm^{-3}). [f]Precipitation and formation of unidentified products was observed; formation of 4-hydroxyacetophenone was not detected.

Table 6. Disappearance Quantum Yields (Φ) of 1b and 1c at pH = 5.6[a]

compound	Φ
1b	0.44 ± 0.02
1c	0.040 ± 0.002
1g	0.52 ± 0.05

[a]Buffered solutions (phosphate buffer ($c = 5.6 \times 10^{-2}$ mol dm^{-3}) titrated by DCl of **1b** and **1c** ($\sim 7 \times 10^{-3}$ mol dm^{-3}) were irradiated at λ = 313 nm; the quantum yields (Φ) were calculated from the solution absorbance and ^{1}H NMR data using valerophenone as the actinometer;[35] the reaction conversions were <20%.

Our results suggest that primary and secondary aliphatic amines are excellent substrates for pHP caging and for decaging photochemically as their ammonium salts. They can be efficiently released in high chemical yields and are accompanied by a photo-Favorskii rearrangement of the chromophore, a previously established advantageous feature of pHP photodeprotection.[1,9] In general, the α-aminoketone moiety is protonated on nitrogen at pH < 7.4, forming an ammonium ion with a high pK_a ($^+$NH) (Table 2) which thereby transforms it into a relatively good leaving group for photoheterolysis reactions. In addition, irradiation of the form A (at pH = 5.6) does not lead to acetophenone formation (photoreduction) even at relatively high concentrations of propan-2-ol, as an H atom donor. As evident from the diminishing quantum yield that accompanies increases in pH, the photoheterolysis is strongly favored when the ammonium ion (form A) is favored over the free amine (Forms C, D). This straightforward explanation suggests that the ground-state chromophore properties might govern the course of the reaction.

Additional factors that could influence the populations of the various protonated forms in the excited state include the speciation of either the singlet and triplet states or both. However, we have not determined the influence of pH on these species which may, in fact, display significantly altered reactivity relative to their ground state protomers. We have not determined the triplet state acidities[27] nor their relative effect on the reaction efficiencies.

We assume that a deprotonated form B (zwitterion; Figure 1), which still possesses a protonated amino group (pK_a > 9.6), is photochemically less efficient, as demonstrated by Givens, Wirz, and co-workers where pH effects showed that the phenolate form of pHP chromophore had a lower release efficiency.[6] In fact, a considerably lower release efficiency was found for **1c** (Φ = 0.04). A comparably low efficiency for photorelease of deoxythymidine from pHP caged deoxythymidine (*vide supra*) at pH = 7.4 has been reported.[24] However, a direct comparison of a caged nucleobase with the aliphatic 4-hydroxyphenacyl amines **1a–c** is less relevant due to the reduced basicity and thus different leaving group ability of the heterocyclic thymidine nitrogen.

Pump–Probe Spectroscopy. Transient absorption spectra were obtained for **1a** ($c = 7 \times 10^{-4}$ mol dm^{-3}) in aqueous acetic acid (pH 4) with 266 nm excitation in 0.1 ps steps up to a delay of 6.8 ps. The initial spectra were weak transients that subsequently rose to a much stronger absorption band. Factor analysis of the series of spectra revealed two components. Fitting the data with a single exponential kinetic function

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produced the species spectra (Figure 4), which are attributed to the lowest excited singlet, ^{1}**1a*** (λ_{max} 320 nm, τ = 2.4 ± 0.4 ps)

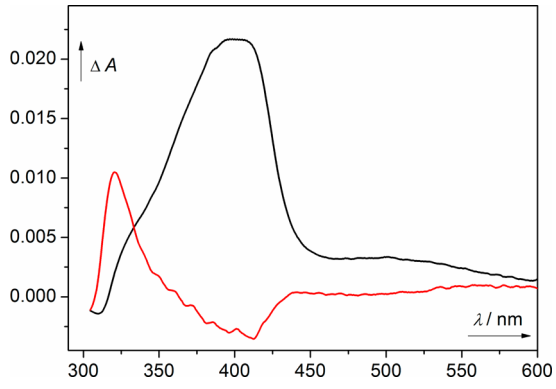
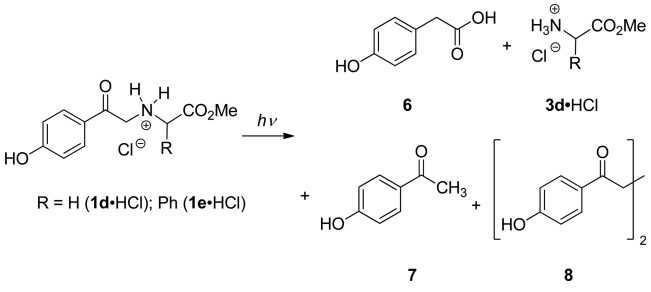


Figure 4. Transient spectra of the singlet (red) and triplet (black) excited states of **1a** in aqueous acetic acid (pH = 4) obtained by the global analysis of the pump−probe data.

and the triplet state, ^{3}**1a*** (λ_{max} = 400 and 510 nm). The triplet excited state is generally reported to be the reactive state that releases the leaving group generating a short-lived biradical intermediate. The biradical subsequently undergoes the Favorskii rearrangement (Scheme 1).[6] Unlike our studies on phosphate esters,[1,27] the release of amines (a much poorer leaving group than phosphate) gave no detectable signal of the biradical intermediate.[7]

The Effect of pH on the Photochemistry of 1d and 1e. The photoproduct distribution from pHP ammonium derivatives of the amino acids **1d,e** is strongly influenced by pH. Caged methyl esters of glycine (**1e**) and phenylalanine (**1d**) when irradiated in aqueous buffers ranging between pH 3.9 and 8.0 at 313 nm (Scheme 4, Table 7) gave the photo-Favorskii

Scheme 4. Photochemistry of 1d and 1e



product **6** in high chemical yield in the lower pH media. However, at pH 7.4 and above, the rearrangement products were increasingly replaced by 4-hydroxyacetophenone (**7**) accompanied by small amounts of the dimer 1,4-bis(4-hydroxyphenyl)butan-1,4-dione (**8**) with increasing pH until they became the major products as shown for **1e**.

The released free amino acid esters (**3d** and **3e**) were identified among the photoproducts. The product ratios of **3d** correlated with appearance of **6** at pH = 4 and 5.6, thus their formation is unambiguously tied to the photo-Favorskii rearrangement. At pH 7.4, the photoproduct concentrations were not determined because of the complexity of the side products.

Irradiation of **1e** at pH 5.6 in formate buffer (an H atom donor) gave a high yield of the photo-Favorskii product **6**,

Table 7. Photochemistry of 1d and 1e over a pH Range of 4.0−7.4[a]

compound	pH	yield **3** (%)[f]	yield **6** (%)[f]	yield **7** (%)[g]	yield **8** (%)[g]
1d	4.0[b]	87	87	11	1
1d	5.6[b]	67	70	14	8
1d	7.4[d]	n.d.	49	33	7
1e	5.6[c]	n.d.	93	7	n.o.
1e	5.6[d]	n.d.	46	55	n.o.
1e	5.6[d,e]	n.d.	41	62	n.o.
1e	7.4[d]	n.d.	n.o.	99	n.o.

[a]Buffered solutions of **1d** and **1e** (~7 × 10^{-3} mol dm^{-3}) were irradiated at λ = 313 nm; the reaction conversions: 71−94%. n.d. = not determined. n.o. = not observed. [b]Acetate buffer (c = 4.3 × 10^{-2} mol dm^{-3}) titrated by DCl. [c]Formate buffer (pH = 5.6; c = 4.3 × 10^{-2} mol dm^{-3}) titrated by DCl. [d]Phosphate buffer (c = 5.6 × 10^{-2} mol dm^{-3}) titrated by DCl. [e]Propan-2-ol (c = 5.6 × 10^{-2} mol dm^{-3}) added to the solution. Determined by [f]^{1}H NMR and [g]HPLC.

whereas with phosphate buffer (pH 7.4), a mixture of **6** and **7**, was observed. Addition of propan-2-ol at pH = 5.6 did not change the ratio of **6**:**7** suggesting that factors influencing the formation of **7** other than ease of hydrogen abstraction are also significant.

Figure 5 shows the pH dependence for disappearance quantum yields of **1d**. These are compared with the three major

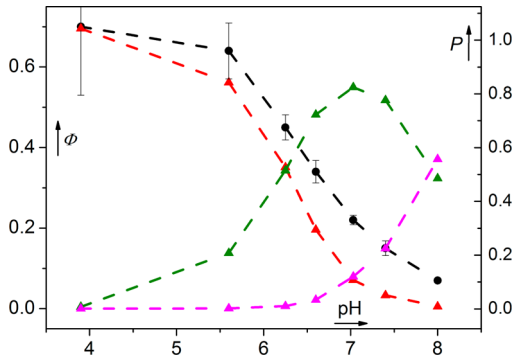


Figure 5. Disappearance quantum yield (Φ, black circle, left ordinate) of **1d** as a function of pH. Plots of the populations (P, right ordinate) as a function of pH for the three major acid−base forms A (red triangle), C (magenta triangle), and D (green triangle) are superimposed on the quantum yield plot (see Figure 2 for the protomer structures). The standard deviations for Φ were calculated from at least 8 measurements. The dashed lines are provided for visualization of the trends.

ground-state acid−base species whose concentrations are determined by the pH-dependent equilibrium concentrations of A, C, and D (for the protomer structures, see Scheme 2). The highest value of the quantum yield for **1d**, Φ = 0.70, was determined at pH 3.9 which decreased to 0.07 when the pH was increased to 8.0 (Table 8).

Distinctive features of the compounds **1d** and **1e** are the low basicity of their amino groups, rendering the protonated amino group more acidic than the phenolic OH group. A substantial decrease in the disappearance quantum yields of **1d** occurred upon increasing the pH above 6 (Figure 5), which is clearly related to a decrease in the population of the protonated amine A. Thus, in the region where the ammonium ion pK_a (NH) is above 6.2−7, the photo-Favorskii reaction is not observed due to the poor leaving group ability of the unprotonated amines

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Table 8. Disappearance Quantum Yields (Φ) of 1d as a Function of pH[a]

pH	Φ (1d)
3.9[a]	0.70 ± 0.03
5.6[b]	0.64 ± 0.01
6.25[b]	0.45 ± 0.01
6.6[b]	0.34 ± 0.04
7.03[b]	0.22 ± 0.02
7.4[b]	0.15 ± 0.01
8.0[b]	0.070 ± 0.004

[a]Acetate buffer; pH = 3.9; $c = 4.3 \times 10^{-2}$ mol dm^{-3}; titrated by DCl. [b]The phosphate buffer ($c = 5.6 \times 10^{-2}$ mol dm^{-3}; titrated by DCl) of **1d** and **1e** (~7×10^{-3} mol dm^{-3}) were irradiated at λ = 313 nm; the quantum yields (Φ) were calculated from the change in solution absorbance and ^{1}H NMR data using valerophenone as an actinometer.[35] Conversions were kept below 20%.

which are poor leaving groups. In contrast to the behavior of **1a−c** where only a decrease in reaction efficiency is observed, homolytic processes compete with the release of the amino acid for **1d** and **1e** resulting in concomitant formation of ketones **7** and **8**. These reduction products became the dominant products at pH ≥ 5.6.

Acetophenone derivatives such as **7** or **8** are common products of the homolytic photocleavage of phenacyl esters and halides. These reactions can be initiated either by a photoinduced electron or hydrogen atom transfer to the phenacyl group from suitable electron or H atom donors.[36] The resulting phenacyl anion radicals or ketyl radicals undergo leaving group elimination to give the phenacyl radicals which are reduced or couple to form acetophenone or 1,4-diphenylbutan-1,4-diones, respectively.[37,38] When amines are the electron/H atom donors, their corresponding oxidation products, such as imines or iminium salts, are commonly observed as well.[38−41] A similar photochemical cleavage was also reported for α-aminoketones in alcohols for which homolysis of the C−N bond was proposed.[41,42]

Alternatively, amino acid derivatives **1d** and **1e** could undergo Norrish type II photochemical reactions.[43−45] This reaction could be initiated by an intramolecular electron transfer from the nitrogen atom (free base) to the excited carbonyl group followed by a proton shift from the γ-position to give a 1,4-biradical intermediate that fragments into a ketone and imine or cyclizes to a four-membered azetidine derivative. The contribution of such a process would also be limited by pH where the form D would be available. A direct cleavage pathway, observed for some aliphatic α-ketoamines,[41,43] may also contribute to the photochemistry of **1d** and **1e**.

Photochemistry of 1f. The photochemistry of **1f** was studied to evaluate the effects of the 4-hydroxyl group deprotonation from a derivative with a quaternary ammonium group. The exhaustive irradiation of **1f** performed in acetate (pH 4) or phosphate (pH 8.4) buffers gave complex mixtures of the photoproducts (Scheme 5, Table 9). The product ratios

Table 9. Photochemistry of 1f at pH = 4.0 and 8.4[a]

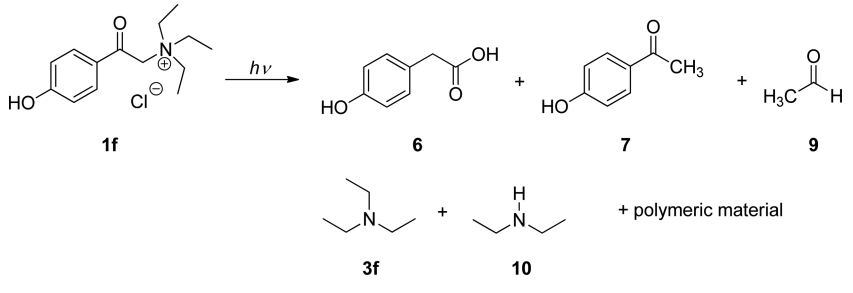
pH	yield **6** (%)	yield **3f** (%)	yield **7** (%)	yield **9** (%)	yield **10** (%)
4.0[b]	20	51	18	24	45
8.4[c]	6	53	19	13	43

[a]Buffered solutions of **1b** and **1c** (~7×10^{-3} mol dm^{-3}) were irradiated at λ = 313 nm; the reaction conversions: 95−98%; determined by ^{1}H NMR. [b]Acetate buffer ($c = 5.0 \times 10^{-2}$ mol dm^{-3}) titrated by DCl (c = 0.6 mol dm^{-3}). [c]Phosphate buffer ($c = 5.0 \times 10^{-2}$ mol dm^{-3}) titrated by DCl (c = 0.6 mol dm^{-3}).

were essentially independent of pH, whereas the observed reaction efficiencies at pH 8.4 were nearly an order of magnitude lower than those observed at pH 4, indicating a substantially decreased reactivity of the excited triplet phenolate in comparison with the corresponding protonated phenol. Both triethylamine (**3f**) and diethylamine (**10**) were identified among the photoproducts; their concentrations were determined from their ethyl group ^{1}H NMR signals. Only a small amount of the photo-Favorskii product **6** was formed as was also true for the radical product **7**; other polymeric photoproducts on the NMR tube walls were not identified.

The ammonium salt **1f** was synthesized as a proxy of the ammonium salts **1a−c** in the forms A and B. However, its complex photochemical behavior eluded straightforward, simple comparisons. A minor contribution of photo-Favorskii reaction pathway at the expense of reactions typical for α-amino ketones alluded to other factors that must be dominating the photochemistry. A major structural difference is the lack of a proton on the ammonium nitrogen in **1f** vis-à-vis structures **1a−c**. Quaternary trialkyl phenacyl ammonium salts, well-known as photoinitiators for radical polymerization,[33,46,47] undergo homolysis as the primary step, but detailed mechanistic studies have not been reported. Sarker and co-workers studied the mechanism of a photochemical cleavage of *N,N,N*-tributyl-*N*-acetobenzo[*b*]thiophene ammonium borates which share structural similarity with the phenacyl ammonium salts. The authors proposed a sequence of one-electron reductions of the excited ketone by borate, followed by homolysis of the C−N bond leading eventually to a phenacyl radical and tertiary amine.[48] Acetaldehyde (**9**) and diethylamine (**10**) most likely arise from Norrish type II reaction and reductive cleavage of 4-hydroxyphenacyl group. A more detailed investigation of these processes is beyond the scope of this work and will be addressed in subsequent studies.

Scheme 5. Photochemistry of 1f



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CONCLUSIONS

The 4-hydroxyphenacyl group is an effective photoremovable protecting group for elementary primary and secondary aliphatic amine functional groups when photolyzed in aqueous solutions at pH below ~7.5. The reaction is accompanied by nearly quantitative formation of 4-hydroxyphenylacetic acid via a photo-Favorskii rearrangement. The process is pH dependent, and the quantum yields, sensitive to the population of the protonated form, increase when the pHP-protected nitrogen is the protonated ammonium ion. When the pK_a of the ammonium group is below that of the 4-hydroxylphenyl (phenolic) group, as is the case for the two α-amine-protected amino acids in slightly basic media, a combination of the lower leaving group ability of the amino group and deprotonated phenoxide (pK_a 7.9) greatly reduces the photorelease efficiency at pH > 7. Instead, homolysis of the C−N bond and a likely Norrish type II cleavage process for γ-C−H bonds dominate. Taken together, the application of pHP photoremovable groups shows promise for biological applications for primary and secondary amines at or below physiological pH.

EXPERIMENTAL SECTION

Materials and Methods. The reagents and solvents of the highest purity available were used as purchased, or they were purified/dried using standard procedures when necessary. Synthetic steps were performed under ambient atmosphere unless stated otherwise. The primary pHP ammonium chlorides (**1g,h**; for NMR, see Figures S25−S28) were used as purchased. ^{1}H, ^{13}C, and ^{15}N NMR spectra were recorded on a 500 MHz spectrometer at 30 °C. The chemical shifts (δ) are reported in ppm relative to that of the residual peak of a nondeuterated solvent[49] (except for D_2O) or sodium 3-(trimethylsilyl)-2,2,3,3-tetradeuteropropionate (δ = 0.084 ppm);[50] the coupling constants (J) are reported in Hz. The ^{15}N shifts were obtained from ^{1}H−^{15}N gHMBC and were referenced to the nitrogen signal of acetonitrile-d_3 (δ = 246 ppm).[51] The deuterated solvents (except for D_2O) were kept over activated 3 Å molecular sieve (8−12 mesh) under dry N_2. HPLC−MS data were obtained using a liquid chromatograph equipped with a C-18 (3 μm, 2.1 × 100 mm) column and UV−vis and ESI/QQQ detectors (nitrogen flow: 8 dm^3 min^{-1}; gas temperature: 300 °C; nebulizer: 45 psi; V_{cap}: 2000 V; fragmentor voltage: 135 V). HRMS data were acquired by a UPLC/MS−TOF apparatus equipped with C-18 (1.7 μm, 2.1 × 50 mm) column and ESI/TOF detector (nitrogen flow: 11 dm^3 min^{-1}, gas temperature: 300 °C; vaporizer: 250 °C; nebulizer: 40 psi; sheath gas temperature: 350 °C; sheath gas flow: 11 dm^3 min^{-1}; V_{cap}: 2000 V; skimmer: 65 V; fragmentor voltage: 135 V). Mobile phases consisted of ammonium acetate (0.005 mol dm^{-3})/acetonitrile. UV absorption spectra and the molar absorption coefficients were obtained on a UV−vis spectrometer with matched 0.2 or 1.0 cm quartz cells. Most of the experiments were performed in aqueous (buffered or nonbuffered) solutions; in some cases, acetonitrile was added to facilitate dissolution of the studied compounds. The melting points were determined on a noncalibrated Kofler's hot stage or in open-end-capillary tubes using a noncalibrated melting point apparatus. The pH values of solutions were determined using a glass electrode calibrated with certified buffer solutions at pH = 4, 7, or 10.

General Procedure for the Synthesis of 1a−e. The ammonium salts were prepared by modification of a previously published method.[52] K_2CO_3 (0.62 g, 2.32 mmol) was added to a stirred solution of amine (**3a−f**, 2.32 mmol) in methanol (20 mL) at 20 °C, and the mixture was stirred for several minutes. 2-Bromo-1-(4-hydroxyphenyl)ethanone (**2**) (2.32 mmol), prepared according to a known procedure,[53] was dissolved in methanol (15 mL) and added dropwise to the reaction mixture over a period of 1 h (the reaction progress was followed by TLC). Methanol was then evaporated under reduced pressure, and the product was purified by column chromatography (mobile phases: 5% methanol in dichloromethane or dichloromethane/petroleum ether/ethyl acetate, 1:1:0.5, v/v). After evaporation of the solvents, the resulting free amine **1** (a thick oil layer) was dissolved in a small amount of methanol, and the corresponding ammonium salt was precipitated by adding a solution of 37% aqueous HCl or 48% aqueous HBr in propan-2-ol (1:4 v/v; 1 mol equiv of an acid). The mixture was stirred at 4 °C for several hours. The resulting crystals were filtered and dried under reduced pressure. The crude product was recrystallized from a methanol/diethyl ether mixture (1:10, v/v).

*2-(Diethylamino)-1-(4-hydroxyphenyl)ethanone Hydrochloride (**1a**).* Prepared according to the general procedure. Yield 23%. White solid. Mp: 209−211 °C (lit. 204−206 °C with decomp.).[54] ^{1}H NMR (500 MHz, CD_3OD): δ (ppm) 1.36 (t, 6H, J = 7.3 Hz), 3.33 (q, 4H, J = 7.3 Hz), 4.86 (s, 2H), 6.97 (d, 2H, J = 8.8 Hz), 7.95 (d, 2H, J = 8.8 Hz) (Figure S8). ^{13}C NMR (126 MHz, CD_3OD): δ (ppm) 9.5, 51.1, 58.9, 116.8, 126.4, 132.4, 165.5, 190.4 (Figure S9). HRMS (APCI$^+$) m/z: calcd for $C_{12}H_{18}NO_2$ [M + H]$^+$ 208.1338; found 208.1334.

*1-(4-Hydroxyphenyl)-2-(piperidin-1-yl)ethanone Hydrobromide (**1b**).* Prepared according to the general procedure. Yield 43%. White solid. Mp: 239−241 °C. ^{1}H NMR (500 MHz, CD_3OD): δ (ppm) 1.94−2.04 (m, 6H), 3.23−3.67 (m, 4H), 4.90 (s, 2H), 7.00 (d, 2H, J = 8.8 Hz), 8.01 (d, 2H, J = 8.8 Hz) (Figure S10). ^{13}C NMR (126 MHz, CD_3OD): δ (ppm) 22.6, 24.1, 55.8, 62.4, 116.9, 126.8, 132.3, 165.3, 190.1 (Figure S11). HRMS (APCI$^+$) m/z: calcd for $C_{13}H_{18}NO_2$ [M + H]$^+$ 220.1338; found 220.1334.

*2-Amino-1-(4-hydroxyphenyl)ethanone Hydrochloride (**1c**).* Prepared according to the general procedure. Yield 75%. White solid. Mp: 237−239 °C (lit. 248−250 °C with decomp.).[55] ^{1}H NMR (500 MHz, CD_3OD): δ (ppm) 4.55 (s, 2H), 6.96 (d, 2H, J = 8.8 Hz), 7.97 (d, 2H, J = 8.8 Hz) (Figure S12). ^{13}C NMR (126 MHz, CD_3OD): δ (ppm) 45.8, 116.9, 126.9, 132.1, 165.2, 191.4 (Figure S13). HRMS (APCI$^+$) m/z: calcd for $C_8H_{10}NO_2$ [M + H]$^+$ 152.0712; found 152.0705. This compound has also been characterized elsewhere.[55,56]

*Methyl Ester of N-[2-(4-hydroxyphenyl)-2-oxoethyl]glycine Hydrochloride (**1d**).* Prepared according to the general procedure. Yield 41%. White crystals. ^{1}H NMR (500 MHz, CD_3OD): δ (ppm) 4.00 (s, 3H), 4.29 (s, 2H), 4.89 (s, 2H), 7.08 (d, 2H, J = 9.3 Hz), 8.04 (d, 2H, J = 9.3 Hz) (Figure S14). ^{13}C NMR (126 MHz, CD_3OD): δ (ppm) 48.2, 53.2, 54.2, 117.0, 126.6, 132.3, 164.7, 168.5, 191.2 (Figure S15). HRMS (APCI$^+$) m/z: calcd for $C_{11}H_{14}NO_4$ [M + H]$^+$ 224.0923; found 224.0916. This compound has also been described elsewhere.[57]

*Methyl Ester of N-[2-(4-hydroxyphenyl)-2-oxoethyl]-phenylalanine Hydrochloride (**1e**).* Prepared according to the general procedure. Mp: >160 °C (decomp.). Yield 36%. White solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 3.09 (dd, 1H, $J1$ = 13.6 Hz, J_2 = 9.5 Hz), 3.48 (dd, 1H, J_1 = 13.7 Hz, J_2 = 5.1 Hz), 3.59 (s, 3H), 4.31 (dd, 1H, J_1 = 9.4 Hz, J_2 = 5.2 Hz), 4.75 (d, 1H, J = 17.5 Hz), 4.84 (d, 1H, J = 17.4 Hz), 6.94 (d, 2H, J = 8.6 Hz), 7.25−7.38 (m, 5H), 7.92 (d, 2H, J = 8.6 Hz), 9.61 (bs, 2H, −NH$_2^+$−), 10.67 (bs, 1H, −OH) (Figure S16). ^{13}C NMR (126 MHz, DMSO-d_6): δ (ppm) 34.8, 50.7, 53.5, 60.2, 115.6, 124.9, 127.3, 128.6, 129.2, 131.0, 134.7, 163.5, 168.7, 189.8 (Figure S17). ^{15}N NMR (DMSO-d_6) δ (ppm) 45. HRMS (APCI$^+$) m/z: calcd for $C_{18}H_{20}NO_4$ [M$^+$ + H] 314.1392; found 314.1387.

*1-(4-(Benzyloxy)phenyl)-2-bromoethanone (**4**).* This compound was prepared from 4-hydroxyacetophenone using a published two-step procedure[8] and chromatographed (EtOAc/n-hexane, 1:30, v/v) to give pure compound. Yield: 80% (over two steps). White microcrystalline powder. Mp: 91.0−91.4 °C (lit. 91 °C).[58] ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.40 (s, 2H), 5.16 (s, 2H), 7.05 (d, 2H, J = 9.1 Hz), 7.34−7.46 (m, 5H), 7.98 (d, 2H, J = 9.1 Hz) (Figure S18). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 30.8, 70.5, 115.2, 127.4, 127.7, 128.6, 129.0, 131.6, 136.2, 163.5, 190.1 (Figure S19). MS (EI): m/z = 306 (<1), 304 (<1), 211 (<1), 120 (<1), 92 (8), 91 (100), 65 (5). FTIR (cm^{-1}): 3062, 3029, 3004, 2949, 1690 (C═O), 1595, 1505, 1455, 1419, 1386, 1324, 1302, 1254, 1198, 1171, 1120, 1007, 987, 920, 862, 767, 749, 706, 695, 624, 565, 553, 512. This compound has also been characterized elsewhere.[59]

*[2-(4-Benzyloxyphenyl)-2-oxoethyl]triethylammonium Bromide (**5**).* This procedure was adopted according a known procedure.[60] Freshly distilled dry triethylamine (295 μL, 2.12 mmol) was added

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dropwise to a stirred mixture of 1-(4-(benzyloxy)phenyl)-2-bromoethanone (**4**) (648 mg, 2.12 mmol) in acetone (2 mL) under inert atmosphere. The reaction mixture was stirred overnight at 20 °C while white precipitate appeared. Acetone (1 mL) was then added to the reaction mixture, and the precipitate was filtered. The solid was washed with another portion of acetone (2 × 1 mL) and dried under high vacuum. No further purification was necessary. Yield: 578.4 mg (84%). White microcrystalline powder. Mp: 164.7−165.4 °C (lit. 162−164 °C).[61] ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 1.22 (t, 9H, J = 7.2 Hz), 3.61 (q, 6H, J = 7.5 Hz), 5.10 (s, 2H), 5.27 (s, 2H), 7.21 (d, 2H, J = 8.8 Hz), 7.35 (t, 1H, J = 7.4 Hz), 7.41 (t, 2H, J = 7.2 Hz), 7.47 (d, 2H, J = 7.2 Hz), 8.04 (d, 2H, J = 8.8 Hz) (Figure S20). ^{13}C NMR (126 MHz, DMSO-d_6) δ (ppm) 7.6, 54.0, 58.4, 69.6, 115.0, 127.2, 127.7, 128.0, 128.5, 130.8, 136.2, 163.4, 189.9 (Figure S21). ^{15}N NMR (DMSO-d_6) δ (ppm) 64. FTIR (cm^{-1}): 2999, 2972, 2944, 2819, 1688 (C═O), 1596, 1510, 1466, 1453, 1438, 1420, 1402, 1379, 1304, 1260, 1231, 1174, 1154, 1105, 1081, 1047, 1001, 980, 941, 904, 862, 840, 810, 759, 708. 648, 630, 587, 552, 515, 506. HRMS (ESI$^+$−TOF) m/z: calcd for $C_{21}H_{28}NO_2$ [M]$^+$ 326.2120; found 326.2111. This compound has also been characterized elsewhere.[61]

*Triethyl-[2-(4-hydroxyphenyl)-2-oxoethyl]ammonium Bromide (**1f**).* Hydrogen was bubbled through a mixture of **5** (578 mg, 1.78 mmol) and Pd (100 mg, 10% w/w on charcoal) in methanol (10 mL) until no starting material was observable (5 μL aliquots were taken every 3 h; the solvent was removed, and remaining material was dissolved in DMSO-d_6 and analyzed by ^{1}H NMR; ca. 30 h was needed to complete the reaction). The solvent mixture was then filtered to remove Pd/C, and the solvent from the filtrate was removed under vacuum to yield pure title compound. No further purification was necessary. Yield: 376 mg (83%). White microcrystalline powder. Mp: 188.1−189.7 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 1.22 (t, 9H, J = 7.2 Hz), 3.60 (q, 6H, J = 7.2 Hz), 5.02 (s, 2H), 6.92 (d, 2H, J = 8.9 Hz), 7.94 (d, 2H, J = 8.9 Hz), 10.71 (bs, 1H, −OH) (Figure S22). ^{13}C NMR (126 MHz, DMSO-d_6) δ (ppm) 7.5, 53.9, 58.2, 115.5, 125.6, 131.0, 163.6, 189.5 (Figure S23). ^{15}N NMR (DMSO-d_6) δ (ppm) 65 (Figure S24). FTIR (cm^{-1}): 3422 (br), 3112, 2900, 2810, 1680 (C═O), 1618, 1556, 1545, 1500, 1442, 1430, 1412, 1360, 1290, 1225, 1172, 1143, 1104, 1066, 1054, 1005, 978, 833, 788, 728, 711, 694, 632, 611, 571, 518, 507. UV−vis (acetate buffer (pH = 4.02, c = 5.0 × 10^{-2} mol dm^{-3}), c (**1f**) = 4.17 × 10^{-5} mol dm^{-3})): λ (log ε) = 288 (λ_{max}; 4.24), 313 (3.71) nm (dm^3 mol^{-1} cm^{-1}) (Figure S29). UV−vis (phosphate buffer (pH = 8.37, c = 5.0 × 10^{-2} mol dm^{-3}), c (**1f**) = 3.67 × 10^{-5} mol dm^{-3})): λ (log ε) = 313 (4.07), 338 (λ_{max}; 4.36) nm (dm^3 mol^{-1} cm^{-1}) (Figure S29). HRMS (ESI$^+$−TOF) m/z: calcd for $C_{14}H_{22}NO_2$ [M]$^+$ 236.1645; found 236.1643.

Note: A prolonged treatment of **1f** with H_2/Pd/C led to further decomposition of **1f**.

Irradiation Experiments. Solutions of the compounds **1a**−**f** (c ∼ 7 mmol dm^{-3}) and trimethylsilyl propionate (TSP; c ∼ 1 mmol dm^{-3}) as an internal standard were prepared in buffered D_2O (**1a**, **1c**, **1d**, and **1f**) or D_2O/CD_3CN mixture (5:2 v/v) (**1b** and **1e**) (the composition and concentration of buffers is specified for each experiments in the Results and Discussion section). The pH of the solution was adjusted by addition of DCl or NaOD in D_2O (c = 4.3 × 10^{-3} mol dm^{-3}). Preparative irradiations of the solutions were accomplished in NMR cuvettes using 313 nm light isolated from a 40 W medium-pressure mercury arc using a band-pass filter (Figure S30). The progress of the reaction was followed by ^{1}H NMR; the internal standard was used to determine the concentrations of the products and reaction conversions. At conversions >83%, irradiation was stopped, and the final mixture was spiked stepwise with the analytical standards (all anticipated photoproducts) and analyzed by ^{1}H NMR to confirm their identity.

Determination of pK_a by ^{1}H NMR titration. Solutions of the compounds **1a**−**f** (c ∼ 7 mmol dm^{-3}), Na_2HPO_4 (c ∼ 70 mmol dm^{-3}), and sodium 3-(trimethylsilyl)-2,2,3,3-tetradeuteropropionate (c ∼ 1 mmol dm^{-3}) as an internal standard were prepared in D_2O (for **1a**, **1c**, and **1f**) or D_2O/CD_3CN mixture (5:2, v/v) (for **1b** and **1e**). The pH of the solution was decreased to ∼3 by addition of DCl in D_2O, and the solution was titrated by stepwise addition of 2−10 μL of NaOH in D_2O. After each addition, the solution was carefully mixed, pH of the solution was determined, and the ^{1}H NMR spectrum was recorded. The titration was usually stopped at pH > 13. The titration curves were constructed by plotting the chemical shifts (δ) of the hydrogen atoms adjacent to the groups that participate in the acid−base equilibria against pH. The chemical shifts were referenced to TSP. The curves had typically a sigmoidal shape and gave the pK_a corresponding to pH value at the inflection point. The pK_a values were then obtained by fitting the points of the titration curve with a function relating δ to pH and pK_a (Figures S2 and S3):

$$\delta = \frac{\delta_A + \delta_B 10^{(pH - pK_a)}}{1 + 10^{(pH - pK_a)}}$$

Determination of pK_a by UV titration. The changes in the UV spectra of the pHP derivatives (c = 0.1 × 10^{-3} mol dm^{-3}) in phosphate buffer solutions (c ∼ 70 × 10^{-3} mol dm^{-3}) as a function of the pH and the volume of a titration agent (aq KOH) were recorded. The deconvolving of the spectra led to the pK_a determination.

Quantum Yields. Aqueous buffered solutions of the pHP derivatives were irradiated in a quartz cell (l = 0.2 cm) on an optical bench consisting of a high-pressure 200 W Hg lamp and a 1/8 m monochromator with grating 200−1600 nm set to 313 nm. The starting material concentration was ∼7 × 10^{-3} mol dm^{-3}. Valerophenone (c = 3.2 × 10^{-3} mol dm^{-3} in n-hexane; the acetophenone formation: Φ = 0.30)[35,62] was used as an actinometer. The irradiated samples were analyzed using ^{1}H NMR (3-(trimethylsilyl)-2,2′,3,3′-tetradeuteropropionic acid salt was used as an internal standard) or GC (hexadecane was used as an internal standard). The reaction conversion was always kept below 20% to avoid the inference of photoproducts. The relative standard deviations for multiple (at least 8) measurements were below 10% in all measurements.

Picosecond Transient Absorption. Picosecond transient absorption in the UV−vis region was obtained with the pump−supercontinuum probe technique using a Ti/Sa laser system (775 nm, pulse energy 1.0 mJ, full width at half-maximum <150 fs, operating frequency 425.6 Hz). A part of the beam was fed into a noncollinear optical parametric amplifier. The output at 532 nm was compressed to <50 fs pulses, and the frequency was doubled by a β-barium borate crystal to 266 nm with pulse energy of 1.6 μJ. The probe beam was generated by focusing the 775 nm beam into a CaF_2 plate with 4 mm path length that produced a super continuum spanning a wavelength range of 270−620 nm. The pump and probe beams were focused to a 0.2 mm spot on the sample that was flowing in an optical cell with a thickness of <1 mm. The probe beam and a reference signal obtained by passing the solution next to the pump beam were spectrally dispersed and registered with two NMOS sensors (512 pixels). The pump−probe cross-correlation was <100 fs over the entire spectrum. Measurements on short time scales (up to 50 ps) were corrected for chirp using a program which we developed. To improve the signal-to-noise ratio, the data were averaged over multiple pump−probe scans (three to six scans with 400 shots per temporal point). The spectra of the given species were obtained by global analysis method.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01770.

Titration data; preparative irradiation data; NMR and absorption spectra; output spectrum of a medium-pressure Hg lamp (PDF)

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Notes

The authors declare no competing financial interest.

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