Efficient photodecarboxylation of 3- and 4acetylphenylacetic acids in aqueous solution

Lawrence A. Huck, Musheng Xu, Kaya Forest, and Peter Wan

Abstract: The photochemistry of 3- and 4-acetylphenylacetic acids (6 and 7) has been studied in aqueous solution. This work is a continuation of research efforts aimed at understanding the structural effects on the efficacy for benzyl carbanion photogeneration via photodecarboxylation. The nitro group (at the 3- and 4-positions) is known to be an exceptionally good activating group on the benzene ring — because of its enhanced electron-withdrawing effect in the excited triplet state — for photodecarboxylation and the related photo-retro-aldol type process. It is shown in this work that the acetyl group is an equally good activating group for the photodecarboxylation. Thus, the photochemistry of 6 and 7 parallels much of what was observed for the corresponding nitrophenylacetic acids 1 and 2. Both 6 and 7 photodecarboxylate efficiently ($\Phi_d = 0.60$ and 0.22, respectively, at pH 7) via the carboxylate form, to give observable (by laser flash photolysis) benzyl carbanion or related intermediates. The meta isomer 6 displays an acid-catalyzed pathway for photodecarboxylation at pH < 3 and along with its enhanced overall reactivity, is consistent with a meta effect of the acetyl group. Triplet state reactivity is inferred from sensitization and laser flash photolysis experiments. Based on the results of this work, the acetyl group may now be viewed as an "enhanced" electron-withdrawing group (in the excited state) when attached to a benzene ring (i.e., in acetophenone derivatives) that is capable of inducing ionic reactions, which is not the traditional photochemistry that is expected from such compounds.

Key words: photodecarboxylation, acid catalysis, acetophenone, photogenerated carbanion, enol, enolate.

Résumé : On a étudié la photochimie des acides 3- et 4-acétylphénylacétiques (6 et 7) en solution aqueuse. Ce travail est une continuation des efforts de recherche déployés pour comprendre les effets structuraux sur l'efficacité de la photogénération du carbanion benzyle par le biais d'une photodécarboxylation. Il est connu que, en raison de l'augmentation de leur effet électroaffinitaire dans l'état triplet excité, les groupes nitro (en positions 3 et 4) activent le noyau benzénique d'une façon exceptionnelle lors de réactions de photodécarboxylation et autres processus apparentés du type photo-rétro-aldolique. Dans ce travail, on a démontré que le groupe acétyle est aussi un bon groupe activant pour la réaction de photodécarboxylation. La photochimie des composés 6 et 7 est donc parallèle à ce qui a été observé avec les acides nitrophénylacétiques correspondants, 1 et 2. Les composés 6 et 7 se décarboxylent d'une façon efficace ($\Phi_d = 0,60$ et 0,22 respectivement, à un pH de 7), par le biais de la forme carboxylate, pour conduire à la formation du carbanion benzyle et d'autres intermédiaires apparentés qui peuvent être observés par photolyse éclair au laser. À des pH < 3, l'isomère méta, 6, donne lieu à une photodécarboxylation impliquant une catalyse acide et, combiné avec sa plus grande réactivité globale, cette observation est en accord avec un effet méta du groupe acétyle. On déduit la réactivité de l'état triplet d'expériences de sensibilisation et de photolyse éclair au laser. Sur la base des résultats de ce travail, on peut considérer que, dans l'état excité, l'effet électroaffinitaire d'un groupe acétyle attaché à un noyau benzénique (comme dans les dérivés de l'acétophénone) est rehaussé, qu'il est capable d'induire des réactions ioniques ce qui ne correspond pas à la photochimie traditionnelle à laquelle on peut s'attendre avec de tels composés.

Mots clés : photodécarboxylation, catalyse acide, acétophénone, carbanion photogénéré, énol, énolate.

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Introduction

Decarboxylation is one of the simplest extrusion reactions in organic chemistry with wide-relevance in both organic synthesis (1) and in biological chemistry (1, 2). Photodecarboxylation is also well-known and has been studied exten-

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sively for a variety of organic substrates, where a number of mechanistic pathways are known to operate for the loss of CO₂ initiated by light (3). With respect to the photodecarboxylation of aromatic compounds, phenylacetic acids have been the most studied as they provide the obvious basis for Hammett-type studies, by varying substituents on the phenyl ring (3). Although we are not aware of any extended systematic studies in this approach — perhaps thwarted by the fact that the parent and many simple alkyl-substituted phenylacetic acids react with only low quantum efficiency ($\Phi < 0.02$) (3) — it is known that 3- and 4-nitrophenylacetic acids (1 and 2, respectively, and related compounds) both react with very high quantum efficiency in the carboxylate form ($\Phi = 0.6$) (4) via nitrobenzyl carbanion intermediates (e.g.,



3-nitrobenzyl carbanion (3) in eq. [1]). More recently, we have shown (5) that both the benzoyl (PhCO) and acetyl (CH₃CO) moieties also act as "enhanced" electronwithdrawing groups (when attached to a benzene ring) in the excited state, capable of mediating highly efficient photodecarboxylations of the corresponding substituted phenylacetic acid, providing a rational explanation for the previously reported efficient photodecarboxylation of ketoprofen (4) (via benzyl carbanion 5, eq. [2]), a nonsteroidal anti-inflammatory drug that is known to be phototoxic (6). In this work, we detail our complete results on a study of the photodecarboxylation of 3- and 4-acetylphenylacetic acids (6 and 7, respectively) and show that their photochemical behaviour essentially parallels that observed for the corresponding nitro-substituted compounds 1 and 2. Moreover, the results show that the acetyl group may be thought of as an enhanced "electron-withdrawing" group in the excited state, capable of inducing photochemistry that would not have been normally be anticipated when these compounds are viewed as substituted acetophenones.

Results and discussion

Product studies

The substrates for study (6 and 7) were readily prepared from the corresponding methylacetophenones (8 and 9) by

initial NBS bromination of the methyl group, followed by substitution of the bromine by cyanide ion, and subsequent acid hydrolysis. Photolysis of 6 in H₂O-CH₃CN (1:1, pH 7, water portion, 10⁻³ mol L⁻¹, 254 or 300 nm, Rayonet RPR 100 photochemical reactor, 1-10 min, deoxygenated by argon purge) gave exclusively the corresponding photodecarboxylation product 8 in high yield (>80%, eq. [3]). Quantitative conversion was observed at sufficiently long photolysis times. No reaction was observed in the absence of light or when photolyzed in neat CH₃CN, the latter consistent with photoreactivity via the carboxylate ion (vide infra). Photolysis in D₂O-CH₃CN (1:1, pD 1 and 7) gave exclusively the corresponding α -deuterated product 8- α D, consistent with the formation of a benzyl-carbanion-type intermediate in the photodecarboxylation. The overall reaction yield was only about 10%-20% lower in D₂O, indicative of a secondary solvent isotope effect for reaction, although the exact source of this effect is not known.

Similar photolysis of the para-isomer 7 gave two products at all conversions, the expected photodecarboxylation product 9 and a "dimer" 10 (formally derived from the coupling of two 4-acetylphenylmethyl radicals) (eq. [4]). Independent photolysis of 9 did not produce 10. Photolysis in D₂O– CH₃CN gave the α -deuterated product 9- α D, consistent with the formation of a benzyl-carbanion-type intermediate; no deuterium was incorporated into dimer 10. The ratio of



Table 1. Ratio of products **9** vs. **10** observed in the photodecarboxylation of **7**.^{*a*}

pH ^b	9 (%)	10 (%)
2.5	90	10
3.2	83	17
5.2	80	20
7.0	78	22
8.0	79	21
10.2	77	23
12.0	72	28

^{*a*}Relative yields were calculated by ¹H NMR. Estimated errors: $\pm 10\%$ of quoted value. Conversions were 30%–70%. The relative yields were independent of conversion. ^{*b*}pH of the aqueous portion (H₂O–CH₃CN, 1:1).

products 9 vs. 10 was found to be pH dependent (Table 1), with increasing yield of the dimer 10 (maximum relative yield $\approx 30\%$) with increasing pH. This trend is consistent with a mechanism in which the initially formed benzyl carbanion intermediate (19a) can react via two pathways, simple protonation to give 9 and a more complex "bimolecular" pathway (disproportionation-type route, vide infra) to give 10. The protonation pathway would be favoured at lower pH, and this was indeed observed. Since the dimer 10 was observed as a photoproduct under relatively low lamp intensities (Rayonet photochemical reactor), it is unlikely that it arises via secondary photolysis of the anticipated intermediate carbanion (19a) of the photodecarboxylation (vide infra).

The above results observed for 4-acetylphenylacetic acid (7) is very similar to what is known in the photodecarboxylation of 4-nitrophenylacetic acid (2) (4) (Scheme 1). Photodecarboxylation of 2 gave a mixture of the expected 4nitrotoluene (11) via simple protonation of the initially formed 4-nitrobenzyl carbanion (12) and a "dimeric" product (4,4'-dinitrobibenzyl, 13). The relative yield of dimer 13 is enhanced at higher pH, becoming the major (>80%) product at pH > 10. Thermally generated 12 (via the deprotonation of 11 using strong bases and where there is no possibility of photoexcitation of the carbanion 12) also gave 13 (7). The mechanism for the formation of 13 from 12 appears to be complex. Radical ions are believed to be involved (7) as strong EPR signals are observed. For the photodecarboxylation pathway, Craig and Pace (8) suggested the possibility of dimerization of the initially formed 12 based on kinetic studies for its decay, to give the radical dianion 14 (expected to be EPR active and consistent with the EPR signals observed) (8), which on work-up, is oxidized to give 13. The very long lifetime of photogenerated 12 ($\tau \approx 60$ s, aqueous solution, pH 7) (7) would indicate slow reaction via simple protonation of the anion (carbon protonation is generally "slow" even in thermodynamically favourable cases), and hence, the possibility of dimerization to give radical dianion 14. Such a mechanism does not operate for the 3-isomer 1 since the corresponding benzyl carbanion intermediate 3 is expected to be shorter lived. Indeed, the 3-nitrobenzyl carbanion (3) has never been detected as a transient, although the reason for this is still not clear.

The high yields and clean photochemistry observed for both **6** and **7** is further evidence for the enhanced activating effect of the acetyl group for photodecarboxylation. Moreover, no products were observed that are derived from the photochemistry of the carbonyl end of the molecule (e.g., via photoreduction or hydrogen abstraction), which is consistent with the notion that this group participates only as an enhanced electron-withdrawing group. Without the acetyl group, phenylacetic acid itself photodecarboxylates with only marginal quantum yields (<0.02) (3). That there is substantial charge transfer character (with negative charge polarized towards the carbonyl oxygen) in the reactive excited state of these compounds is further evidenced by observation of acid catalysis for the photodecarboxylation of **6** (vide infra).

Quantum yields

Quantum yields for photodecarboxylation were measured as a function of pH, using the photodecarboxylation of ketoprofen (4, $\Phi_d = 0.75$ (6*a*)) as a secondary standard (Fig. 1). H_2O-CH_3CN (1:1, v/v) was employed as the solvent in these studies because of experimental difficulties in performing semipreparative photolysis in 100% water. All the quoted pH are of the aqueous portion prior to mixing except for pH 4-8, where the pH was measured in the mixed solvent as adjustment to the pH had to be made with NaOH upon dissolution of the substrate. Since the quantum yield plot is for qualitative purposes only, the exact pH values are of less consequence. The quantum yields for photodecarboxylation (Φ_d) for both 6 and 7 are substantial at pH 7 (0.60 and 0.22, respectively), indicative of the highly activating nature of the acetyl group. For both compounds, the highest quantum yields were observed for the carboxylate form of the molecule (in the region where $pH > pK_a$; estimated pK_a for these compounds \approx 3 to 4). Indeed, this is suggestive that only the carboxylate form is reactive in photodecarboxylation, as is the case for most any lacetic acids reported to date (3, 4). This is indeed the case for the para isomer 7 since the quantum yield vs. pH plot for this compound approaches zero at

Scheme 1.



Fig. 1. Plots of quantum yields for photodecarboxylation (Φ_d) vs. pH for acetylphenylacetic acids **6** (squares) and **7** (circles) in H₂O–CH₃CN (1:1). The short-dashed line shows the expected trend for **6** if acid catalysis does not operate; the long-dashed line shows the resolved acid-catalyzed photodecarboxylation pathway.



pH < 1. For 3-acetylphenylacetic acid (**6**), the quantum yield is substantial (≈0.13) in acidic solution, which is indicative of an acid-catalyzed mechanism that operates only for the meta isomer. As shown in Fig. 1, the short-dashed line represents the expected trend in the absence of an acidcatalyzed pathway. The long-dashed line is the "resolved" contributing acid-catalyzed pathway. The "plateau" region observed in the pH 2 to H_o –2 region is therefore the sum of the acid- and "base"-catalyzed mechanisms. It should be emphasized at this point that product studies of **6** in the acid region discussed here also gave only one photoproduct (viz., **8**). Additionally, photolysis of **6** at pD 1 (where the mechanism is believed to be almost exclusively in the acidcatalyzed regime) gave **8-αD** exclusively. That is, the quan-

tum yield vs. pH plot observed for 6 in Fig. 1 over the entire pH region is due to photodecarboxylation and not some other contributing photochemical reaction that may have been overlooked in the product studies.

The above "unusual" photoreactivity displayed by the meta acid **6** may be interpreted as another example of the well-known "meta effect" for the photochemistry of substituted benzenes that has been well-documented and studied by Zimmerman (9). That is, the meta-acetyl group in **6** can activate (in the excited state, by electron withdrawal) the corresponding attached acetic acid moiety more than a corresponding para-acetyl group. This results in a more reactive compound (as manifested in the higher quantum yields observed for **6** at all pH) as well as the operation of an observable acid-catalyzed pathway (vide infra).

Nanosecond laser flash photolysis (LFP) and reaction mechanisms

Although the results presented so far, based on product studies and quantum yield measurements vs. pH, show a close analogy in photochemical behaviour between the nitrophenylacetic acids (1 and 2) and the acetylphenylacetic acids (6 and 7), LFP results show mechanistic details for 6 and 7 that appear to be more complex than those reported for 1 and 2. LFP studies of 6 and 7 were first performed in dry CH₃CN, where there is no photoreaction. Only one strong and broad ($\Delta OD \approx 0.12$) transient formed immediately after the laser pulse was observed for both compounds, with λ_{max} 330 nm (Fig. 2, shown for 7), which was efficiently quenched by oxygen. This transient exhibited the same decay kinetics over the 330-430 nm region of the spectrum and hence assignable to one transient. For 6, the lifetime (all single exponential fits) was 800 ns under N2 and 50 ns under O₂; for 7, 1200 ns under N₂ and 170 ns under O2. This transient is assigned to the triplet state, in agreement with the known triplet state absorption for acetophenone itself (λ_{max} 330 nm (10)), although there is a

Fig. 2. Transient observed on LFP of **7** in 100% CH₃CN (266 nm excitation, N₂ purged). The signal at 340 nm is assigned to the triplet state. (130 ns (\blacklozenge), 220 ns (\square), 410 ns (\blacklozenge), 3000 ns after the laser pulse (×)). Inset: first-order decay at 340 nm; $\tau \approx 1000$ ns.



Fig. 3. Transient observed on LFP of **6** in H₂O–CH₃CN (1:1, pH 7) (266 nm excitation, N₂ purged). The transient is assigned to carbanion **15** or **16**. The decay is first order (130 ns (\blacklozenge), 280 ns (\square), 480 ns (\blacklozenge), 3000 ns after the laser pulse (×)). Inset: first-order decay at 340 nm; $\tau \approx 400$ ns.



weak residual longer lived signal at ca. 310 that was not assigned.

LFP studies of **6** and **7** were then carried out in H₂O– CH₃CN (1:1, at several different pH), a solvent where these compounds photodecarboxylate efficiently (except for **7** at pH < 2). The transient observed immediately upon the laser pulse for **6** in pH 7 is shown in Fig. 3. The spectral band is narrower and weaker than that observed in 100% CH₃CN, with λ_{max} at 340 nm. The same decay kinetics (single exponential decay) was observed across the whole spectral range with no significant residual signals. In addition, the transient is significantly longer lived in D₂O (about twofold) and is somewhat sensitive to oxygen but not to the same extent as the transient observed in 100% CH₃CN (Table 2). Therefore, although this transient has absorption in about the same spectral region as the triplet state assigned above, it *cannot*

Table 2. Lifetimes of observed transients for 6 and 7 by LFP.

	Observed lifetimes (ns) ^a				
λ^b	6 (In H_2O) ^c	6 (In $D_2O)^c$	7 (In $H_2O)^c$	7 (In $D_2O)^c$	
310			4600 (600)	4400 (630)	
320			3400 (400)	3200 (460)	
340	390 (220)	910 (190)	1800 (260)	1700 (300)	
400	460 (140)	920 (190)	1700 (420)	3900 (710)	

^{*a*}Lifetimes obtained from first-order decays at the respective wavelength under N₂, except for 310, 320, and 340 nm of **7**, which did not obey firstorder kinetics and the lifetimes are estimated based on force fitting to a single exponential decay. Values in brackets obtained under O₂. Estimated error: $\pm 10\%$ of quoted value. All transients were observed immediately after the laser pulse.

^bWavelength at which decay was monitored. Corresponds to λ_{max} for **6** at 340 nm and for **7** at 310 and 400 nm (shoulder).

^{*c*}At pH(D) = 7. Cosolvent is 50% CH₃CN.

be the triplet state. Indeed, the absence of the triplet state in aq. CH₃CN would suggest that it may be the reactive state in the photodecarboxylation, given that aromatic ketones are known to intersystem cross very efficiently. Triplet sensitization experiments were carried out in which D₂O-CD₃CN (1:1) was replaced with D₂O-acetone- d_6 (1:1, with $\lambda_{ex} =$ 300 nm), which resulted in 30% higher yield (when acetone d_6 was used). Since most of the exciting light is absorbed by acetone in these experiments, the inference is that the triplet state of **6** is reactive towards photodecarboxylation, consistent with the LFP data. However, we cannot rule out reaction from the singlet state, although such a pathway is probably insignificant.

Scaiano and Monti and their respective co-workers (6b-6d) have carried out extensive LFP studies of the photodecarboxylation of ketoprofen (4), a reaction that is closely related to the ones being studied in the present work. They assigned a transient with λ_{max} at 330 and 580 nm as owing to carbanion 5, although its spectral characteristics suggested that this anion might have substantial contribution from the radical anion (non-Kekulé) resonance form 5a.



Lifetimes of this species has been reported to be about 200 ns in aqueous solution with much longer lifetimes when photogenerated in some organic solvents (6b-6d). In addition, a simple benzyl anion is known to absorb at ca. 350 nm (11). In view of these literature precedents and the observed primary solvent isotope effect on decay of the observed 340 nm LFP transient for **6**, it seems reasonable that it be assigned to (singlet ground state) benzyl carbanion **15a/15b** (Scheme 2). It is assumed that if the benzyl carbanion was initially photogenerated in its triplet state that intersystem crossing has occurred during the laser pulse. We cannot rule out formation of the corresponding (ground state) non-Kekulé enol **16** at this pH since the pK_a of some aromatic ketyls are known to be in the 7 to 8 range (6c). Indeed,

Scheme 2.



protonation at oxygen would be diffusion controlled in this case (at pH 7 or lower), further arguing that the transient may actually be the non-Kekulé biradical 16. This species would still be quenchable by oxygen and sensitive to D_2O . LFP studies at pH 3 gave essentially the same transient but at pH 0, only very weak signals were observed, consistent with a change in reaction mechanism as required from data presented in Fig. 1. The acid-catalyzed photodecarboxylation pathway is given in eq. [5]. Support for this mechanism comes from the recent work of Wirz and co-workers (12) who showed that aromatic ketones such as benzophenone and acetophenone are readily photoprotonated via the triplet excited state, giving rise to reactive electronically excited carbocations that can undergo overall hydration (which for the parent systems studied are entirely reversible). In the case of acetophenone - phenylacetic acid 6, such a photoprotonation would give rise to 17a/17b, since Wirz and co-workers (12) have also shown that most of the positive charge of such cations reside at the meta positions (a form of meta activation (9)). An activated species such as 17b would be expected to decarboxylate (with concerted loss of the carboxylic acid proton to water), to generate a species such as 18 (which may or may not be identical to 16). In any event, in an acid medium, we anticipate that 18 will quickly form 8. This mechanistic scheme also gives an explanation as to why acid catalysis for photodecarboxylation was not observed for the para-acid 7 since the positive charge of the protonated species would not be expected to be localized significantly at the para position. The question of why the quantum yields measured in acid reach a plateau below pH 1 (Fig. 2) can be explained simply by noting that 17a/17b can deactivate back to ground state 6 without continuing on to 18. In addition, triplet excited state 6 could also suffer simple nonproductive quenching by protons, which would compete with the acid-catalyzed photodecarboxylation process itself. Thus, one would not expect the quantum yields to continue to rise until quantum yield of unity is reached.

LFP results for the para-isomer 7 are more complex. Although strong signals (Δ OD up to 0.1, Fig. 4) were observed immediately upon the laser pulse, three major transients could be discerned at 310, 355, and 400 nm (Table 2). At least two transients are contained within the broad absorp-



Scheme 3.



Fig. 4. Transients observed on LFP of **7** in H₂O–CH₃CN (1:1, pH 7, 266 nm excitation, N₂ purged); 500 ns (\blacklozenge), 800 ns (\square), 1600 ns (\blacklozenge), 13 000 ns after the laser pulse (×)). The transient at 400 nm (shoulder) is assigned to **19** or **21** and decays with first-order kinetics (inset) with $\tau \approx 1700$ ns.



tion in the 300–380 nm region, where the decays do not obey simple first-order kinetics, likely caused by the overlapping absorptions; only the 400 nm transient exhibited first-order decay. This increased complexity is not surprising since this compound gave two photoproducts (9 and 10) at all pH. Analogous experiments to 6 (vide supra) were performed to identify as many of the observed transients as possible, within the scope of the time resolution of the laser equipment. When H₂O was replaced with D₂O, an increase in lifetime (by about twofold) of the 400 nm transient was observed, while the lifetimes of the other transients were essentially unaffected. The products of the photodecarboxylation of 7 are formally derived from a benzyl carbanion 19 (to give 9) and a benzyl radical 20 (to give 10). Therefore, we assign the 400 nm transient to (ground state) carbanion 19a/19b (Scheme 3), although we cannot rule out that it is in fact the corresponding enol 21. The mechanism of photodecarboxylation of 7 (Scheme 3) proceeds in a similar fashion as proposed for **6**. After extrusion of CO_2 (via the carboxylate form), a benzyl carbanion (19) is generated, which can follow two possible routes to the product. It is either carbon protonated immediately to give 9 or is protonated at the oxygen to give enol 21. Either pathway eventually leads to product 9. The LFP transient at 400 nm could be reasonably assigned to either 19 or 21. Compared to the analogous transient 15/16 for the meta acid 6, the present transient is longer lived since the structure would have better resonance stablization. Improved resonance stabilization also explains the observed red shift (≈60 nm) of this transient.

The benzyl radical **20** is likely contained within the broad strong 300–380 nm absorption. These transients are all sensitive to oxygen, as would be required for such a radical. The parent benzyl radical itself is known to absorb at \approx 315 nm (11). Although our results cannot discern among the various mechanisms possible for formation of **10**, we propose that one possible pathway is formation of **20** via oxidation of **19** (either by residual oxygen or by absorption of a photon). Another possibility is the coupling of two molecules of **19**, giving a diradical dianion, which is then oxidized, similar to that proposed for **2** (Scheme 1). However, the much shorter lived **19** (1700 ns) compared to the para nitro analogue **12** (60 s) makes this less likely. However, it would appear that the longer lifetime of **19** compared to the corresponding meta carbanion **15** does allows for the minor "radical" pathway giving rise to the corresponding dimer **10**.

Summary

We have shown that acetophenone derivatives 6 and 7 undergo efficient photochemistry that is best rationalized as being due to the enhanced electron-withdrawing character of the acetyl group in the triplet excited state. The photochemistry mirrors some of the observed behaviour for the much-studied nitrophenylacetic acids 1 and 2. The triplet state is reactive, although we cannot rule out residual singlet state reaction. Our results suggest that new types of photochemistry via ionic intermediates may be available for aromatic ketones, which will require a reevaluation of the present theoretical understanding of ketone photochemistry, at least in polar solvents such as water.

Experimental

General

¹H NMR spectra were recorderd on a Bruker AC300 (300 MHz) instrument in CDCl₃ unless otherwise specified. MS and HR-MS were obtained on a Kratos Concept H (EI) instrument. UV–vis spectra were recorded on a Varian Cary 5 instrument. Acetonitrile (HPLC or spectral grade) used for LFP experiments was dried by distillation from calcium hydride. Organic extracts were dried over anhydrous magnesium sulfate and filtered. pH(D) values were measured using a Fisher Accumet 915 pH meter.

Materials

3-Acetylphenylacetic acid (6)

3-Methylacetophenone (Aldrich, 5.17 g, 38 mmol) was added to a solution consisting of 100 mL CCl₄, 1.2 equiv. Nbromosuccinimide (8.23 g, 46 mmol), and a catalytic amount of benzoyl peroxide, and refluxed for 20 h under N₂. The bromination product was isolated by first evaporation of the solvent and subsequent dissolution in CH₂Cl₂ (with back-wash with water). This crude material was then dissolved in 10% H₂O-CH₃CN and refluxed for 4 h with 1.1 equimolar of NaCN. The resulting crude cyano derivative was hydrolyzed directly with concd. HCl (refluxed in 50 mL for 5 h). The crude acid product was isolated by evaporation of the solvent to give a brown solid, which was then dissolved in a minimum of hot water, filtered, and cooled. The crude product was recrystallized again in water to yield a white powder (0.38 g, 12% overall yield); mp (uncorrected) 96-99 °C (lit. value (13) 106 °C). ¹H NMR (300 MHz) & 2.59 (s, 3H, CH₃), 3.71 (s, 2H, ArCH₂), 7.43 (m, 2H, ArH), 7.86 (m, 2H, ArH), 10.8 (in acetone-d₆, br, COOH). ¹³C NMR (250 MHz) & 26.6 (CH₃), 40.7 (CH₂), 127.5 (ArCH), 128.9(ArCH), 129.3 (ArCH), 133.8 (ipso), 134.1(ArCH), 137.5 (ipso), 176.6 (CO₂H), 197.9 (R₂CO). HR-MS calcd. for C₁₀H₁₀O₃: 178.0630; found: 178.0631.

4-Acetylphenylacetic acid (7)

The desired product was synthesized in a similar procedure and with comparable yield to **6** previously. The compound is a white powder, mp (uncorrected) 106–108 °C (lit. value (13) 119 °C). ¹H NMR (300 MHz, CDCl₃) & 2.58 (s, 3H, CH₃), 3.70 (s, 2H, ArCH₂), 7.36 (d, J = 8 Hz, 2H, ArH), 7.92 (d, J = 8 Hz, 2H, ArCH₂), 7.36 (d, J = 8 Hz, 2H, ArH), 7.92 (d, J = 8 Hz, 2H, ArCH₂), 7.36 (d, J = 8 Hz, 2H, ArH), 7.92 (d, J = 8 Hz, 2H, ArCH₂), 7.36 (d, J = 8 Hz, 2H, ArH), 7.92 (d, J = 8 Hz, 2H, ArCH₂), 7.36 (d, J = 8 Hz, 2H, ArH), 7.92 (d, J = 8 Hz, 2H, ArCH₂), 12.4 (in acetone- d_6 , br, COOH). ¹³C NMR (250 MHz) & 26.6 (CH₃), 40.8 (CH₂), 128.7 (CH), 129.7 (CH), 136.2 (*ipso*), 138.6 (*ipso*), 176.1 (CO₂H), 197.8 (R₂CO). HR-MS calcd. for C₁₀H₁₀O₃: 178.0630; found: 178.0629.

Product studies

Preparative photolyses for 6 and 7 were carried out with samples (10-100 mg) dissolved in the appropriate solvent (40–100 mL) and transferred to a 100 mL quartz tube. The solution was irradiated in a RPR-100 photochemical reactor fitted with 254 nm or 300 nm lamps with continuous cooling (by a cold finger) and purging by a stream of argon for approximately 10 min before and continuously during irradiation (via a long stainless steel needle). Photolysis times ranged from 1 to 30 min, depending on the conversion desired, the efficiency of the reaction, and the size of the sample. After photolysis, aqueous samples were acidified (if necessary) and extracted with CH₂Cl₂. Direct evaporation of the organic solvent was used when samples were irradiated in wholly organic solvents. As the photoproducts are somewhat volatile, the temperature was kept under 30 °C during evaporation and the flask was returned to atmospheric pressure as soon as the solvent was removed. Typical experiments are described in the following.

Photolysis of 6 (pH 7)

Compound **6** (50 mg) was dissolved in 100 mL of H₂O– CH₃CN (1:1) and the pH was adjusted to 7 using aq. NaOH. The solution was irradiated using 4 × 254 nm lamps for 15 min. After photolysis, the solution was made acidic with concd. HCl (to pH < 2) and extracted with CH₂Cl₂ (3 × 40 mL). The solvent was dried over MgSO₄ and concentrated on a rotary evaporator. The ¹H NMR (300 MHz) was obtained in CDCl₃ and gave a spectrum identical to that of the commercial 3-methylacetophenone δ : 2.40 (s, 3H, ArCH₃), 2.58 (s, 3H, COCH₃), 7.37 (m, 2H, ArH), 7.74 (m, 2H, ArH). Conversion to **8** was 100%. MS (*m*/*z*): 134 (M⁺).

Photolysis of 6 $(pH \approx 0)$

Compound **6** (50 mg) was dissolved in 10% H₂SO₄– CH₃CN (1:1). Procedure as for pH 7 previously. The NMR spectrum of the product was the same as pH 7, with unreacted **6**. Conversion to **8** was 15% by ¹H NMR.

Photolysis of 6 (pD 7)

Compound **6** (100 mg) was dissolved in 100 mL of D₂O–CH₃CN (1:1) and the pD was adjusted to 7 with a solution of NaOD–D₂O. The ¹H NMR (300 MHz) spectrum of the photoproduct (76% yield) was identical to that of commercial 3-methylacetophenone except that the aromatic methyl group was monodeuterated (product **8**- α **D**). It was separated from the product mixture using column chromatography (CH₂Cl₂, $R_f = 0.73$): δ : 2.38 ("t", 2H, J = 2 Hz, ArCH₂D), 2.58 (s, 3H, COCH₃), 7.34 (m, 2H, ArH), 7.74 (m, 2H, ArH).

Photolysis of 7

Compound 7 (100 mg) was dissolved in 80 mL of H₂O-CH₃CN (1:1) and the pH was adjusted to 7.5 using aq. NaOH. The solution was irradiated using 254 nm lamps for 30 min. After photolysis, the solution was made acidic with concd. HCl (so the pH < 2) and extracted with CH₂Cl₂ (3 \times 40 mL). The solvent was dried with MgSO₄ and concentrated. The products were separated by preparative TLC (5% EtOAc-CH₂Cl₂) to give two photoproducts, 4methylacetophenone (9, 78%) and a dimer 10 (22%). The 1 H NMR (300 MHz) spectrum of 9 was identical to that of the commercial 4-methylacetophenone δ : 2.25 (s, 3H, ArCH₃), 2.42 (s, 3H, COCH₃), 7.20 (d, J = 8 Hz, 2H, ArH), 7.80 (d, J = 8 Hz, 2H, ArH). MS (EI, m/z): 134 (M⁺). Dimer 10: ¹H NMR (300 MHz) & 2.58 (s, 6H, CH₃CO), 3.00 (s, 4H, ArCH₂-), 7.20 (d, 4H, J = 8 Hz, ArH), 7.85 (d, 4H, J =8 Hz, ArH). MS (EI, m/z): 266 (M⁺).

Triplet sensitization of 6

Compound **6** (9.1 mg) was dissolved in 3.0 mL of D₂O– CD₃CN (2:1). Two aliquots (0.5 mL) were removed and diluted, one was with 0.5 mL CD₃CN and the other with 0.5 mL acetone- d_6 . The solutions (8 × 10⁻³ mol L⁻¹) were placed into NMR tubes and purged with argon. The solutions were photolyzed for 90 s (8 × 300 nm lamps). Photodecarboxylation yields (by ¹H NMR) were 33% and 43% for D₂O–CD₃CN vs. D₂O–acetone- d_6 solutions, respectively.

Quantum yields

Photodecarboxylation quantum yields for **6** and **7** were determined using relative methods that involved comparison of the yields of decarboxylated product between ketoprofen (**4**) with a known quantum yield (secondary actinometric standard) of 0.75 (6) and those of the compounds in question, as determined by ¹H NMR integration. A known amount of standard was dissolved in CH₃CN-H₂O (1:1, 2 × 10^{-3} mol L ⁻¹ adjusted to pH 7) and photolyzed as above for 1 min (4 lamps, 254 nm). An equimolar amount of the compound of unknown quantum yield was irradiated under the same conditions and decarboxylation determined by ¹H NMR integration of the benzyl methyl protons.

Nanosecond laser flash photolysis (LFP)

LFP studies were carried out at the University of Victoria laser flash photolysis facility. A Spectra-Physics Nd: YAG laser (266 nm, ~10 ns, <30 mJ/pulse) was used for excitation and signals were digitized with a Tektronix TDS 520 recorder. Samples of OD ~ 0.4 at 266 nm were prepared and

irradiated in 7 mm quartz cells. Flow cells were used to obtain spectra and kinetic data. Runs using static cells in aqueous solution gave irreproducible results because of efficient depletion of substrate because of efficient photochemical decarboxylation. Solutions were purged (with N₂ or O₂) prior to and continuously during LFP studies.

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