Protecting Groups That Can Be Removed through Photochemical Electron Transfer: Mechanistic and Product Studies on Photosensitized Release of Carboxylates from Phenacyl Esters

Anamitro Banerjee and Daniel E. Falvey*

Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742

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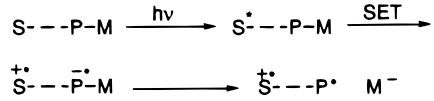
Photolysis of electron-donating photosensitizers in the presence of various phenacyl esters ($PhCOCH_2-OCOR$) results in C−O bond scission leading to the formation of acetophenone ($PhCOCH_3$) and the corresponding carboxylic acid (RCO_2H). Preparative experiments showed that the carboxylic acids are generated in high or quantitative isolated yields. It is argued that this reaction is initiated by a photoinduced electron transfer from the excited state sensitizer to the phenacyl ester. The latter process forms the anion radical of the phenacyl ester which in turn undergoes rapid C−O bond scission leading to the phenacyl radical and the corresponding carboxylate anion. This mechanism is supported by the following observations. (1) The phenacyl esters quench fluorescence from the sensitizers. (2) Analysis of the redox potentials of the sensitizer excited states and the substrates shows that the proposed electron transfer step is exergonic by 15−20 kcal/mol. (3) The byproducts are indicative of the proposed ion radical intermediates. In particular *N*-methylaniline is detected when *N*,*N*-dimethylaniline is used as a sensitizer. (4) Competing processes are observed in phenacyl esters whose acid components are themselves labile to single-electron transfer. For example, phenacyl 4-bromophenylacetate showed bromide elimination in competition with deprotection.

Introduction

There has been much recent interest in the use of photoremovable protecting groups (PRPGs).[1−9] These are species that can be attached to a key functional group of a molecule rendering it inert to some particular reaction conditions. PRPGs are distinct from conventional protecting groups in that the PRPGs are released when the caged molecule is exposed to light. In biochemical applications such a protected molecule is often referred to as a "caged" substrate (e.g., caged ATP,[10] caged neurotransmitters[11]).

PRPGs provide a general way of using light to trigger or activate chemical or biochemical reactions that are not themselves photochemical in nature. The use of light is often desirable as it allows for precise temporal control (using pulsed sources) and spatial control (using masks or focused beams) of reactions. A general phototriggering strategy is to introduce one reagent to the reactive system in caged form and then release it using light. For example, Hess and co-workers have used caged neurotransmitters to study the opening of ion channel proteins in whole cells. The use of light in these studies allowed fast laser flash photolysis methods to be applied to this important physiological process even though it is not inherently a photochemical reaction. Similar strategies have been applied to a wide variety of problems including time-resolved X-ray crystallography,[12] time-resolved studies on calcium ion effects on nerve and muscle cells,[13−15] and various aspects of combinatorial chemistry.[16,17]

Scheme 1. General Strategy for Photorelease Using Photoinduced Electron Transfer



Recent efforts in this laboratory have been directed at the design of PRPGs whose release is activated through photoinduced electron transfer (PET) mechanisms.[18−20] Our general strategy is described by the mechanism in Scheme 1.[21] The photorelease system consists of a protecting group P attached to a substrate molecule M and a photosensitizer S. The latter is either a chromophore that is covalently tethered to P or else a separate

* Corresponding author. E-mail: df37@umail.umd.edu. Fax: 301-314-9656.

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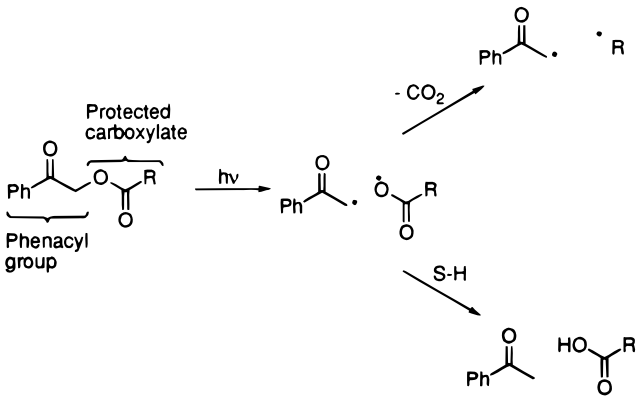
Scheme 2. Direct Irradiation of Phenacyl Esters



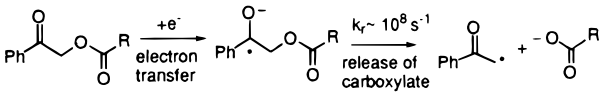
additive. The light is first absorbed by the S creating its excited state S*. The latter transfers an electron to the caged molecule, creating the anion radical P-M$^{\bullet-}$. The molecule is released in its anionic (i.e., conjugate base) form as M$^-$.

The selection of this PET strategy was guided by two considerations. Firstly, the use of PET to activate the leaving group lends itself to modular design of PRPG systems; that is, the light absorption step is decoupled from the release or bond scission step. For this reason it is possible to separately optimize light-absorbing properties of S while maintaining a constant mechanism and rate for the release step. The only constraint in the selection of S is that it has to be able to successfully deliver an electron to P-M upon photolysis. In contrast most previously studied PRPGs (e.g., the 2-nitrobenzyl groups studied by Trentham[22] and Hess,[23] the benzoin-derived groups studied by Givens[6] and Pirrung,[24] or the 2-benzoylbenzyl ethers studied by Porter[3]) are unitary in design. The chromophore group in this case becomes intimately involved in the mechanism of the release step. Consequently, any changes that are made in the light-absorbing properties of the chromophore are likely to change the mechanism and/or the rate of release.

A second consideration was that it was desirable to release the substrate in its conjugate base form rather than as a free radical or a cation. Generally, most of the functional groups that would be protected (e.g., hydroxy groups, carboxylic acids, amines, amides, etc.) are highly unstable as radicals or cations and would likely undergo undesired secondary fragmentation reactions or rearrangements leading to undesired side products. It was for this reason that we targeted the radical anion, rather than the radical cation, of the caged molecule as the intermediate to be generated through PET.

Some years ago, Sheehan and Umezawa[25] reported that *direct* irradiation of phenacyl esters[26] could provide modest yields of deprotected carboxylic acids. The mechanism reported for this reaction involves homolytic C−O bond scission to give an acyloxy radical and a phenacyl radical (Scheme 2). The success of this approach relies on a rapid H atom transfer to the former to give the acid. This process competes with facile decarboxylation. Perhaps concern about the competing decarboxylation process has prevented widespread adoption of this photorelease strategy.

The present report focuses on the development of protecting groups that are released via a reductive PET mechanism. Tanner et al.[27] showed that one-electron reduction of phenacyl benzoate and phenacyl acetate causes rapid elimination of benzoate and acetate anions, respectively (eq 1). Intramolecular competition experi-

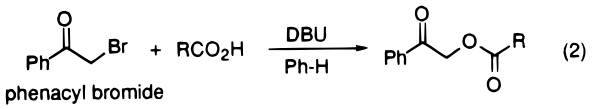


(1)

ments indicated that the carboxylate anion is released from the anion radical with $k_{rel} = 10^8$ s^{-1}. Herein it is demonstrated that excitation of electron-donating photosensitizers in the presence of various phenacyl esters ($PhCOCH_2OC(O)R$) results in the release of the corresponding carboxylates (RCO_2^-) in high to quantitative *isolated* yields. This procedure is applicable to a wide variety of carboxylic acid substrates. It is further shown that the mechanism proceeds via the PET pathway outlined in Scheme 1.

Results and Discussion

The protection of carboxylic acids with the phenacyl group follows well-described procedures.[28] The corresponding carboxylic acid is dissolved in benzene and treated first with a base, diazabicyclo[5.4.0]undec-7-ene (DBU), and then with phenacyl bromide (eq 2). Reactions



(2)

were generally complete after several minutes, and the yields were usually above 90%. It was found that when even a slight excess of DBU was employed, a red color accompanied by a complex mixture of products would form. It was for this reason that DBU was added in subequivalent (0.7−0.8 equiv) amounts. In that case only a slight yellow color accompanies addition of phenacyl bromide and the product is formed cleanly. The acids that were thus protected are listed in Table 1.

On the basis of Tanner's[27] study discussed above, we reasoned that a similar elimination of carboxylate anions from phenacyl esters could be effected through photosensitization using excited state electron donors (Scheme 1). To this end *N,N,N′,N′*-tetramethylbenzidine (TMB), *N,N,N′,N′*-tetramethylphenylenediamine (TMPD), and *N,N*-dimethylaniline (DMA) were employed as sensitizers (Chart 1). These compounds are potent single-electron donors in their excited states due to their low excited state oxidation potentials (E_{ox}*) which are −3.48 V vs Fc/Fc$^+$ for TMB, −3.56 V for TMPD, and −3.35 V for DMA.

Preparative photolysis experiments validate the photosensitization strategy. UV photolyses were carried out on CH_3CN solutions containing the sensitizers and the

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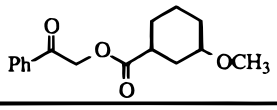
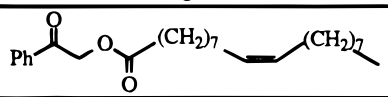
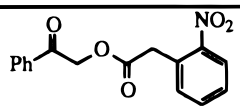
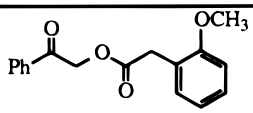
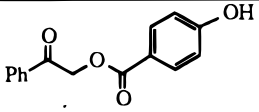
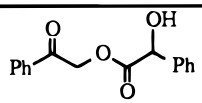
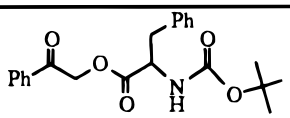
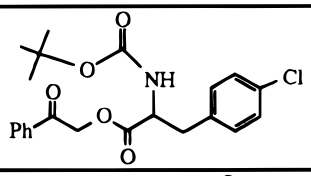
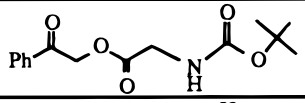
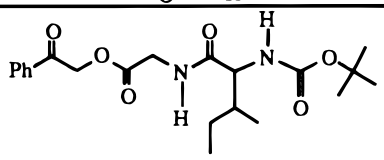
Table 1. Protection and Deprotection Yields of Various Phenacyl Esters

Entry	Protected acid	Protection yield (%)	Sensitizer	Deprotection Yield (%)
1		91	TMPD	100
2		95	TMPD	100
3	$PhCOCH_2OCOCH_2Ph$	96	DMA TMPD TMB	79 76 100
4		84	DMA	68[a]
5		87	TMPD	100
6	$PhCOCH_2OCOPh$	72	DMA	93
7		50	TMPD	82
8		94	DMA	100
9		60	DMA	100
10		91	TMPD	81
11		94	TMPD	100
12		65	DMA	94

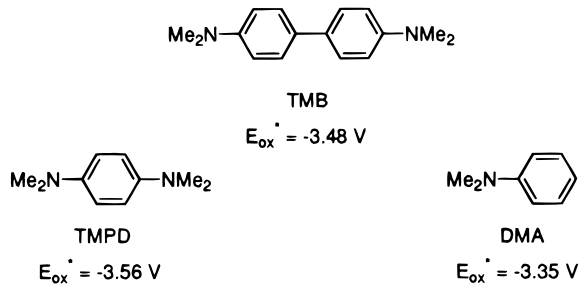
[a] After 15 h of photolysis.

phenacyl esters listed in Table 1. In most of these cases, the deprotection reaction proceeds cleanly and efficiently following eq 3. High yields of the corresponding carboxylic acid are isolated. Approximately 100 mg of ester is completely converted within 2 h when irradiated with a 150 W Hg vapor lamp. *We emphasize that the reported yields refer to materials that were isolated and weighed in milligram quantities.*

$$PhCOCH_2OCOR + ArN(Me)_2 \xrightarrow{h\nu} PhCOCH_3 + ArNHMe + RCO_2H \quad (3)$$

A number of different carboxylic acids were photoreleased in this manner in order to determine which functional groups would be compatible with the PRPG system. Aromatic acids, such as benzoic acid (entry 6) and its 4-hydroxy derivative (entry 7), were readily protected and deprotected. The strategy also can be applied to aliphatic acids as exemplified by experiments with phenylacetic acid (entry 3) and 3-methoxycyclohexanoic acid (entry 1). The compatibility of several functional groups with the PRPG system was similarly investigated. Both aromatic as well as aliphatic ether linkages are compatible, as demonstrated with 2-methoxyphenylacetic acid (entry 5) and 3-methoxycyclohexanoic acid (entry 1). Likewise hydroxy groups are compatible as illustrated with mandelate (entry 8) and 4-hydroxybenzoate (entry 7). Protection and deprotection

Chart 1. Electron-Donating Photosensitizers Used in Photorelease Experiments



experiments on oleic acid (entry 2) show that unconjugated alkenes present no difficulties.

Many applications of photorelease involve amino acids, peptides, and similar compounds. It was therefore of specific interest to determine if such species can be successfully caged and released using the electron transfer method. Our protocol was thus applied to *N-tert*-butylcarbamate (*t*-Boc) derivatives of phenylalanine (entry 9), glycine (entry 11), and 4-chlorophenylalanine (entry 10) as well as an isoleucine−glycine dipeptide (entry 12). These substrates also gave generally satisfactory results. These experiments show that neither the amide nor the carbamate functional groups interfere with photosensitized release of the carboxylate group.

Fluorescence quenching experiments were carried out in order to determine which excited state of the sensitizer was responsible for initiating release. Phenacyl 2-methoxyphenylacetate and phenacyl *N-t*-Boc-glycine were chosen as representative examples of protected substrates. These protected compounds were found to quench the fluorescence of the sensitizer, TMPD. Stern−Volmer analyses indicate that the quenching processes occurs at or near the diffusion limit (the quenching rate constants being 1.61×10^{10} and 1.44×10^{10} M^{-1} s^{-1}, respectively, for phenacyl 2-methoxyphenylacetate and phenacyl *N-t*-Boc-glycine). These experiments indicate that the substrates interact with the excited singlet states of the sensitizers.

All excited state electron transfers compete with nonradiative relaxation of the excited state sensitizer. In order for such a process to occur with measurable efficiency, it is necessary that the initial charge transfer step be exothermic or only very slightly endothermic. One way to assess the feasibility of a proposed electron transfer reaction is to determine the driving force for the charge transfer step (ΔG_{ct}, in kcal/mol). The latter can be determined from the oxidation potential of the donor (E_{ox}, in V), the reduction potential of the acceptor (E_{red}, in V), and the energy of the excited state from which the charge transfer occurs (E_{oo}, in kcal/mol), along with a correction for the desolvation and attraction of the ion pair, $e^2/R\epsilon$ following eq 4:

$$\Delta G_{ct} = 23.03\left(E_{ox} - E_{red} - \frac{e^2}{R\epsilon}\right) - E_{oo} \qquad (4)$$

The E_{ox} and E_{oo} values for the three sensitizers are available from previous work. In order to estimate E_{red} for typical phenacyl-protected carboxylates, cyclic voltammograms (CVs) of phenacyl phenylacetate and *O*-phenacyl-*N-t*-Boc-phenylalanine were measured. In each case an irreversible cathodic wave is detected at −2.65 V (vs Fc/Fc^+). Following Wayner et al.,[29] we assign this wave to a two-electron process caused by reduction of the phenacyl ester followed by rapid reduction of the phenacyl radical fragment. Using the $E_{1/2}$ value of −2.65 V as an estimate of the E_{red} for the phenacyl esters, taking the values stated above for the sensitizer E_{ox}*, and applying eq 4 gives a ΔG_{ct} ca. −20 kcal/mol − −15 kcal/mol. That the presumed charge transfer step is exothermic is consistent with the electron transfer mechanism.

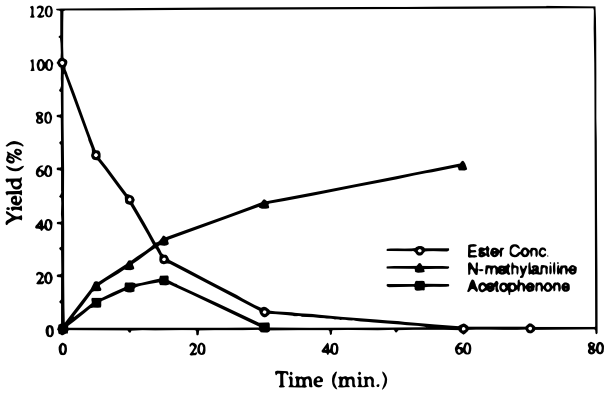


Figure 1. Time dependence of reactant and product concentrations from the sensitized photolysis of phenacyl phenylacetate by DMA in CH_3CN.

Byproducts detected from the deprotection reactions are also consistent with the anticipated PET mechanism. Both *N*-methylaniline and acetophenone were detected by HPLC analysis of the reaction mixture generated from deprotection of phenacyl phenylacetate sensitized by DMA (eq 3). *N*-Methylaniline grows in proportionately to the disappearance of the phenacyl ester. Acetophenone also grows in at low photolysis conversions but then is consumed by secondary photolytic reactions. This behavior is illustrated in Figure 1. The *N*-methylaniline product is particularly diagnostic for the one-electron oxidation of DMA and is unlikely to arise from a simple energy transfer mechanism.

Scheme 3 outlines the specifics of the proposed mechanism for the photorelease of phenacyl esters using DMA as the sensitizer. Initial charge transfer leads to the cation radical of DMA ($DMA^{\bullet+}$) along with the anion radical of the phenacyl ester. The latter is expected to fragment rapidly to produce the carboxylate anion (RCO_2^-) and the phenacyl radical ($PhC(O)CH_2\bullet$). A direct transfer of a H atom from $DMA^{\bullet+}$ to $PhC(O)CH_2\bullet$ leads to the formation of the iminium ion $Ph(Me)N{=}CH_2^+$. This iminium ion is hydolyzed either by traces of water in the reaction medium or upon workup to give *N*-methylaniline. Alternatively the RCO_2^- generated in the fragmentation could deprotonate $DMA^{\bullet+}$. This is corroborated by the work of Mariano et al.[30] wherein it is demonstrated that the cation radical of DMA is strongly acidic and rapidly deprotonated by $CH_3CO_2^-$. This proton transfer would lead to the easily oxidizable α-amino radical, $Ph(Me)NCH_2\bullet$. Electron transfer from this radical to $PhC(O)CH_2\bullet$ produces the acetophenone enolate and would lead to the same intermediates and products. Our experiments are incapable of distinguishing between this pathway involving sequential proton and electron transfer and the H atom transfer pathway shown in Scheme 3.

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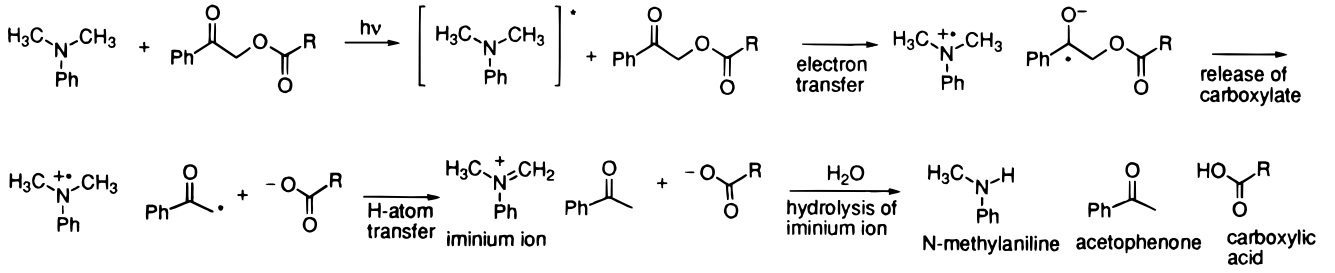
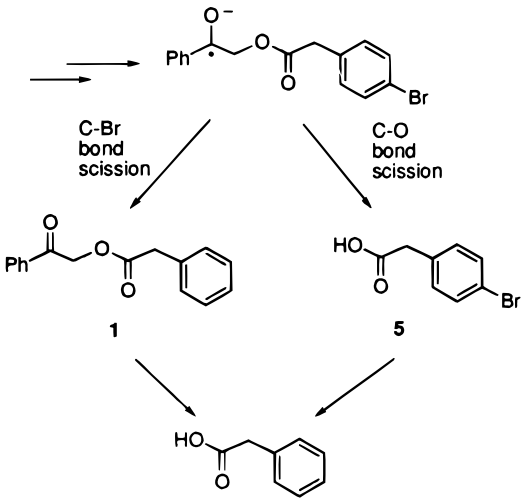
(30) Zhang, X.; Yeh, S.-R.; Hong, S.; Freccero, M.; Albini, A.; Falvey, D. E.; Mariano, P. S. *J. Am. Chem. Soc.* **1994**, *116*, 4211−4220.

Scheme 3. Mechanism of DMA-Sensitized Deprotection of Phenacyl phenylacetate



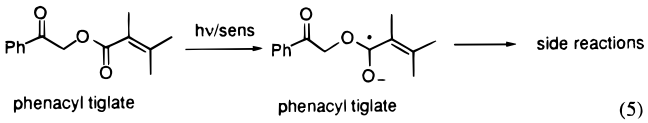
Scheme 4. Competing Bromide and Carboxylate Elimination



The electron transfer mechanism predicts some limitations on the types of carboxylates that can be released using this process. In particular, if the carboxylate possesses functionality that is more easily reduced than the phenacyl group and further reacts rapidly and irreversibly upon one-electron reduction, then undesired side reactions are likely to compete with the photorelease. It is known that aryl halides rapidly eliminate halide anions upon one-electron reduction.[31] The phenacyl ester of 4-bromophenylacetic acid was prepared and subjected to the photosensitized deprotection conditions. In this case a mixture of products was formed. This consisted of (1) 4-bromophenylacetic acid, which arises from the desired release pathway; (2) phenacyl phenylacetate, which arises from competing loss of bromide; and (3) phenylacetic acid, which arises from the two photoreactions occurring in succession (Scheme 4). Deprotection appears to be faster than the very rapid competing bromide elimination. The two primary products, 4-bromophenylacetate and phenacyl phenylacetate, are formed in a ratio of 5:1.

The behavior of the aryl bromide substrate can be compared with that of *N*-*t*-Boc-4-chlorophenylalanine, an aryl chloride (Table 1, entry 10). In the latter case, the yield of the desired acid was high (84%) and none of the dehalogenated product could be detected. This can be attributed to the differing labilities of the two types of halides. Aryl chloride anion radicals generally have lifetimes that are several orders of magnitude longer than those of the corresponding bromides. For example, 4-chloroacetophenone eliminates chloride ion with a rate constant of 3×10^3 s^{-1}, while 4-bromoacetophenone eliminates with a rate constant of 3.2×10^7 s^{-1}.[32]

Competing electron transfer reactions also prevent clean deprotection of α,β-unsaturated carboxylates. The α,β-unsaturated ester group is reduced at slightly less negative potentials then the phenacyl group. CV experiments were carried out on phenacyl tiglate (eq 5). An



(5)

irreversible wave was detected with a peak at −2.45 V—a value 200 mV more positive than that observed for phenacyl phenylacetate. On the basis of this experiment, it seems likely that the preferred site of reduction is the α,β-unsaturated carbonyl group on the ester fragment rather than the aryl ketone of the phenacyl group. Preparative photosensitized release experiments were also carried out on this substrate, and a complex mixture of products was obtained. Apparently, the anion radicals of such α,β-unsaturated esters react irreversibly.

Phenacyl 2-nitrophenylacetate (entry 4) is an interesting case. It is clear that the nitrophenyl group is more easily reduced than the phenacyl group. In fact, CV experiments on this compound show a reduction wave at −1.5 V (Figure 2). This wave is reversible at high scan rates and becomes irreversible at slow scan rates. Because it occurs at a potential that is 1.0 V more positive than simple phenacyl esters, this wave is attributed to formation of a nitrophenyl-localized anion radical. The sensitizer DMA has $E_{ox}^* = -3.35$ V, and as such it is capable of reducing both the phenacyl group (−2.65 V) and the nitrophenyl group (ca. −1.5 V). Despite the possibility of competing electron transfer to the nitrophenyl group, this 2-nitrophenylacetate is deprotected in reasonable chemical yields. However, significantly longer photolysis times are required.

We propose a mechanism involving electron transfers to both the phenacyl group and the nitrophenyl group (Scheme 5). The nitrophenyl-localized anion radical does not undergo any (significant) competing reactions other than back-electron transfer to the sensitizer cation radical. This is supported by the CV experiments which show that the reduction wave for the phenacyl 2-nitrophenylacetate becomes irreversible only at very slow (100 mV/s) scan rates. Thus the corresponding anion radical is relatively unreactive, and electron transfer to this group represents an unproductive pathway. Formation of the phenacyl-localized anion radical results in a partitioning between exergonic electron transfer to the nitrophenyl group and a rapid C−O bond scission. It is also possible that the desired carboxylate release could occur through an intramolecular electron transfer reaction from the

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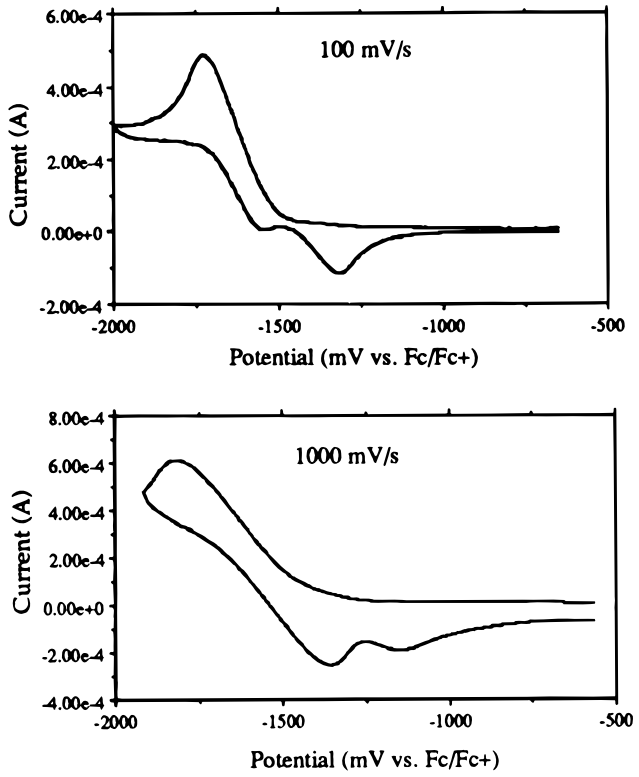


Figure 2. Cyclic voltammogram of phenacyl 2-nitrophenylacetate in CH_3CN. Scan rates are 100 mV/s (upper panel) and 1000 mV/s (lower panel).

nitrophenyl group to the phenacyl group. However, we regard this as unlikely as it would be endergonic by approximately 23 kcal/mol.

Conclusions

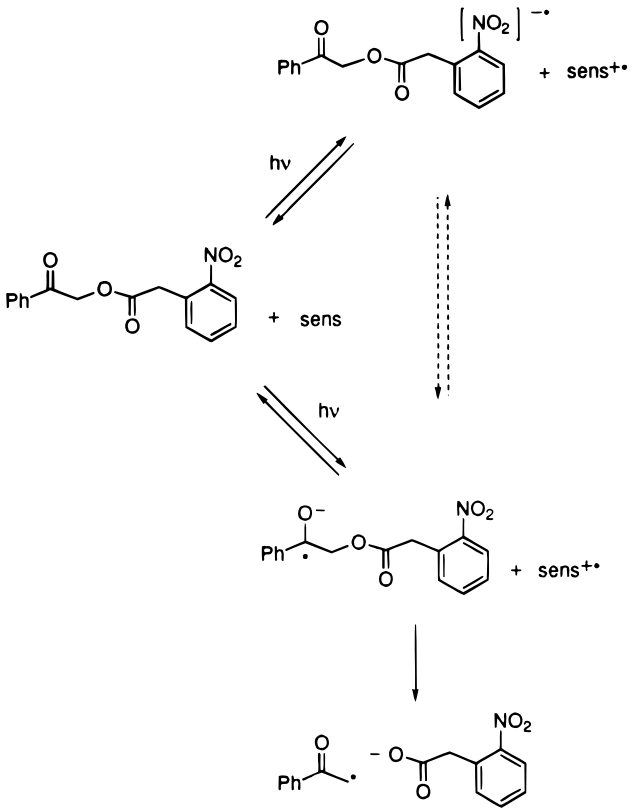
This work shows that reductive photochemical electron transfer can be used to remove phenacyl protecting groups from carboxylic acids. Preparative experiments show that high isolated yields of the released substrates can be realized. Fluorescence quenching experiments, detection of characteristic byproducts, and analysis of the substrate and sensitizer redox potentials all support the predicted photochemical electron transfer mechanism. Low yields or mixtures of products were observed when the carboxylic acids contain functional groups that react rapidly upon one-electron reduction. While these latter experiments reveal some limitations to this photorelease strategy, they also provide further support for the proposed mechanism.

Experimental Section

General. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Acetonitrile and dichloromethane were distilled from CaH_2 under anhydrous N_2 atmosphere through a vacuum-sealed column (30 cm) packed with glass helices. ^{1}H NMR spectra were run at 200 MHz and ^{13}C NMR spectra at 55.1 MHz. *J* values are reported in Hz. Mass spectra were performed using EI (70 eV), CI, or FAB.

Preparative photolysis reactions were performed using a 400 W Xe lamp and an Ace-Hanovia 450 W medium pressure Hg vapor lamp. The CW Xe arc lamp was also used to carry out control reactions. A 295 nm cutoff filter was used in each case to ensure that the light was absorbed by the sensitizer rather than the substrate.

Scheme 5. Mechanism of Deprotection for Phenacyl 2-Nitrophenylacetate



Reactions were analyzed using Rainin Instrument HPLC with an analytical C_{18} reversed phase column. Appropriate mixtures of water and acetonitrile were used to resolve the sensitizer and ester peaks at 254 nm.

CV data were obtained from BAS CV-50 W in the CV mode. All measurements were taken after purging samples with N_2 using glassy carbon working, platinum auxiliary, and Ag/AgCl reference electrodes with $[NBu_4][PF_6]$ (0.13 M) as the supporting electrolyte. Ferrocene/ferrocenium (Fc/Fc^+) couple was found at 455 mV vs Ag/Ag^+, and the potentials shown in the waveform in Figure 2 are adjusted to this reference.

General Method for Synthesis of Phenacyl Esters. A mixture of diazabicycloundecene (DBU) (~0.018 mol) and the acid (~0.020 mol) was dissolved in about 40 mL of benzene. Phenacyl bromide (~0.015 mol) was then added to the mixture and stirred under nitrogen at room temperature for about 2 h. The resulting solution was then washed three times each with 50 mL of 10% HCl and saturated Na_2CO_3 solution. The organic layer was dried over $MgSO_4$, and the solvent was removed to obtain the crude product which was then recrystallized from diethyl ether. All esters were judged to be >95% pure by their ^{1}H NMR spectra and in most cases by the observation of sharp melting points. For those compounds which did not crystallize, HPLC analysis was also used to confirm their purity.

Phenacyl 3-methoxycyclohexanoate (1:1 cis and trans mixture): yield 2.002 g (91%) from 1.566 g of acid, yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.37−2.15 (m, 16H), 2.39−2.57 (m, 2H), 2.81−3.28 (m, 2H), 3.33 (s, 3H), 3.36 (s, 3H), 5.33 (s, 4H), 7.43−7.60 (m, 6H), 7.89 (d, J = 7, 4H); ^{13}C NMR ($CDCl_3$) δ 192.2, 192.1, 175.2, 174.2, 134.2, 133.7, 128.7, 127.6, 78.4, 74.6, 65.8, 65.7, 55.6, 41.6, 37.8, 34.0, 32.0, 31.5, 29.4, 28.3, 28.2, 23.3, 19.9; EI-MS *m*/*z* (rel. intensity) 276 (M^+, 0.2), 246 (9), 157 (72), 141 (70), 137 (18), 127 (24), 120 (31), 112 (43), 108 (50), 105 (100), 91 (66), 81 (89), 77 (92), 71 (78), 54 (75), 50 (67).

Phenacyl oleiate: yield 2.468 g (95%) from 2.151 g of acid, yellow oil; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6, 3H), 1.26−2.16 (m, 26H), 2.49 (t, 2H), 5.33 (s, 4H), 7.43−7.60 (m, 3H), 7.89 (d, J = 7.2H); EI-MS *m*/*z* (rel. intensity) 400 (M^+, 1), 382 (5), 280 (21), 266 (100), 236 (16), 221 (16), 207 (16), 193 (10), 179 (13), 105 (72), 98 (13), 91 (12), 77 (24), 70 (23), 68 (21), 54 (43).

Phenacyl tiglate: yield 2.135 g (94%) from 1.329 g of acid, white solid; mp 40−42 °C; ^{1}H NMR ($CDCl_3$) δ 1.82 (d, J = 7, 3H), 1.90 (s, 3H), 5.40 (s, 2H), 7.03 (q, J = 7, 1H), 7.35−7.62 (m, 3H), 7.92 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 192.5, 167.2, 138.5, 134.3, 133.6, 128.6, 127.8, 127.6, 65.9, 14.3, 11.9; EI-MS m/z (rel. intensity) 218 (M^+, 23), 188 (25), 118 (30), 105 (100), 91 (45), 81 (90), 77 (84), 65 (18), 55 (87), 51 (67).

Phenacyl phenylacetate: yield 4.890 g (96%) from 4.085 g of acid, yellowish white crystalline solid; mp 43−46 °C (lit.[33,34] mp 50 °C); ^{1}H NMR ($CDCl_3$) δ 3.83 (s, 2H), 5.35 (s, 2H), 7.31−7.60 (m, 8H), 7.90 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 192.0, 171.0, 134.2, 133.8, 133.6, 129.4, 128.8, 128.6, 127.8, 127.2, 66.4, 40.9; EI-MS m/z (rel. intensity) 254 (M^+, 2), 118 (30), 105 (100), 91 (34), 77 (18).

Phenacyl 2-nitrophenylacetate: yield 4.818 g (84%) from 3.633 g of acid, yellow crystals; mp 92−94 °C; ^{1}H NMR ($CDCl_3$) δ 4.21 (s, 2H), 5.36 (s, 2H), 7.0−8.2 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 191.7, 169.4, 148.6, 134.0, 133.8, 133.5, 133.4, 129.2, 128.7, 127.6, 125.1, 66.4, 39.1; CI-MS m/z (rel. intensity) 300 (M + 1, 2), 136 (19), 118 (51), 105 (100), 92 (16), 77 (92).

Phenacyl 2-methoxyphenylacetate: yield 2.312 g (87%) from 1.997 g of acid, yellow oil; ^{1}H NMR ($CDCl_3$) δ 3.72 (s, 3H), 3.78 (s, 2H), 5.23 (s, 2H), 6.78−6.91 (m, 2H), 7.20−7.47 (m, 5H), 7.79 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 191.9, 170.8, 157.2, 133.9, 133.3, 130.6, 128.4, 128.3, 127.3, 122.3, 120.1, 110.2, 65.9, 55.0, 35.0; EI-MS m/z (rel. intensity) 284 (M^+, 66), 148 (89), 121 (91), 105 (100), 91 (90), 77 (80), 66 (61), 51 (66).

Phenacyl 4-bromophenylacetate: yield 1.543 g (83%) from 1.333 g of acid, white solid; mp 80−82 °C; ^{1}H NMR ($CDCl_3$) δ 3.78 (s, 2H), 5.36 (s, 2H), 7.24 (d, J = 8, 2H), 7.45−7.65 (m, 5H), 7.89 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 191.8, 170.5, 134.1, 133.9, 132.5, 131.7, 131.1, 128.9, 127.7, 121.3, 66.4, 40.2; EI-MS m/z (rel. intensity) 334 (M + 2, 2), 332 (M^+, 2), 197 (63), 195 (63), 171 (61), 169 (61), 118 (2), 105 (100), 90 (51), 86 (22), 84 (30), 77 (77), 63 (22), 50 (48).

Phenacyl benzoate: yield 1.738 g (72%) from 2.00 g of acid, white solid; mp 118−120 °C (lit.[35] mp 117−120 °C); ^{1}H NMR ($CDCl_3$) δ 5.57 (s, 2H), 7.42−7.65 (m, 6H), 7.96 (d, J = 7, 2H), 8.14 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 192.0, 166.0, 134.3, 133.8, 133.3, 130.1, 129.9, 129.4, 128.8, 127.8, 66.4; EI-MS m/z (rel. intensity) 240 (M^+, 0.3), 118 (26), 105 (100), 78 (88).

Phenacyl 4-hydroxybenzoate: (CH_3CN) yield 50%, yellow solid; mp 184−186 °C; ^{1}H NMR ($CDCl_3$−DMSO-d_6) δ 5.60 (s, 2H), 6.88 (d, J = 9, 2H), 7.51−7.70 (m, 3H), 7.92 (d, J = 9, 2H), 7.99 (d, J = 7, 2H), 9.53 (s, 1H); ^{13}C NMR ($CDCl_3$−DMSO-d_6) δ 191.1, 163.7, 160.8, 132.6, 132.2, 130.2, 127.3, 126.1, 118.4, 113.8, 64.8; EI-MS m/z (rel. intensity) 257 (M + 1, 3), 256 (M^+, 15), 122 (8), 121 (93), 119 (1), 118 (7), 106 (8), 105 (100), 93 (10), 77 (18), 66 (12), 53 (5).

Phenacyl mandelate: yield 5.052 g (94%) from 3.393 g of acid, white solid; mp 78−80 °C (lit.[36] mp 84−84.5); ^{1}H NMR ($CDCl_3$) δ 3.70 (d, J = 5, 1H), 5.29 (d, J = 16, 1H), 5.43 (d, J = 16, 1H), 5.42 (s, 1H), 7.20−7.65 (m, 8H), 7.83 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 191.2, 173.0, 137.9, 134.0, 128.9, 127.7, 126.9, 73.1, 67.1; CI-MS m/z (rel. intensity) 271 (M + 1, 2), 253 (55), 120 (96), 107 (85), 105 (100), 91 (59), 77 (92).

Phenacyl *N*-*t*-Boc-phenylalanine: yield 0.392 g (60%) from 0.345 g of acid, white solid; mp 139−142 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 9H), 2.96 (dd, J_1 = 9, J_2 = 14, 1H), 3.29 (dd, J_1 = 4, J_2 = 14, 1H), 4.52 (m, 1H), 5.44 (d, J = 7, 2H), 5.58 (d, J = 8, 1H), 7.23−7.71 (m, 8H), 7.95 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 193.4, 173.7, 138.2, 135.2, 134.9, 130.5, 130.0, 129.5, 128.7, 127.8, 67.9, 56.0, 38.2, 28.5; EI-MS m/z (rel. intensity) 383 (M^+, 0.1), 266 (52), 192 (24), 131 (14), 120 (22), 105 (62), 91 (29), 77 (19), 57 (100).

Phenacyl *N*-*t*-Boc-4-chlorophenylalanine: yield 0.397 g (91%) from 0.344 g of acid, white solid; mp 101−102 °C; ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 9H), 3.12 (dd, J_1 = 7, J_2 = 14, 1H), 3.33 (dd, J_1 = 6, J_2 = 14, 1H), 4.75 (m, 1H), 4.99 (d, J = 8), 5.31 (d, J = 16, 1H), 5.52 (d, J = 16, 1H), 7.24 (dd, J_1 = 17, J_2 = 9, 4H), 7.47−8.67 (m, 3H), 7.92 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 191.4, 171.3, 134.7, 134.1, 132.9, 130.9, 129.0, 128.7, 127.8, 66.4, 54.1, 37.6, 28.3; FAB-MS m/z (rel. intensity) 418 (M + H, 1), 364 (1), 362 (3), 200 (2), 198 (4), 156 (12), 154 (45), 119 (8), 105 (17), 77 (10), 57 (100), 55 (26).

Phenacyl *N*-*t*-Boc-glycine: yield 1.482 g (94%) from 1.237 g of acid, white solid; mp 60−62 °C; ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 9H), 4.12 (d, J = 5, 2H), 5.14 (s, 1H), 5.41 (s, 2H), 7.48−7.64 (m, 3H), 7.89 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 191.5, 169.9, 155.6, 134.0, 128.8, 127.7, 79.9, 66.4, 42.2, 28.2; CI-MS m/z (rel. intensity) 294 (M + 1, 3), 238 (19), 194 (16), 118 (18), 105 (100), 93 (13), 77 (15), 58 (62).

Phenacyl *N*-*t*-Boc-Ile-Gly: yield 0.129 g (40%) from 0.136 g of acid, white solid; mp 136 °C dec; ^{1}H NMR ($CDCl_3$) δ 0.90 (m, 6H), 1.13 (m, 3H), 1.41 (s, 9H), 3.95 (m, 1H), 4.12 (dd, J_1 = 4, J_2 = 6, 2H), 5.46 (s, 2H), 7.5−7.7 (m, 3H), 7.98 (d, J = 7, 2H); ^{13}C NMR ($CDCl_3$) δ 173.2, 170.5, 135.0, 130.0, 128.8, 67.8, 41.4, 38.2, 28.6, 25.4, 15.9, 11.8; CI-MS m/z (rel. intensity) 407 (M + 1, 1), 406 (M^+), 333 (22), 308 (18), 228 (35), 215 (37), 186 (100), 105 (20), 86 (34), 77 (12).

Photolysis of Phenacyl Esters. The phenacyl esters (~4 × 10^{-4} mol) were photolyzed for 2 h (16 h in the case of 2-nitrophenylacetate ester) in the presence of a large excess (~2.5 × 10^{-3} mol) of the sensitizer in 150 mL of acetonitrile as the solvent. Corex filter was used in each case (Pyrex filter was used when TMPD was used as the electron donor). The conversion rate was analyzed using HPLC. The products were dissolved in dichloromethane, and the acid was extracted into the aqueous layer with dilute NaOH or $NaHCO_3$ solution. The aqueous layer was then acidified with HCl and the acid extracted with dichloromethane. The organic layer was dried over $MgSO_4$, and the solvent was evaporated to yield the acid which was then weighed and analyzed by ^{1}H NMR and compared to the ^{1}H NMR of the authentic acid. Samples of all the authentic acids were obtained from commercial sources.

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Supporting Information Available: ^{1}H NMR of all the phenacyl esters (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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