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Protecting Group Release Through Photoinduced Electron Transfer: Wavelength Control Through Sensitized Irradiation

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Abstract: Phenacyl esters (benzoylmethyl esters, $PhCOCH_2$–OCOR) release carboxylic acids upon photolysis using photosensitizers that are good one-electron donors in the excited state. Herein it is demonstrated that this procedure can be used to control the wavelength of light required to trigger the release. A variety of sensitizers having different absorption profiles are employed and in each case high isolated yields of carboxylic acids are achieved. It is further demonstrated that this method be extended into the visible (>400 nm) region of the spectrum.

Protecting groups that are photochemically releasable are becoming increasingly important in multi-step syntheses, combinatorial chemistry, time-resolved studies of biochemical processes, and in new photolithographic technology.[1] Most currently popular photoreleasable protecting groups such as phenacyl esters[2] and benzoin derivatives[3] use light in the UV-B region of 300-350 nm. While this is appropriate in certain applications, it would also be desirable to use higher wavelengths of light to carry out these procedures. First, this would avoid problems with competing absorption by the substrates and thus widen the applicability of such technology. Second, high-wavelength light sources are generally more readily available, less expensive, safer to operate, and do not require special glassware. It is a long term goal of ours to develop a suite of photoreleasable protecting groups each responsive to a different wavelength of light.

Elsewhere[4] we have advocated a modular approach to the design of photosensitive protecting groups where the light absorption step is controlled by an antenna unit (or chromophore) that is distinct from the release unit (scissile bond). In this way it is possible to separately optimize the properties of the two components. A specific example of that approach was demonstrated using a phenacyl (benzoylmethyl) ester linkage as the release unit and an electron-donating photosensitizer as the antenna. In that report, we demonstrated that various carboxylic acids could be quantitatively released by this methodology. The carboxylic acids ranged from long chain aliphatic acids to aromatic acids to biologically relevant dipeptides. We also showed the compatibility of this technology with various functional groups. Mechanistic and product studies confirmed that the pathway involved one-electron reduction of the phenacyl group followed by a facile α C–O bond scission of its anion radical which rapidly releases the carboxylate anion (Scheme 1). Tanner et al.[5] showed that the anion radical of the phenacyl ester has a lifetime of about 5 ns and released the carboxylate anion with $k_{rel} = 10^8\ s^{-1}$ as demonstrated using intramolecular competition experiments. The phenacyl radical generated from the fragmentation then abstracts a hydrogen atom to form acetophenone (Scheme 1). On the basis of this electron transfer mechanism it was argued that wavelength control could be achieved through the choice of an appropriate sensitizer. However the practical examples demonstrated in the earlier study were limited to several aniline derivatives with absorption maxima no higher than 335 nm. The present study utilizes a wider variety of photosensitizers and thereby demonstrates that wavelengths approaching the visible can be used in this photorelease strategy. Phenacyl phenylacetate is chosen as the model protected acid that would release phenylacetic acid upon sensitized irradiation.

The protection of the acid was carried out by well descibed procedures.[4] About 0.8 equivalents of

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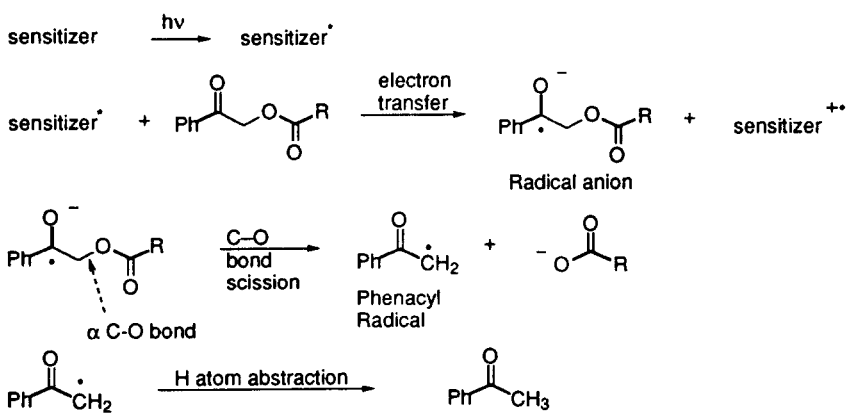
phenacyl bromide was added to a solution of DBU and the acid in benzene. The resulting mixture was stirred for about 2 h at room temperature. The resulting solution was washed with 10 % HCl, and $NaHCO_3$, dried over $MgSO_4$ and the solvent was evaporated to obtain dry solid. The ester was isolated in quantitative yields. It was then recrystallized from diethyl ether and characterized by standard spectroscopic techniques.

The deprotection reactions were carried out on the ester and sensitizer solutions in Pyrex tubes. The anionic sensitizers were generated *in situ*, whereas the neutral sensitizers were obtained from commercial sources. Since isolation of the released functionality is of utmost importance for most of the applications of this technique, phenylacetic acid was isolated and quantified for all the sensitizers. Approximately 20-50 mg each of the sensitizer and ester were dissolved in acetonitrile, purged with argon for about 10 minutes, and photolyzed with an appropriate filter using a xenon-arc lamp for about 2 h. The acid released was isolated using basic extraction,[4] weighed and characterized by spectroscopic techniques.

In order to determine the initial products, the the solutions were examined by ^1H NMR prior to work-up steps in certain cases. In these cases, nearly one equivalent sensitizer was added to a solution of the ester in CD_3CN. The tube was then sealed and purged with argon for about 10 minutes. The concentration of ester was determined by ^1H NMR using an internal standard (hexamethyldisiloxane). The reaction mixture was then photolyzed using a xenon-arc lamp and an appropriate filter for about 2 h. The amount of acid released was determined by ^1H NMR.

Scheme 1.



The mechanism in Scheme 1 predicts that any sensitizer capable of delivering an electron to the phenacyl group will initiate the desired release of the carboxylate anion. The free energy change for this initial electron transfer is given by the difference between the excited state oxidation potential of the sensitizer (E_{ox}^*) and E_{red}, the reduction potential of the phenacyl group (ca. -1.94 V vs. SCE[4]). Maximal rates of electron transfer are usually seen when ΔG_{et} is at least 10 kcal/mol negative.[6] Thus any sensitizer with E_{ox}^* more negative than -2.0 V ought to deliver an electron to the phenacyl substrate. This appears to be the case. All of the sensitizers that were effective have E_{ox}^* values that ranged from -2.24 V to -3.25. Another criterion in choosing the sensitizer is its E_{ox} values. If the E_{ox} value of the sensitizer is sufficiently low so that it can transfer an electron to the ester from its ground states, then the undesirable dark reaction would occur. Thus all the successful

sensitizers had E_{ox} values ranging from 0.20 V to 1.1 V.

One important criteria for choosing the sensitizer was that it absorbs in or near the visible wavelengths. Figure 1 shows the absorption spectra of some of the sensitizers and the phenacyl ester. The phenacyl ester has a weak absorption band above 300 nm corresponding to n-π^* transition (ε_0^{320} = 60 M^{-1} cm^{-1}), whereas the sensitizers (except 9-methylcarbazole) absorb near 400 nm. High wavelength cutoff filters (390 nm or 400 nm) were used in this study to ensure that the radiation was absorbed only by the sensitizers and not by the ester.

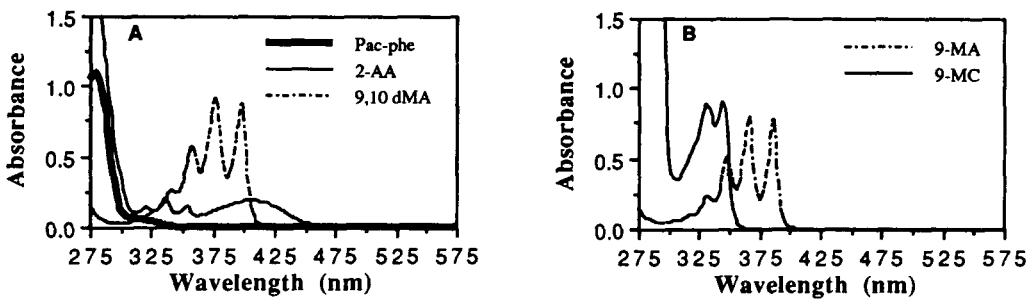


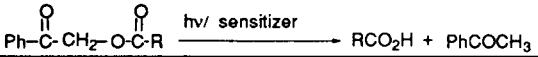
Figure 1. UV absorption of phenacyl phenylacetate (*Pac-phe*) and few of the sensitizers used in the study. The phenacyl ester has a weak absorption tail above 300 nm. 9-methylcarbazole (*9-MC*) has an absorption peak at 348 nm, whereas the anthracene derivatives have λ_{max} close to 400 nm. 2-aminoanthracene (*2-AA*) is the only sensitizer that absorbs above 400 nm. Therefore 2-aminoanthracene was used as the sensitizer for deprotection with visible light.(*9, 10 dMA* = 9, 10-dimethylanthracene; *9-MA* = 9-methylanthracene).

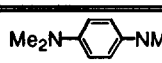
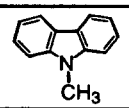
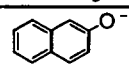
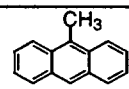
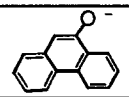
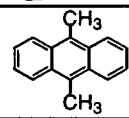
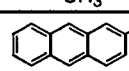
As seen in Table 1, sensitizers with absorption maxima spanning from 332 nm to 407 nm are effective at promoting photorelease. Of the sensitizers examined in this study, 9,10-dimethylanthracence (No. 6) provided the highest yields and the shortest irradiation times while at the same time being excitable with high wavelength light. The monomethyl derivative, 9-methylanthracene (no. 4), is also an effective sensitizer. However its lower wavelength absorption band and its propensity for photodimerization render it somewhat less desirable than the dimethyl derivative. The highest wavelength sensitizer, 2-aminoanthracene (No. 7), allows for photolysis in the low wavelength visible region of the spectrum. However the required irradiation times are longer and the isolated yield is somewhat lower. Also examined were two anionic photosensitizers, 2-naphtholate and 2-phenanthrolate (No. 3 and 5).[7] These are compatible with aqueous media (provided it is kept sufficiently basic). However in the absence of a sacrificial reductant (e.g. ascorbate), very low yields of product were obtained. Apparently the aryloxy radical formed in the initial electron transfer are unstable and consume the substrate and/or products through some uncharacterized side reactions. The conditions reported here use ascorbic acid. The latter regenerates the sensitizer by donating a H atom (or electron) to the aryloxy radical. *N*-Methylcarbazole (No. 2) also sensitizes release, although it absorbs at wavelengths only slightly higher than the original arylamines. Data from *N,N,N,N*-tetramethylphenylene diamine[4] (No. 1) are included for comparison purposes.

The experiments here demonstrate that through the choice of an appropriate sensitizer, photolytic release of carboxylates can be achieved using light of wavelengths as high as 400 nm. In addition to the practical benefits of being able to control photolysis wavelengths, this also provides further confirmation of the proposed

electron transfer mechanism.[4] Future work will be directed at (1) designing visible light sensitizers with improved electron transfer efficiencies and photostabilities; and (2) preparing covalently linked sensitizer-phenacyl systems.

Table 1. Photosensitized Release of Phenylacetic acid from Phenacyl Phenylacetate.



No.	Sensitizer	λ_{max} (nm)	E_{ox} (V vs. SCE)	E_{ox}^* (V vs. SCE)	Cond[a].	%Yield (conv)
1		332	0.20	-3.25	>320 nm, 2 h	76 (100)[c]
2		345	1.10	-2.46	>320 nm, 3 h	88 (100)[c]
3		349	0.54	-2.70	350 nm, 3 h[b]	70 (100)[c]
4		387	0.96	-2.46	>390 nm, 2 h >320 nm, 2.5 h	83 (29)[d] 78 (100)[c]
5		382	0.34	-2.57	350 nm, 3.5 h[b]	86 (100)[c]
6		398	0.87	-2.23	>390 nm, 2.0 h. >390 nm, 2.0 h	90 (100)[c] 96 (100)[d]
7		407	0.44	-2.25	>400 nm,15 h >390 nm, 5 h	97 (74)[d] 70 (90)[c]

[a] Unless otherwise noted the irradiation were carried out on samples containing 20-50 mg each of the ester and sensitizer dissolved in 50 mL CH_3CN. Samples were purged with N_2 and then irradiated with a 350 W Xe lamp using high-pass glass filters.

[b] Irradiation carried out on solutions in Pyrex vessels using a Rayonette photoreactor with broad-band fluorescent lamps having emission maxima at 350 nm. The solutions consisted of 110 mg of ester, 130-180 mg sensitizer, 780-900 mg of ascorbic acid, and 1.1 g KOH, in 80% aqueous CH_3OH.

[c] Yields were determined gravimetrically following isolation of phenylacetic acid.

[d] Yields determined by ^1H NMR integration of the phenylacetic acid peak relative to an internal standard. In these cases samples contained 10-20 mg each of ester and sensitizer, and 1-2 mL of CD_3CN.

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References

1. (a) Willner, I.; Willner, B. In *Biological Applications of Photochemical Switches*; H. Morrison, Ed.; Wiley: New York, 1993; pp. 1-110. (b) Corrie, J. E. T.; Trentham, D. R. In *Biological Applications of Photochemical Switches*; H. Morrison, Ed.; Wiley: New York, 1993; pp. 243-304. (c) Pillai, V. N. R. In *Organic Photochemistry*; A. Padwa, Ed.; Marcel Dekker: New York, 1987; Vol. 9; pp. 225-323.
2. Givens, R. S.; Jung, A.; Park, C.-H.; Weber, J.; Bartlett, W. *J. Am. Chem. Soc.* **1997**, *119*, 2453-2463.
3. Pirrung, M. C.; Bradley, J.-C. *J. Org. Chem.* **1995**, *60*, 1116-1117.
4. Banerjee, A.; Falvey, D. E. *J. Org. Chem.* **1997**, *62*, 6245-6251.
5. Tanner, D. D.; Chen, J. J.; Chen, L.; Leulo, C. *J. Am. Chem. Soc.* **1991**, *113*, 8074-8081.
6. Scannell, M. P.; Fenick, D. J.; Yeh, S.-R.; Falvey, D. E. *J. Am. Chem. Soc.* **1996**, *119*, 1971-1975.
7. Legros, B., Vandereecken, P.; Soumillion, J. P. *J. Phys. Chem.* **1991**, *95*, 4752-4761.