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C−O Bond Fragmentation of 4-Picolyl- and *N*-Methyl-4-picolinium Esters Triggered by Photochemical Electron Transfer

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Photochemical reduction of several 4-picolyl- and *N*-methyl-4-picolinium esters was examined using product analysis, laser flash photolysis, and fluorescence quenching. It is demonstrated that the radical (anions) formed in these reactions readily fragment to yield a carboxylic acid and a 4-pyridylmethyl radical intermediate. The high chemical and quantum yields observed for these photoreactions suggests that these esters can be used as photolabile protecting groups.

Introduction

Photoinduced electron transfer (PET) processes have attracted the interest of a generation of chemists. Previous work has elucidated many of the factors that control the rates of these reactions.[1,2] Therefore, many current efforts are aimed at identifying and demonstrating useful applications of these processes. Applications include solar energy conversion,[3−5] photolithography,[6] molecular electronics,[7,8] and the design of novel synthetic transformations. With regard to the latter, it has long been recognized that PET is capable of generating high-energy radical and radical ion pairs. Such radical pairs are interesting because they are often capable of undergoing bond-forming or bond-fragmentation reactions that are difficult to carry out using conventional techniques. For example, Mariano and others have explored PET triggered C−Si fragmentations.[9,10] These reactions form nucleophilic α-amino radicals, which were demonstrated to be useful in the formation of new carbon−carbon bonds. Other examples include the reactions of phthalimide derivatives triggered by PET from an alkyl-tethered donor group to the phthalimide chromophore.[11]

We have had a longstanding interest in applying photoinduced electron-transfer reactions to the controlled photorelease of functional molecules. Photoreleasable protecting groups are important in applications such as photolithographic fabrication of DNA chips,[12−14] photoregulation of proteins and cellular signaling pathways,[15−17] time-resolved X-ray crystallography,[18] and solid-phase peptide and nucleotide synthesis.[14,19] Photolabile groups are also being used in multistep organic syntheses[20,21] and in biological systems.[22,23]

A specific interest in photoremovable protecting groups (PRPGs) has lead us to explore PET-triggered C−O bond scission in phenacyl esters (**1,** Scheme 1**)**. It was demonstrated that the phenacyl group could be released with high efficiencies and with excellent chemical yields of the released substrate.[24,25] A particularly attractive feature of this PET-based PRPG system is that the light absorption step is decoupled from the bond-breaking step. Through choice of an appropriate PET sensitizer, it is, in principle, possible to make the system responsive to any desired photolysis wavelength. Because the same protecting group anion is generated with each sensitizer, the kinetics and mechanism of the release step remain constant. This contrasts with more conventional PRPG systems, such as those based on nitrobenzyl, or benzoin

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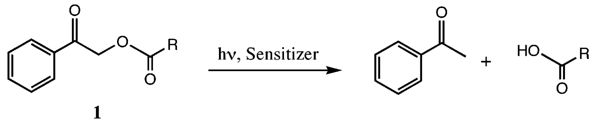
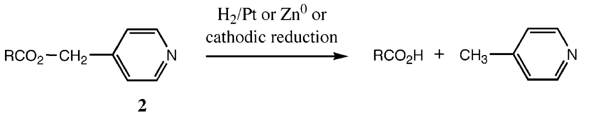
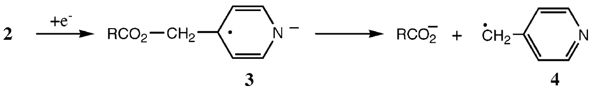
SCHEME 1



SCHEME 2



SCHEME 3



chromophores, which have the light absorption and bond-breaking steps occurring at the chromophore. In these cases, attempts to tune the light absorption properties of the protecting group often adversely affect the rate of bond scission. However, one significant limitation of the phenacyl-based protecting groups is the fact that they are reduced only at very negative potentials (−2.2 V vs SCE). This led us to investigate alternative radical ion bond scission reactions.

The 4-picolyl group (i.e., 4-pyridylmethyl) has been used as a carboxyl protecting group in peptide synthesis.[26,27] Previous reports indicate that they can be released using cold alkali, catalytic hydrogenation, reducing metals, or electrolytic reduction[28] (Scheme 2). The latter two reactions were of specific interest to us. Although the mechanisms had not been examined in detail, we hypothesized that these bond cleavages might occur via the anion radical of the ester (Scheme 3). Some related radical heterolytic cleavage reactions have been characterized for β-(phosphatoxy)alkyl and β-(acyloxy)alkyl radicals. However, simple examples of the latter also undergo a 1,2-shift.[29−31]

If the mechanism in Scheme 3 is correct, then it should be possible to effect a similar reaction via photochemical reduction. Such a reaction would be interesting not only from a mechanistic point of view, but it might lead to the development of improved PRPGs. What follows describes experiments on the PET reduction of picolyl and *N*-methylpicolinium esters. Through photoproduct analysis, fluorescence quenching, laser flash photolysis, and related experiments it is demonstrated that these esters do in fact suffer a C−O fragmentation following one-electron reduction.

Results and Discussion

Various 4-picolyl esters (**2**) can be readily prepared by the reaction of 4-pyridylcarbinol with acid chlorides and triethylamine in benzene[32] or alternately by combining the corresponding carboxylic acids with 4-pyridylcarbinol and dicyclohexylcarbodiimide (DCC) in methylene chloride. [28] The photosensitizers employed in this study are listed in Table 1, along with some relevant photophysical parameters including their excited-state oxidation potentials (E_{ox}* in V). The latter are derived from published values for the singlet-state energies (E_{oo} in kcal/mol) and their (ground-state) oxidation potentials (E_{ox} in V vs SCE) using eq 1.[33]

$$E_{ox}^* = E_{ox} - E_{oo}/23.06 \tag{1}$$

As shown in Table 1, TMB is the strongest excited-state reductant, having an $E_{ox}^* = -3.17$ V (vs SCE). The least powerful excited-state reductant is triphenylamine (TPA), which has an E_{ox}* value of −2.06 V. Pyrene and 9-methylcarbazole have intermediate values of −2.17 and −2.46 V, respectively.

Preparative photolyses of the 4-picolyl esters in the presence of various electron-donating sensitizers were carried out to determine if C−O bond scission would occur, releasing the corresponding carboxylic acids. The 4-picolyl esters listed in Table 2 were subjected to filtered (>320 nm) irradiation with several photosensitizers, using a 200 W Hg lamp. At these wavelengths the sensitizers, but not the esters, absorb the light. The photolysis solution consisted of 4.0 mM of ester and 4.0−4.5 mM of sensitizer. In each case, an identical solution was held in the dark as a control sample. The photolysis and dark control solutions were then analyzed by ^{1}H NMR and the yields of the carboxylic acids, as well as the amount of ester consumed, were determined by integration of the acid peaks relative to an internal standard.

The 4-picolyl esters release carboxylic acids only when TMB is used as the sensitizer. When other sensitizers such as 9-MC and pyrene were employed, no detectable conversion of the ester was observed, even upon longer exposure times (upto 8 h). We attribute this to the fact that the picolyl group is difficult to reduce. It has been reported that pyridine has E_{red} of −2.62 V vs SCE.[33] The 4-picolyl esters are likely to have a similar potential. Thus, TMB is able to reduce these esters with an exergonic PET step, whereas PET is predicted to be endergonic for pyrene and 9-MC.

The 4-picolyl esters **2** were converted to *N*-methylpicolinium esters in an attempt to increase the reduction potential of the group, thereby allowing for PET with a wider array of sensitizers. The reduction potentials of *N*-alkylpyridinium salts are reported to be about −1.7 V,[33] suggesting that the *N*-alkylated derivatives would be better electron acceptors. Picolyl esters **2** were *N*-methylated with methyl iodide to give the corresponding iodide salts **5**. These iodide salts display a charge-transfer band around 350−400 nm, depending on the solvent (see below). To avoid any ambiguities resulting from competing absorption by the sensitizers and the charge-transfer band the iodide counterion was exchanged for perchlorate, yielding **6** as illustrated in Scheme 4. These perchlo-

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TABLE 1. Properties of Photosensitizers Used in Photocleavage Experiments[33]

sensitizer	E_{ox}^*(V vs SCE)	E_{oo}(kcal/mol)	τ[33] (ns)	λ_{max} (nm)
N,*N*,*N′*,*N′*-tetramethylbenzidine (TMB)	−3.17	83.0	9.4	350
9-methylcarbazole (9-MC)	−2.46	82.1	16.0	345
pyrene	−2.17	76.8	190.0	370
triphenylamine (TPA)	−2.06	70.1	17.0	305

TABLE 2. Sensitized Photofragmentation of 4-Picolyl Esters 2

compd	R	sensitizer	conditions	% acid formed[a,b]	% ester consumed[a,b]
2d	$C(CH_3)_3$	TMB	3 h, rt, MeOH	14	31
2e	$CH(C_6H_5)_2$	TMB	3 h, rt, MeOH	43	53
2f	$CH_2C_6H_4CH_3$	TMB	3 h, rt, MeOH	29	30

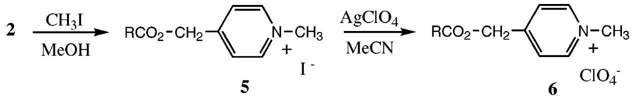
[a] Photolysis solution was 2.5−3.0 mL of a 4 mM solution of ester and 4.0−4.5 mM sensitizer. [b] Yields were determined by ^{1}H NMR integration of the carboxylic acid peak relative to an internal standard. [c] Estimated error ± 5%.

TABLE 3. Sensitized Photofragmentation of *N*-Methyl-4-picolinium Esters 6

compd	R	sensitizer	conditions[a]	% acid formed[b,c]	% ester consumed[b,c]
6a	CH_3	9-MC	3 h, rt, MeOH	62	65
6b	C_6H_5	TMB	3 h, rt, MeOH	30	26
6c	$CH_2C_6H_5$	9-MC	3 h, rt, MeOH	45	41
6c	$CH_2C_6H_5$	TMB	3 h, rt, MeOH	92	87
6c	$CH_2C_6H_5$	Pyrene	3 h, rt, MeOH	84	92
6c	$CH_2C_6H_5$	TPA	3 h, rt, MeOH	77	79
6d	$C(CH_3)_3$	9-MC	3 h, rt, MeOH	43	43
6e	$CH(C_6H_5)_2$	9-MC	3 h, rt, MeOH	74	78
6f	$CH_2C_6H_4CH_3$	9-MC	3 h, rt, MeOH	21	25
6g	$CH_2C_6H_4Br$	9-MC	3 h, rt, MeOH	49	58
6h	$CH{=}CHC_6H_5$	9-MC	3 h, rt, MeOH	22	64

[a] Photolysis solution was 2.5−3.0 mL of a 4 mM solution of ester and 4.0−4.5 mM sensitizer. [b] Yields were determined by ^{1}H NMR integration of the carboxylic acid peak relative to an internal standard. [c] Estimated error ± 5%.

SCHEME 4



rate salts absorb below 320 nm, with some esters displaying a weak absorption tail above 320 nm.

Eight examples of **6**, listed in Table 3, were prepared. Sensitized photolyses of these salts were carried out using a 200 W Hg lamp, with a 320 nm cutoff filter and 9-MC as the sensitizer. Control experiments were also carried out on several esters without the sensitizers, under identical photolysis conditions. Analysis of the photoproducts was carried out in the same manner as described for **2**. The carboxylic acids were chosen with a view to demonstrate photorelease in various aliphatic as well as aromatic esters. Also, as the photoproduct analysis was carried out by ^{1}H NMR peak integration, it was desirable to use carboxylic acids with peaks distinct from those of the sensitizers.

In the absence of the sensitizer, irradiation of the picolinium salts afforded no photoproducts. Under sensitized irradiation, the esters released the free carboxylic acids efficiently. For the simple aryl and alkyl esters **6a**−**f** the conversions were clean and the amount of carboxylic acid formed was, within experimental error, the same as the amount of ester consumed. It was observed that the amount of ester consumed was not the same for the different esters, although the chemical yields of the carboxylic acids were consistently quantitative.

An interesting case was *N*-methylpicolinium 4-bromophenylacetate **6g**. Previous PET studies with the corresponding phenacyl esters demonstrated the difficulties of reducing the protecting group preferentially over the aryl bromide part of the ester (aryl bromides readily expel the halide ion following one-electron reduction).[20] Phenacyl 4-bromophenylacetate yields a mixture of products upon sensitized photolysis. The latter results from competing electron transfer to the aryl bromide. Along with 4-bromophenylacetic acid, the debrominated phenacyl phenylacetate and phenylacetic acid were also obtained. In contrast, sensitized photolysis of the corresponding picolinium ester **6g** gives only the desired product, 4-bromophenylacetic acid, in good yields. This indicates that the picolinium group is far easier to reduce and can be used for protection of reductively labile carboxylic acids.

The cinnamate ester **6h** was studied to observe the effect of the alkene functionality on efficiency of photorelease. Alkenes, especially highly conjugated ones such as the cinnamate ester, are known to undergo several photochemical reactions and are difficult to photodeprotect. Upon photolysis, we observed release of cinnamic acid, although in low yields and with several byproducts. At higher conversions of the ester, the yields of the free acids were found to diminish. This may be due to the photoreactivity of the cinnamate ester or due to photoreactions of the product cinnamic acid itself, which could be undergoing secondary photochemical processes.

It is possible to initiate the fragmentation of these esters using a variety of sensitizers. As shown in Table 3, four different sensitizers, *N*,*N*,*N′*,*N′*-tetramethylbenzidine (TMB), 9-methylcarbazole (9-MC), pyrene, and triphenylamine (TPA), were employed with ester **6c** and

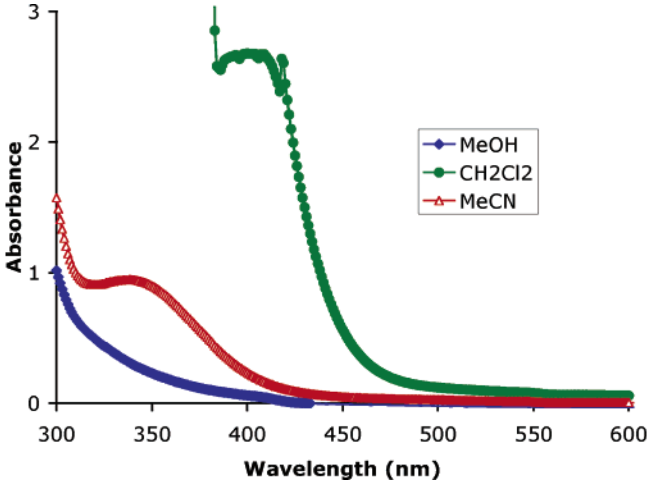


FIGURE 1. Steady-state UV−vis absorption spectrum of ester **5c** in methanol (A), dichloromethane (B), and acetonitrile (C).

SCHEME 5

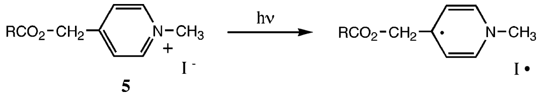


TABLE 4. Photolysis of the Picolinium Iodides 5

compd	R	conditions[a]	% acid formed[b,c]	% ester consumed[b,c]
5a	CH_3	3 h, MeOH[d]	67	74
5b	C_6H_5	3 h, MeOH[d]	32	48
5c	$CH_2C_6H_5$	3 h, MeOH[d]	64	92
5c	$CH_2C_6H_5$	3 h, $MeCl_2$[e]	30	45
5f	$CH_2C_6H_4CH_3$	3 h, MeOH[d]	73	90
5h	$CH{=}CHC_6H_5$	3 h, MeOH[d]	63	71

[a] Photolysis solution was 2.5−3.0 mL of a 4 mM solution of ester. [b] Yields were determined by ^1H NMR integration of the carboxylic acid peak relative to an internal standard. [c] Estimated error ± 5%. [d] Irradiation by Hg lamp, >320 nm cutoff filter. [e] Irradiation by Xe lamp, >390 nm cutoff filter.

in each case efficient release of the free acid was observed upon photolysis.

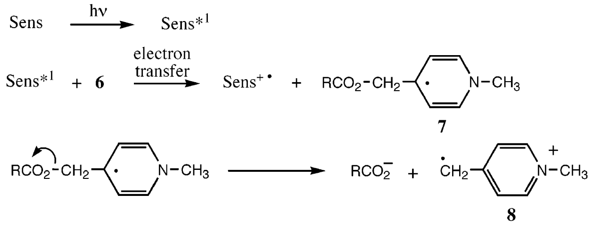
The successful bond cleavage with electron-donating sensitizers led us to explore bond cleavage through direct photolysis. Although the perchlorate salts absorb only at low wavelengths (<320 nm), it was found that the iodide salts absorb between 350 and 450 nm (Figure 1). This is attributed to a charge-transfer absorption of the picolinium/iodide ion pair. Irradiation of such charge-transfer bands creates a species that is a caged radical pair consisting of radical **7** and iodine atom (Scheme 5). Therefore, it was anticipated that photolysis of these salts would also lead to fragmentation of the C−O bond.

Photolysis of the *N*-methyl-4-picolinium iodides in methanol (>320 nm, 200 W Hg lamp) releases the free carboxylic acids in good yields (Table 4). Using the less polar solvents, acetonitrile (MeCN) or dichloromethane ($MeCl_2$) allows for irradiation at higher wavelengths. Entry 4 in Table 4 was obtained by irradiation of ester **5c** in $MeCl_2$ above 390 nm using a Xe lamp. However, in practice, the photolyses proceed more cleanly with MeOH as the solvent. We attribute this to the ability of MeOH to scavenge the radical intermediates resulting from the initial C−O bond scission.

TABLE 5. Quantum Yields for Sensitized Photolysis of 6

compd	R	sensitizer	solvent	quantum yield (%)
6c	$CH_2C_6H_5$	9-MC	MeOH	0.23
6c	$CH_2C_6H_5$	9-MC	MeCN	0.14
6c	$CH_2C_6H_5$	TMB	MeCN	0.05

SCHEME 6. Proposed Mechanism for the Photofragmentation Reaction



To compare the relative efficiencies of sensitized irradiation and direct irradiation of the iodide salts, several quantum yields were determined. First, the quantum yield for the sensitized photorelease was determined for *N*-methylpicolinium phenylacetate. (**6c**). A solution of the ester and an equal amount of sensitizer was irradiated by a xenon lamp for different periods of time, and the rate of disappearance of the ester was determined by ^1H NMR. The quantum yields were found to be around 0.14 for the photorelease process (Table 5). The quantum yield for photorelease from the picolinium iodide salts was found using *N*-methylpicolinium benzoate to be 0.15 in methanol, comparable to the better quantum yields obtained in the sensitized photolysis.

Having established that picolinium esters release the free acids upon irradiation, we now turned our attention to the mechanistic pathway of this photofragmentation reaction. Scheme 6 describes the anticipated reaction mechanism. Upon irradiation, the photosensitizer molecule (Sens) absorbs light preferentially over the substrate and is promoted to its excited singlet state ($Sens^{*1}$). The latter transfers an electron to the picolinium ester. The pyridyl radical **7** subsequently releases the carboxylate anion, along with a pyridylmethyl radical fragment **8**.

As a rule, PET reactions compete with rapid photophysical deactivation of the sensitizer excited state. As a consequence such reactions are expected to proceed efficiently only when the initial electron-transfer step is exergonic. Values for ΔG_{ET} can be estimated for the mechanism in Scheme 6, using the reduction potential of the *N*-methylpicolinium group (E_{red}) and the excited-state oxidation potential of the sensitizers (E_{ox}*). The latter are given in Table 1. In polar solvents, such as MeCN and MeOH, eq 2 provides a reasonable estimate for ΔG_{ET}.

$$\Delta G_{ET} = 23.06(E_{ox}{*} - E_{red}) + 0.06\ \text{eV} \qquad (2)$$

Reduction potentials, E_{red}, of the various *N*-methylpicolinium esters were determined by cyclic voltammetry (CV) experiments. In each case, an irreversible reduction wave is observed with E_{red} between −1050 and −1200 mV (Table 6). The E_{red} values were determined at a scan rate 100 mV/s.

TABLE 6. Reduction Potentials for *N*-Methyl-4-picolinium Esters

compd	R	E_{red}[a] (V) vs SCE
6a	CH_3	−1.09
6b	C_6H_5	−1.01
6c	$CH_2C_6H_5$	−1.08
6d	$C(CH_3)_3$	−1.11
6e	$CH(C_6H_5)_2$	−1.17
6f	$CH_2C_6H_4CH_3$	−1.15
6g	$CH_2C_6H_4Br$	−1.09
6h	$CH{=}CHC_6H_5$	−1.05

[a] Potential at half peak current, obtained from a irreversible wave at a scan rate of 100 mV/sec.

Thus, for the sensitizers employed in this study, ΔG_{ET} is predicted to range between −22.1 kcal/mol (in the case of Ph_3N) and −47.7 kcal/mol (in the case of TMB), using −1.1 V as the E_{red} for esters **6**. Although the reorganization energies (λ) have not been characterized for these particular donor−acceptor pairs, these driving forces are sufficiently large that one would expect diffusion-limited k_{ET} values, given typical values of λ. Thus, we conclude that the thermodynamics of this system are consistent with the mechanism in Scheme 6.

The possibility of ground-state complexation between picolinium salts **6** and the sensitizers led us to examine the UV−vis spectra of mixtures of the perchlorate salts and sensitizers. The UV spectra of the sensitizers were found to be unchanged upon addition of increasing amounts of esters **6**. No charge-transfer bands were observed, and the UV spectra of sensitizers showed little change with addition of esters up to 20 mM (1−2 mM solutions of sensitizer in 3.5 mL methanol were used).

Fluorescence quenching experiments also support the proposed mechanism. Scheme 6 implies that electron transfer occurs from the singlet-excited state of the sensitizer to the picolinium ester. If this occurs, then the fluorescence of the sensitizer should be quenched upon addition of the picolinium substrate. To test this, the fluorescence of the sensitizers was measured with addition of increasing concentrations of picolinium esters **6** and was observed to diminish as a function of the ester concentration. The rate constants for fluorescence quenching were found using a Stern−Volmer analysis and published lifetimes of the sensitizers,[33] to be at or near the diffusion limit (~1.9×10^{10} in MeCN). The rate constant for fluorescence quenching of 9-MC by ester **6e** is 2.4×10^{10} M^{-1} s^{-1}. This result indicates that the sensitizers rapidly react with the esters upon photolysis. The Stern−Volmer plots in a few cases show small deviations from linearity. This observation, along with the higher than expected rate constants for quenching, could indicate some contribution from precomplexation of the sensitizer with the esters, although we could not detect such complexes by UV−vis absorption.

The unalkylated esters **2** likewise quench the fluorescence of the most reactive donor, TMB ($k_q = 1.6 \times 10^{10}$ M^{-1} s^{-1}). The less reactive sensitizer 9-MC is also quenched, but far less efficiently ($k_q = 8.6 \times 10^5$ M^{-1} s^{-1}). The least reactive sensitizers, pyrene and Ph_3N, show no fluorescence quenching when **2** is added. This observation is consistent with our observation of no photofragmentation using the latter sensitizers.

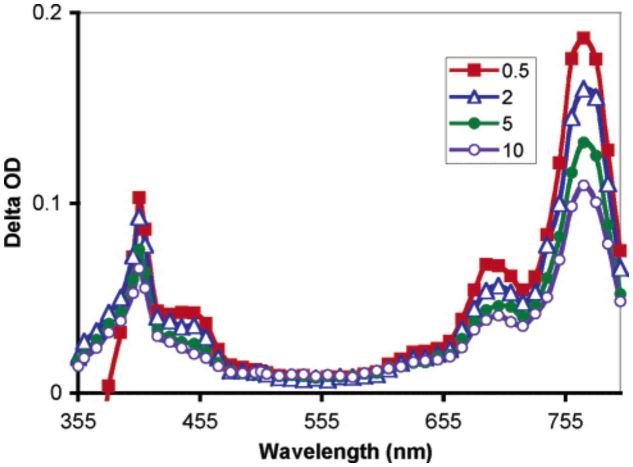


FIGURE 2. Transient absorption spectra from pulsed laser photolysis (355 nm, 50−100 mJ, 6 ns) of 9-MC with *N*-methylpicolinium diphenylacetate perchlorate **6e** in N_2-purged CH_3CN. Times are in microseconds after the laser pulse.

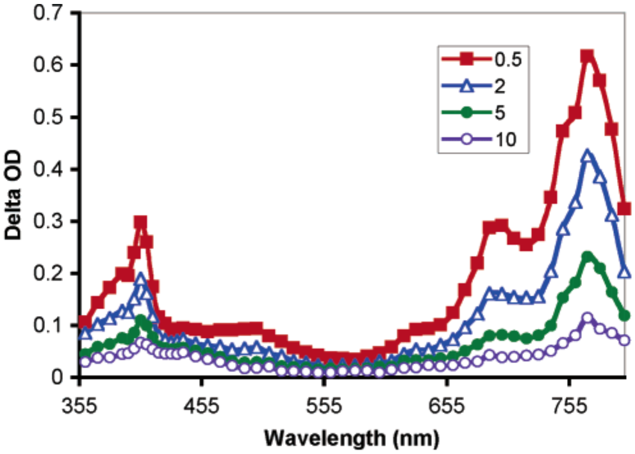


FIGURE 3. Transient absorption spectra from pulsed laser photolysis (355 nm, 50−100 mJ, 6 ns) of 9-MC with **9** in N_2-purged CH_3CN. Times are given in microseconds after the laser pulse.

Laser flash photolysis (LFP) experiments provide further support for the proposed mechanism. Transient UV−vis spectra were obtained following pulsed laser photolysis (355 nm, 50−100 mJ/pulse, 4−8 ns) of MeCN solution containing both the sensitizer (9-MC) and the picolinium ester **6e**. These spectra show strong absorption bands at 410, 690, and 770 nm (Figure 2). The latter two peaks correspond to previously characterized absorptions for the 9-MC cation radicals.[34] The peak at 410 nm is assigned to the reduced *N*-methylpicolinium ion, radical **7**. The other esters (**6a**−**h**) were examined using the same LFP experiment and essentially identical spectra are observed.

The assignment of the 410 nm peak is supported by similar laser flash photolysis experiments carried out on *N*-methylpicolinium perchlorate **9** (Figure 3). This latter ion is expected to be reduced by excited-state sensitizers, forming a radical similar to **7**. As expected, **9** efficiently quenched the fluorescence of 9-MC, with a rate constant of 2.4×10^{10} M^{-1} s^{-1}. However, preparative photolyses carried out with *N*-methyl picolinium perchlorate **9** and

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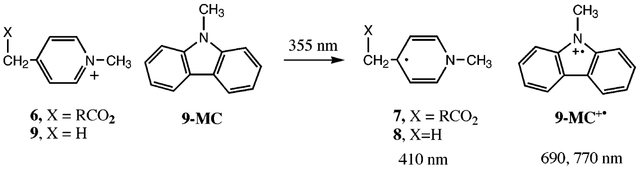
(34) Shida, T. *Electronic Absorption Spectra of Radical Ions*; Elsevier: Amsterdam, 1988.

TABLE 7. Yields of Acids and *N*-Methylpicolinium Ion in the Presence of CHD

compd	R	sensitizer	conditions[a]	% acid formed[b,c]	% ester consumed[b,c]	% *N*-methylpicolinium ion formed[b,c]
6c	$CH_2C_6H_5$	9-M.C	2 h, MeOH	37	40	
6c	$CH_2C_6H_5$	9-M.C	2 h, MeOH, CHD	86	94	76
6c	$CH_2C_6H_5$	9-M.C	2 h, MeCN	26	28	
6c	$CH_2C_6H_5$	9-M.C	2 h, MeCN, CHD	47	46	43
6f	$CH_2C_6H_4CH_3$	9-M.C	2 h, MeOH	17	22	
6f	$CH_2C_6H_4CH_3$	9-M.C	2 h, MeOH, CHD	44	49	38
6h	$CH{=}CHC_6H_5$	9-M.C	2 h, MeOH	26	38	
6h	$CH{=}CHC_6H_5$	9-M.C	2 h, MeOH, CHD	42	57	43
6c	$CH_2C_6H_5$	pyrene	2 h, MeOH	52	51	
6c	$CH_2C_6H_5$	pyrene	2 h, MeOH, CHD	94	99	80

[a] Photolysis solution was 2.5−3.0 mL of a 4 mM solution of ester and 4.0−4.5 mM sensitizer and 20% CHD. [b] Yields were determined by ^1H NMR integration of the carboxylic acid peak relative to an internal standard. [c] Estimated error ± 5%.

SCHEME 7. PET from Sensitizer to Picolinium Moiety



9-MC showed that there is an insignificant change in the solution composition over several hours of photolysis. Thus, we conclude that **9** undergoes reversible electron transfer from the sensitizer to form the *N*-methyl-4-picolyl radical **8** (Scheme 7). The transient absorption spectra obtained by LFP on **9** with 9-MC as sensitizer show the 9-MC cation radical peaks at 690 and 770 nm and a peak at 410 nm as with the esters **6**. Absorption maxima of similar radicals in the literature also support this assignment.[35]

LFP experiments were carried out on esters **6** using the other sensitizers, TMB, pyrene, and TPA as well. In all cases, the observed transient signals agree with the known spectra for the cation radicals of the sensitizers.[34] With 9-MC, pyrene, and TPA, we were able to detect the expected 410 nm peak for the reduced ester. In the case of TMB, the strong absorbance of the TMB cation radical at 470 nm obscures the expected 410 nm peak for the reduced ester.

The unalkylated esters **2** were also examined using LFP. However, we were limited to using TMB as the sensitizer since the other three sensitizers are unable to reduce the ester. No transient peak corresponding to anion radical **3** could be detected. The anion radical of pyridine is known to have a weak absorption around 330 nm,[34] and if radical **3** has a similar absorption, then under our LFP conditions we would be unable to observe it.

The formation of the carboxylic acids in the sensitized photolysis experiments leaves little doubt that the predicted C−O bond scission reaction occurs following PET. However, we were unable to detect the *N*-methyl-4-picolinium methyl radical **8**. To our knowledge, the absorption spectrum of this radical is unknown. Attempts to independently generate and detect radical **8** through LFP (266 nm, 5−15 mJ, 4−6 ns) experiments on *N*-methyl-4-chloropicolinium perchlorate were unsuccessful. The benzyl radical ($PhCH_2^•$) is known to absorb near 320 nm.[36] Thus, it is possible that radical **8** absorbs in a similar region and its signal is obscured by absorptions of the sensitizer and/or the *N*-methyl-4-picolinium group.

SCHEME 8. Trapping of 4-*N*-Methyl-4-picolinium Methyl Radical 8 by CHD

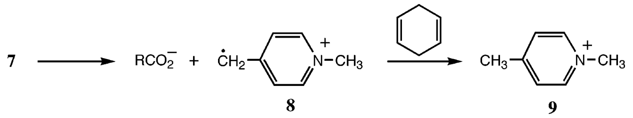


TABLE 8. Quantum Yields with and without CHD

compd	ester	sensitizer	conditions	quantum yield (%)
6c	$CH_2C_6H_5$	9-MC	MeOH	0.23
6c	$CH_2C_6H_5$	9-MC	MeOH, CHD	0.39
6c	$CH_2C_6H_5$	9-MC	MeOH/H_2O, CHD	0.36

To verify the formation of **8**, we carried out trapping experiments using 1,4-cyclohexadiene (CHD). This latter additive is a good H atom donor, having a C−H bond dissociation energy of 76.0 kcal/mol.[37] Thus, it was anticipated that CHD would efficiently trap radical **8** as the *N*-methylpicolinium ion **9** (Scheme 8). This proved to be the case. As shown in Table 7, good yields of the radical product **9** are observed when CHD is included in the photolysis solutions. In the absence of CHD, **9** was not detected in the ^1H NMR of the photolysis solutions. The fate of radical fragment **8** under these conditions is not known with certainty. The absence of a single significant byproduct suggests that this radical decays through a variety of pathways.

Another interesting effect of CHD is the apparent increase in the efficiencies of the sensitized photolysis reported in Table 7. Under comparable, although not rigorously identical, photolysis conditions, a ca. 2-fold increase in the absolute yield of carboxylic acid is observed when CHD is included. This is accompanied by a corresponding increase in the amount of ester that is converted. In the case of ester derivative **6c** this effect was verified by more accurate quantum yield measurements. As shown in Table 8, the quantum yield for ester conversion increases from 0.23 in the absence of CHD to 0.39 when the trap is added.

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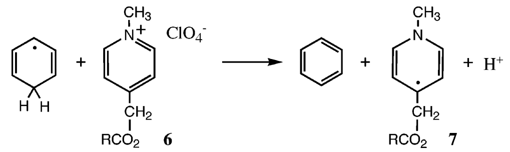
(35) Hermolin, J.; Levin, M.; Kosower, E. M. *J. Am. Chem. Soc.* **1981**, *103*, 4808−4813.

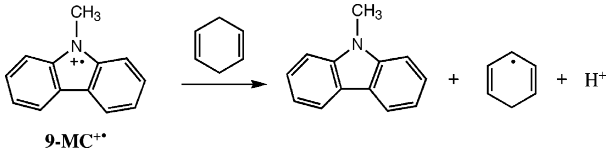
(36) Turro, N. J.; Chow, M.-F.; Chung, C.-J.; Tanimoto, Y.; Weed, G. C. *J. Am. Chem. Soc.* **1981**, *103*, 4574−4576.

(37) Luo, Y.-R. *Handbook of Bond Dissociation Energies in Organic Compounds*; CRC Press: Boca Raton, 2003.

SCHEME 9. Secondary Reduction by CHD Radical



SCHEME 10. Quenching of 9-MC Cation Radical by CHD



One explanation for this is a secondary, nonphotochemical reduction step carried out by the 1, 4-cyclohexadienyl radical byproduct of the H atom transfer reaction. It is possible that this radical reduces an unreacted *N*-methylpicolinium ester **6,** creating the same intermediate radical **7** generated in the PET step (Scheme 9).

The presence of CHD has another interesting effect. The sensitizer (9-MC) cation radical is quenched by this trap (Scheme 10). Repeating this experiment with varying concentrations of CHD and observing the pseudo-first-order decay of the 9-MC cation radical provides a rate constant of 5×10^5 M^{-1} s^{-1} for this process. Although this process has not been studied in detail, it likely involves H atom transfer to carbazole, followed by deprotonation of the highly acidic carbazole conjugate acid. Such a quenching process would prevent 9-MC cation radicals from engaging in back electron transfer with **7**. This suppression of back electron transfer would also increase the quantum yield for the PET process. The relative contribution of this effect and the CHD radical pathway shown in Scheme 9 has yet to be determined.

Conclusions

The experiments described herein demonstrate that the 4-picolyl- and 4-picolinium esters can function as electron acceptors in PET reactions. It is further demonstrated that the resulting (anion) radicals fragment to give a carboxylate anion and pyridylmethyl radical. The high chemical and quantum yields from these fragmentation reactions suggest that such reactions will find use in photorelease applications. These reactions have been carried out by sensitization and as well as by direct photolysis in the case of the iodide salts. The mechanism of the photorelease has been investigated, and the data support the proposed PET based mechanism.

Experimental Section

General Procedures. All ^{1}H and ^{13}C NMR were obtained using a 400 MHz spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) in hertz (Hz). Deuterated CD_3CN or CD_3OD were used for all NMR experiments. Acetonitrile was distilled from calcium hydride under nitrogen atmosphere. UV−vis spectra were recorded on a spectrophotometer.

Cyclic Voltammetry Experiments. All electrochemical experiments were done on a voltammetry analyzer with $[Bu_4N][PF_6]$ as the supporting electrolyte. The electrodes used were a carbon working, a platinum auxiliary, and an Ag/AgCl reference. Ferrocene was used as the internal standard. The CV data were taken in spectroscopic grade dry MeCN after N_2 purging the samples for 10 min. The ferrocene/ferrocenium couple was found around 590 mV and the typical scan speed was 100 mV/s.

Fluorescence Quenching Experiments. Fluorescence quenching experiments were performed on an luminescence spectrometer. Samples in MeCN solvent were placed in 1 cm quartz cuvettes, sealed with rubber septums and purged with N_2 for 10−15 min. Sample concentrations were prepared such that the optical densities at the excitation wavelength were about 0.1−0.4.

Fluorescence Lifetime Measurement. Fluorescence lifetimes were determined by measuring the fluorescence decay on a nanoflash fluorescence apparatus. Samples in MeCN solvent were placed in 1 cm quartz cuvettes, sealed with rubber septums, and purged with N_2 for 10−15 min. Sample concentrations were prepared such that the optical densities at the excitation wavelength were about 0.1−0.4. The fluorescence lifetime of the sensitizer TPA was determined by this procedure.

Quantum Yield Determination. The solutions were photolyzed by the output of a 1000 W Hg−Xe lamp after passing through a spectral energy monochromator set to 355 nm ± 10 nm. Solutions of ester and sensitizer (3.3 mM, OD at 355 about 0.4−0.6) were placed in a 1 cm quartz cuvette and purged with N_2 for 10−15 min. The samples were irradiated for different times, 1.5, 2, 3, and 4 h and the amount of ester converted was determined by ^{1}H NMR integration. Light intensities were measured by a radiometer.

Deprotection Photolysis. A solution of 4−10 mg of the picolinium ester and an equal amount or slight excess of sensitizer was prepared in about 5 mL of CH_3OH (4.0 mM of ester and 4.0−4.5 mM of sensitizer). A 1 mL aliquot from this solution was used as dark control. The solution was purged with nitrogen and irradiated using a 200 W Hg lamp with continuous stirring. A Pyrex filter was used to cut off light below 320 nm to ensure light absorption by the sensitizer alone. A 1 mL aliquot was drawn out of the photolyzed solution. The solvents in the aliquots were evaporated, and the residues were redissolved in CD_3OD and hexamethyldisiloxane was added as the internal standard. The percent yields were determined by ^{1}H NMR integration of the carboxylic acid peaks relative to the internal standard.

In some cases, 4−10 mg each of the picolinium ester and the sensitizer was dissolved in 5 mL of CH_3OH. Half of the solution was used as dark control, and the remaining half was N_2 purged and photolyzed. The solutions were then evaporated and redissolved in CD_3OD with hexamethyldisiloxane as the internal standard and ^{1}H NMR spectra were obtained. The yields were determined as before.

Laser Flash Photolysis. Laser flash photolysis experiments were performed using an Nd:YAG laser as the pump beam source. The laser used was capable of 266 or 355 nm pulses between 4 and 6 ns duration. A 350 MHz digital oscilloscope was used to observe the waveforms. The samples were prepared such that the absorbances were between 1.5 and 2.0 at the excitation wavelength, 355 nm. The samples were placed in 1 cm quartz cuvettes, N_2 (or O_2) purged for 15 min, and stirred continuously during the photolysis.

General Procedures for the Synthesis of Esters 2a−h. Method 1. Esters **2a**−**d** and **2h** were prepared using this procedure.[32] 4-Pyridylcarbinol (3.45 g, 31.6 mmol) was dissolved in 40 mL of benzene, and triethylamine (7.97 mL, 56.8 mmol) was added. A solution of the corresponding acyl chloride (50.5 mmol) in 15 mL of benzene was added dropwise. The reaction mixture was stirred at room temperature for 16 h. H_2O (30 mL) was added, and the organic layer was separated, dried over $MgSO_4$, and concentrated in vacuo.

Method 2. Esters **2e**, **2f**, and **2g** were prepared using this procedure.[28] *N*,*N*′-Dicyclohexylcarbodiimide (DCC) (3.40 g, 16.4 mmol) was added to a solution of the carboxylic acid (16.4 mmol) and 4-pyridylcarbinol (1.62 g, 14.8 mmol) in 50 mL of dichloromethane. The reaction mixture was stirred at room temperature for about 24 h and checked by TLC for disappearance of starting material. The urea precipitate was filtered off, and the filtrate was washed with $NaHCO_3$ (2 × 25 mL) and H_2O (2 × 10 mL). The organic layers were collected and dried over $MgSO_4$, and the solvent was evaporated.

General Procedure for the Synthesis of Methylated Esters 5a−h. A 0.02 mol portion of the corresponding picolyl ester was dissolved in 15 mL of CH_3OH, and methyl iodide (4.26 g, 0.03 mol) was added slowly. The reaction mixture was refluxed at 75 °C for 8 h. The solvent was removed under reduced pressure, and the residue was recrystallized from hot methanol or ethanol.

General Procedure for Counter-Ion Exchange. The picolyl methiodide (5 mmol) was dissolved in a minimum amount of acetonitrile. A solution of silver perchlorate (1.04 g, 5 mmol) in acetonitrile was added, and the reaction mixture was stirred overnight at room temperature. The yellow AgI precipitate was filtered off, and the filtrate was concentrated in vacuo and recrystallized from hot ethanol.

Acknowledgment. This work was supported by the National Science Foundation.

Supporting Information Available: Copies of ^{1}H NMR spectra of **2a**−**h**, **5a**−**h**, **6a**−**h** and **9**, fluorescence data, LFP spectra, and UV spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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