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Photodecarboxylation Study of Carboxy-Substituted *N*-Alkylphthalimides in Aqueous Solution: Time Resolved UV−Vis Spectroscopy and Conductometry

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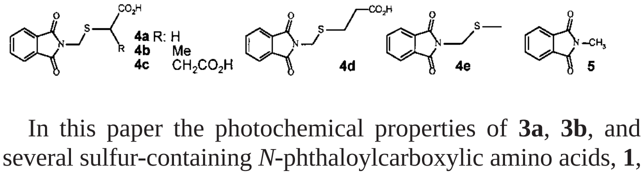
The photophysical and photochemical properties of *N*-phthaloyltranexamic acid (**3b**) and *N*-methylsulfanylmethylphthalimide (**4e**) as well as several sulfur-containing carboxylates, *N*-phthaloylmethionine (**1**), *N*-phthaloyl-*S*-carboxymethylcysteine (**2c**), phthalimidomethylsulfanyl acetic acid (**4a**), and its derivatives **4b-4d** were studied in aqueous solution by time-resolved UV−vis spectroscopy and conductivity using laser pulses at 248 or 308 nm. From the changes in absorption spectra upon continuous irradiation at 290 nm, the quantum yields of substrate decomposition (Φ_d) were measured for various cases. The quantum yields of formation of the lowest triplet state (Φ_{isc}) are small, when Φ_d is large and vice versa. The quantum yields of decarboxylation, $\Phi(-CO_2)$, were determined by conductometry. $\Phi(-CO_2)$ is largest (0.3) for **3b** in argon-saturated aqueous solution at pH 6−10 and decreases in the order **4a**−**c**, **2c**, **1**, and **4d**. The increase of Φ_d vs pH indicates that carboxylic acids exhibit low decarboxylation efficiencies, whereas the corresponding anions effectively eliminate CO_2 and subsequently cyclize. The mechanisms of photochemical decomposition, decarboxylation, and cyclization are discussed.

Introduction

Phthalimide derivatives of natural α-amino acids have been used as chiral building blocks for photochemical reactions.[1−22] Soon after the first report on simple alkyl-substituted compounds[1] we focused on potential electron donor−acceptor couples, derived from methionine,[2] phenylalanine,[3] serine and threonine,[3] cysteine,[4] and several *S*-alkylated cysteines.[7] Besides the intramolecular reactions which mostly result in cyclization, decarboxylation of *N*-phthaloyl α-amino acids has been reported earlier.[12] This reaction has been applied for *ω*-phthalimido alkylcarboxylic acids, where numerous applications for medium and large ring synthesis were developed.[5,6,8] The photochemistry of *N*-phthaloylmethionine (**1**),[2] *N*-phthaloyl-*S*-methyl-*L*-cysteine (**2a**),[4] and of phthalimidocarboxylic compounds containing a *trans*-cyclohexane-1,4-diyl spacer group between the nitrogen and the carboxyl group (**3a**−**c**)[11] has recently been described in detail. For the *N*-phthaloylvaline methyl ester we have proposed that the formation of a photoisomer as the main product upon direct excitation occurs via an upper excited n,π^* triplet state.[10]



In this paper the photochemical properties of **3a**, **3b**, and several sulfur-containing *N*-phthaloylcarboxylic amino acids, **1**, **2c**, (phthalimidomethylsulfanyl)acetic acid (**4a**), and three derivatives **(4b−d**) were studied by time-resolved spectroscopic and conductometric methods. *N*-Methylphthalimide (**5**) and the *N*-phthalimides **4e**, **2a**, **2b**, and **3c**, which do not contain an unprotected carboxy group, were used for comparison. The features of the observable triplet state of **1**, **2**, **3**, and **4** in polar solvents are discussed. The quantum yields of decarboxylation $\Phi(-CO_2)$ were measured by time-resolved conductivity in aqueous solution. The quantum yields of decomposition (Φ_d) which were taken as measure for cyclization are compared with $\Phi(-CO_2)$ and the quantum yields of triplet formation (Φ_{isc}).

Experimental Section

The phthalimides were used as described previously;[1−9] *N*-methylphthalimide (**5**, EGA) and acetonitrile (Merck, Uvasol) were used as received. Water was deionized by a Millipore (Milli Q) system and 2-naphthylglyoxylic acid (2-NG) was the same as used previously.[23] The pH values were adjusted for optical detection with phosphate buffer at pH 7 or borate buffer at pH 9. For conductivity measurements, only $HClO_4$ or NaOH were used. *N*-Alkylphthalimides in alkaline aqueous solution are known to hydrolyze slowly.[18] Therefore, the stability of the *N*-phthalimides in aqueous solution or acetonitrile−water mixtures was checked and continuous irradiation or transient measurements were carried out in appropriate cases within a few minutes after adjusting the pH at 10−11.

Absorption and emission spectra were recorded on a diode array spectrophotometer (Hewlett-Packard, 8453) and a spectrofluorimeter (Perkin-Elmer, LS5), respectively. The 248 or 308 nm output from one of two excimer lasers (Lambda Physik, EMG 200 and EMG 210 MSC; energy below 100 mJ, pulse width 20 ns) was used for excitation. For photodecomposition $\lambda_{irr} = 290$ nm from a Hg−Xe 1000-W lamb in combination with a monochromator, $\lambda_{irr} = 254$ nm from a low-pressure Hg

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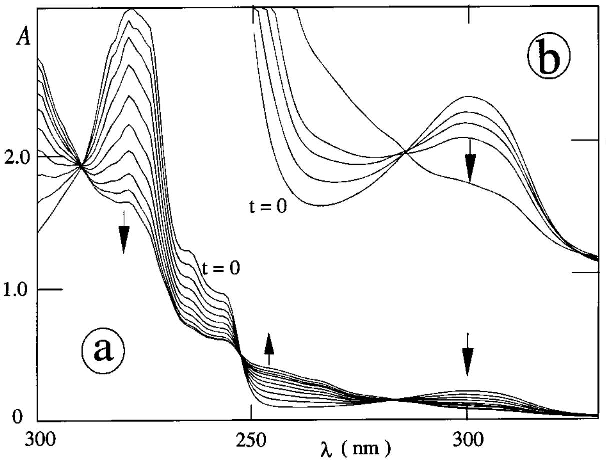


Figure 1. Absorption spectra in argon-saturated aqueous solution of (a) **3a** at pH 3 and (b) **2c** at pH 7, λ_{irr} = 290 nm (initially in 20 s intervals).

lamp or λ_{exc} = 308 nm were used. The concentration was adjusted such that the absorbance (in a 1 cm cell) was 1−2 at λ_{irr}. The laser flash photolysis apparatus and the time-resolved UV−vis spectroscopy and conductivity detection systems have been described elsewhere.[10,11,23,24] Actinometry was performed with aberchrome 540 for λ_{irr} = 290 nm.[25] For HPLC analysis a Nucleosil 5-C18 column (125 × 4.6 mm, 0.8 mL min^{-1}) and 0.1% phosphoric acid in aqueous MeOH (1:1) were used. The product peaks were not analyzed; note that in previous work the various products were described in the presence of organic solvents,[10,11] whereas the phthalimide concentrations in neat aqueous solution are too small in most cases. The measurements were carried out at 24 ± 2 °C.

Results

Photolysis. The phthalimide chromophore has its major absorption maximum at 220 nm and a minor one at ca. 300 nm. Upon continuous irradiation at 290 nm of **3a** in argon-saturated aqueous solution at pH 3, the bands at 220 and 300 nm disappear and the spectrum of the product(s) steadily decreases from 200 nm with isosbestic points at 220, 248, and 282 nm (Figure 1a). Similar changes were obtained for **2c** (Figure 1b), **3a/3b**, **4a**, **4b,** or **4c** at pH 7 in the presence of 1 mM phosphate buffer and at pH 9−10. This behavior was also observed when the phthalimide chromophore was excited with λ_{exc} = 308 nm, 248 nm or λ_{irr} = 254 nm. The changes in absorption at 300 nm vs dose (λ_{irr} = 290 nm) are shown in Figure 2a for several cases. The isosbestic points indicate that decomposition of the products does not take place. These spectral features are due to the conversion in chromophore structure from the aromatic imide to the isoindole-2-one, e.g., **3′** in Scheme 1.

The largest conversion, being mainly due to cyclization,[10] was found for **3a**/**3b** in argon-saturated aqueous solution at pH 6−10. The changes in concentration (C/C$_0$) for **3a** and **4c** vs dose, using HPLC measurements, are consistent (Figure 2b) with those obtained from UV analysis. The quantum yields of decomposition of phthalimides which do not contain a free carboxy group, i.e., **2a, 2b, 4e**, or **5**, are low in aqueous solution, Φ_d < 0.01. Φ_d is moderate for **2c**, **3c**, or **4a**−**c**, and largest for **3a/3b** with Φ_d = 0.3−0.4 at pH 6−10 (Table 1). Compared to aqueous solution, practically no photochemical changes were found in acetonitrile (except for **3a/b**[11]). This is consistent with earlier results on the photodecarboxylation of *N*-phthaloyl γ-amino butyric acid.[5] In most cases the presence of oxygen in aqueous solution at pH 6−10 has no marked effect on Φ_d. For **3a**, however, Φ_d is enhanced by ca. 30% on saturation by oxygen.

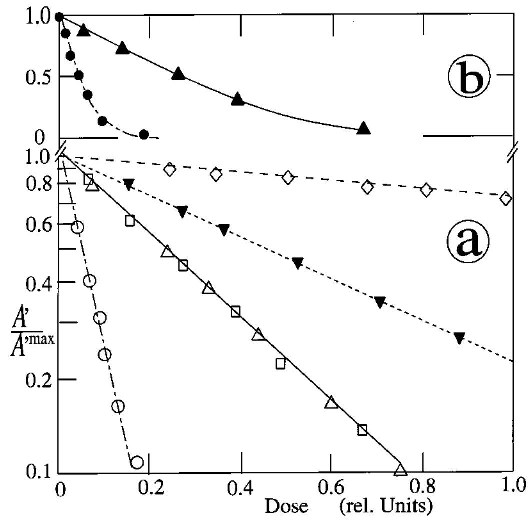
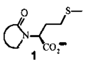
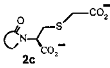
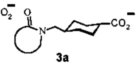


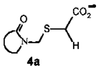
Figure 2. Photoconversion vs dose; (a) changes in absorption at 300 nm of **3b** (○), **4a** (□), **4c** (△), **2c** (▼), and **4d** (◇) in argon-saturated aqueous solution at pH 7 and (b) decrease of the relative HPLC signals of substrate for **3b** (●) and **4c** (▲); λ_{irr} = 290 nm.

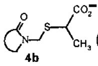
When the initial pH was adjusted at 4−6, e.g., for **3a**, pulsing at 248 nm causes a decrease in the proton concentration, i.e., a rise in pH, whereas in the basic range no clean trend could be measured (not shown). The increase in the OH$^-$ concentration results from the overall photoconversion of the anion of a carboxylic acid to an alkoxide anion, but formation of bicarbonate at pH >8 inhibits the effect of OH$^-$ release (see below). The Φ_d values of **3a/3b** in aqueous solution are significantly smaller on decreasing the pH and reflect a pK_a value at 4.7 (Figure 3 and Table 1). The pK_a values of **2c** and **4a**−**c** are expected to be much smaller (α-mercaptocarboxylic acid vs alkylcarboxylic acid); thus, the drop in Φ_d begins below pH 3. We therefore suggest that the sequence of decarboxylation and cyclization as the major reason for decomposition is less efficient for the carboxylic acid than for the corresponding anion. In aqueous solution at pH 3.3 (natural pH for a concentration of ca. 0.5 mM) the phthalimidocarboxylic compounds under examination (except for **3a/3b**) are mainly present as carboxylic acids. The anions are present at larger pH:

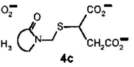

1

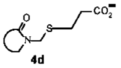

2c


3a


4a


4b


4c


4d

Singlet and Triplet Properties. *N*-Alkylphthalimides exhibit fluorescence with remarkable low quantum yields of Φ_f = 0.01 or less in solution at room temperature.[3,15] For **5** in acetonitrile, where λ_f = 390 nm, Φ_f = 8 × 10^{-4}, and the lifetime τ_f = 0.19 ns, the rate constants are k_f = 4 × 10^6 s^{-1} and k_{isc} = 4 × 10^9 s^{-1}.[22] The fluorescence is even lower for **5** and *N*-propylphthalimide in aprotic media.[17,18] The fluorescence properties are sensitive to solvent polarity and in protic solvents to hydrogen bonding.[18,22] Weak fluorescence has recently been reported for **1** (Φ_f ≤1 × 10^{-3}) and **3b** (4 × 10^{-3}) in aqueous solution.[11] For **2c** and **4a**−**e** in aqueous solution at pH 6−7, Φ_f is also low (≤3 × 10^{-3}) without any significant trend.

SCHEME 1

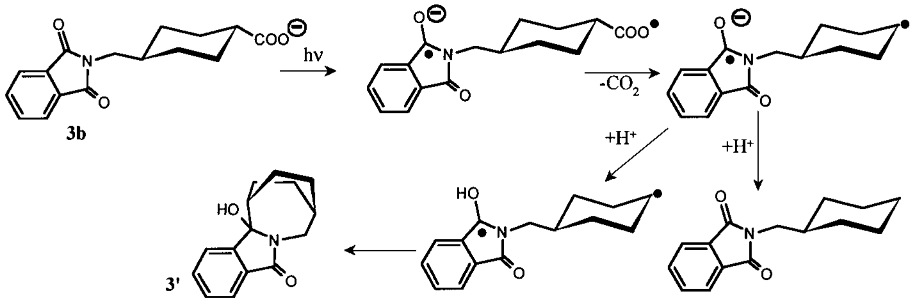


TABLE 1: Quantum Yield Φ_d of Decomposition of Phthalimide Derivatives[a]

	MeCN	H$_2$O, pH 1	H$_2$O, pH 3.5−4.6	H$_2$O, pH 7	H$_2$O, pH 9
1[b]			<0.01	<0.01	
2b	<0.01			<0.01	
2c		0.03	0.05	0.05	0.05
3a[b]	0.2		0.33 (0.39)[c]	0.3	0.4
3b	0.2	0.05	0.3	0.4	0.4
3c	<0.08		*d*	[0.05][e]	
4a	<0.03	0.02	0.1	0.12	0.12 (0.12)
4b	<0.03	0.02	0.1	0.1	0.10 (0.1)
4c	<0.03	0.01	0.12	0.14	0.13 (0.13)
4d	<0.03		<0.01	<0.05	
4e	<0.03			0.01	
2-NG[f]			0.04		0.04

[a] In argon-saturated solution upon irradiation at 290 nm. [b] Taken from ref 11. [c] Values in parentheses refer to saturation with oxygen. [d] Too low solubility. [e] Values in brackets refer to acetonitrile-water (1:1, vol) mixtures. [f] For conversion of 2-naphthylglyoxylic acid into 2-naphthaldehyde, see ref 23.

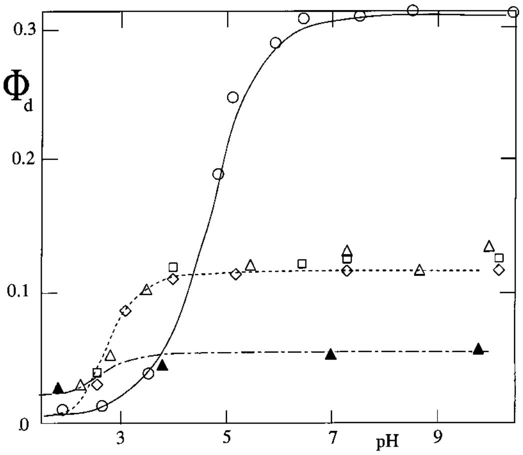


Figure 3. Effect of pH on Φ_d for **2c** (▲), **3b** (○), **4a** (□), **4b** (◇), and **4c** (△) in argon-saturated aqueous solution for λ_{irr} = 290 nm.

TABLE 2: Properties of the Triplet State of Phthalimide Derivatives[a]

compound	λ_{max} (nm)	τ_T (μs)	k_{ox} (10^9 $M^{-1}s^{-1}$)	Φ_{isc}[b]
1	315	3 (5)[c]	1.5	0.05 (<0.05)[c]
2a	<330	3		<0.03
2c	335	3		<0.04
3a	330	5 (5)	1.5	0.6
3b	330	5	1.5	0.6
3c	330	10 (5)	1.5	0.6 (0.5)
4a	340	1	1	0.05 (<0.05)
4b	345	3	1	0.05 (<0.05)
4c	345	<2		0.05 (<0.05)
4d	345	2	1	0.08
4e	335	1	1	0.05

[a] In argon-saturated acetonitrile, λ_{exc} = 248 nm. [b] Using Φ_{isc} = 0.8 for **5** in acetonitrile as reference. [c] Values in parentheses refer to aqueous solution.

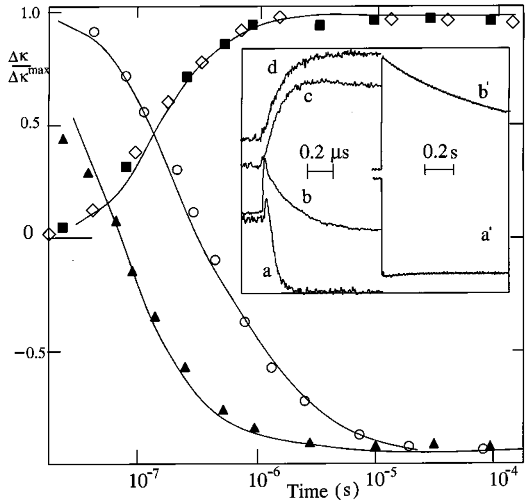


Figure 4. Effect of pH: changes of the $\Delta\kappa$ signal as a function of log time for **4c** in argon-saturated aqueous solution at pH 4 (▲), 5 (○), 9 (◇), and 10 (■); insets: signals at (a) pH 3.6, (b) pH 4.9, (c) pH 8.2, and (d) pH 9.5, and of the slow change at (a′) pH 4 and (b′) pH 10.6; λ_{exc} = 308 nm.

The observed main transient upon direct UV-excitation of **5** has been assigned to the lowest triplet state.[10,11,16] The T−T absorption spectra of the methionine derivative **1** in acetonitrile and other solvents show a $\lambda_{max} \leq 350$ nm. Virtually no triplet could be detected for **1** or the cysteine derivative **2a** in acetonitrile upon 248 or 308 nm laser excitation, in contrast to the case of **5**. The triplet lifetimes in several solvents are in the 1−10 μs range (Table 2). The decay is quenched by oxygen with rate constants of $k_{ox} = (1-2) \times 10^9$ $M^{-1}s^{-1}$. The relative transient absorbances at λ_{max} in acetonitrile, using optically matched conditions and λ_{exc} = 248 nm, are taken as a measure of Φ_{isc} (Table 2). The Φ_{isc} values of **5** are large and not specific for changes in solvent polarity.[10] The triplet yields of **1**, **2a**−**c**, and **4a**−**e** are much smaller than those of **3a**−**c**, and the reference **5**. This indicates that reactions via the lowest triplet state of the first group are rather unlikely and that the photochemical reactivity involves its precursor (see discussion).

Transient Conductivity. In aqueous solution at pH 3.5 and above the phthalimidocarboxylic compounds are mainly present as anions (for **3a**/**3b** see below). A conductivity increase ($\Delta\kappa$: positive for increasing conductivity) concomitant with the laser pulse was observed for carboxyl compounds **1**, **2c**, **3a**/**3b**, and **4a**−**c** in argon-saturated aqueous solution in a broad pH range. A representative case is given for the biscarboxylate **4c** using λ_{exc} = 308 nm (Figure 4). At pH 3.5−5 the $\Delta\kappa$ signal increases within the laser pulse width, decreases rapidly to a value which is much smaller than the initial one (Figure 4a, 4b) and then remains constant for seconds. The rate constant of this fast decay

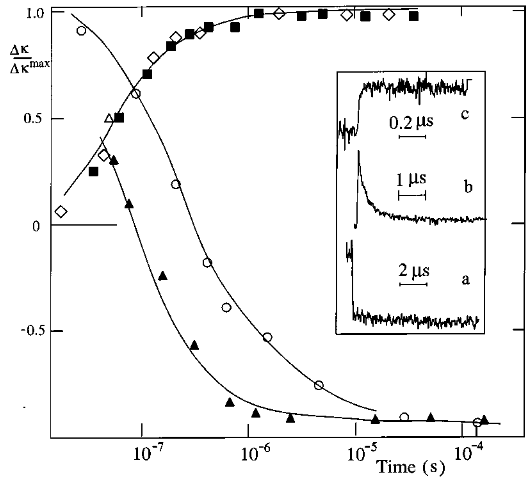


Figure 5. Effect of pH: changes of the $\Delta\kappa$ signal as a function of log time for **1** in argon-saturated aqueous solution at pH 4 (▲), 5 (○), 9 (◇), and 10 (■); insets: signals at pH (a) 3.9, (b) 6, and (c) 10.3; λ_{exc} = 308 nm.

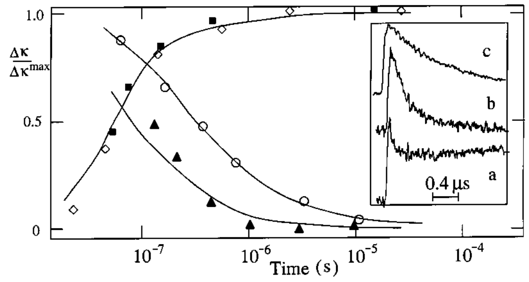
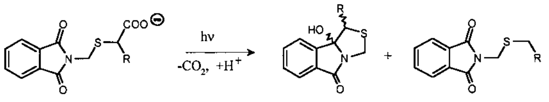


Figure 6. Effect of pH: changes of the $\Delta\kappa$ signal as a function of log time for **3a** in argon-saturated aqueous solution at pH 4 (▲), 5 (○), 9 (◇), and 10 (■); insets: signals for **3b** at pH (a) 3.1, (b) 4.2, and (c) 5.1; λ_{exc} = 308 nm.

depends on the proton concentration (see below). At pH 5.5−8 the conductivity signal increases within <1 μs and then slowly decreases (Figure 4c). When the OH^- concentration is further increased (up to pH 10.5), the signal becomes positive after the pulse, increases further in the submicrosecond range and remains virtually unchanged (Figure 4d). The rate constant of this fast build-up is independent of the hydroxyl concentration; the values are 1.5×10^7 s^{-1} for **1** (Figure 5) and $(0.7-1.1) \times 10^7$ s^{-1} for **3a**/**3b** (Figure 6) and **4a**−**c**.



(1)

The fast increase in $\Delta\kappa$ in aqueous solution at pH 8−11 is ascribed to photoconversion of the phthalimido carboxylate into decarboxylation products and OH^- (eq 1).[8] The equivalent conductivity of the anion ($\Lambda \sim 40$ cm^2 Ω^{-1} mol^{-1}) is much lower than that of OH^- ($\Lambda = 190$ cm^2 Ω^{-1} mol^{-1}). The reason for the primary increase of $\Delta\kappa$ in the acidic range is likewise due to OH^- formation. The subsequent fast pH-dependent decrease of $\Delta\kappa$ is due to the neutralization reaction 2 and the larger equivalent conductivity of H^+ ($\Lambda = 350$ cm^2 Ω^{-1} mol^{-1}) than that of OH^-, i.e., the permanent negative signal is due to proton consumption.

$$H^+ + OH^- \rightleftarrows H_2O \qquad (2)$$

Thus, CO_2 and OH^- are suggested to be formed within the laser pulse width throughout and OH^- remains as conducting species in the alkaline range or is neutralized at lower pH.

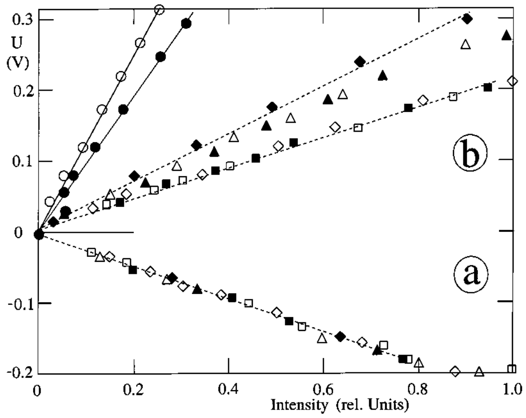


Figure 7. Plots of $\Delta\kappa$ at 1 ms (corrected for optically matched solution) vs laser intensity (I_L^{max} = 0.5 MW cm^{-2}) for **3b** (○, ●), **4a** (□, ■), **4b** (◇, ♦), and **4c** (△, ▲) in argon- and oxygen-saturated aqueous solution (open and full symbols, respectively) at (a) pH 3.6−4.4 and (b) 9−10; λ_{exc} = 308 nm.

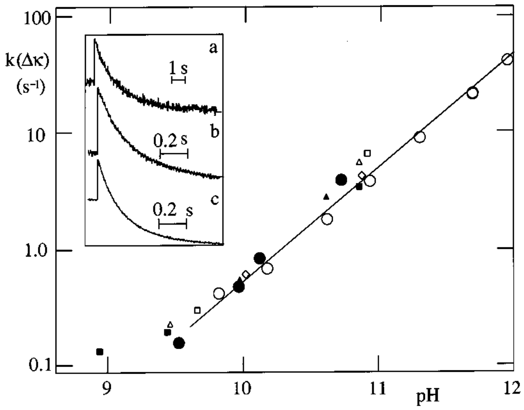


Figure 8. Rate constant of the slow decay of $\Delta\kappa$ vs pH in argon-saturated aqueous solution for 2-NG (●), **3b** (○), **2c** (■), **4a** (□), **4c** (△), and **4d** (◇); insets: (a) for **1** at pH 9.5, (b) for **4d** at pH 9.4, and (c) for **3b** at pH 10.4; λ_{exc} = 308 nm.

In each case for **1**, **2**, and **4a**−**c** in argon-saturated aqueous solution at pH 3.4−4.6 and 9−10, the $\Delta\kappa$ signal at 1 ms after the laser pulse depends linearly on the intensity (I_L) using λ_{exc} = 308 nm (Figure 7) or λ_{exc} = 248 nm; no saturation or two photon processes contribute. For **3a** and **b** in aqueous solution, the time-resolved $\Delta\kappa$ signals at pH 8−10 are similar to the above cases, but they are not negative in the acidic range (Figure 6). The latter effect for **3a** is due to the pK_a around 4.7 and not a consequence of a larger K^+ concentration since the pattern with respect to $[H^+]$ is similar for **3b** under the applied conditions.

On a long time scale the $\Delta\kappa$ signals remain permanently (more than seconds) negative in the acidic pH range, but after the initial increase they decrease below the value prior to the pulse at pH 9−11. This slow decrease of $\Delta\kappa$ in the 0.1−10 s range becomes significantly pH dependent (Figure 8) and is ascribed to formation of bicarbonate, reaction 3,[23,24] which has a markedly smaller equivalent conductivity ($\Lambda \leq 50$ cm^2 Ω^{-1} mol^{-1}) than OH^-.

$$CO_2 + OH^- \rightleftarrows HCO_3^- \qquad (3)$$

A value of k_3 = 8000 M^{-1} s^{-1} is obtained from the slope in Figure 8 of the rate constant of this slow decay vs the OH^- concentration for several phthalimides. Comparable values of

TABLE 3: Transient Conductivity Amplitudes and Quantum Yield of Decarboxylation[a]

compound	$\Delta\kappa/\Delta\kappa^{max}$ pH 3.4−4.6 $\lambda_{exc} = 308$ nm	$\Delta\kappa/\Delta\kappa^{max}$ pH 9−10 $\lambda_{exc} = 248$ nm	$\Delta\kappa/\Delta\kappa^{max}$ pH 9−10 $\lambda_{exc} = 308$ nm	$\Phi(-CO_2)$[b]
1	0.08	0.1	0.06 (0.06)[c]	0.04
2a			<0.02	*d*
2c	0.04	0.1 [0.05][e]	0.04 (0.04)	0.03
3a	*f*	0.9 (0.4)	0.95	0.3
3b	*f*	1.0	1.0 (0.75)	0.35
4a	0.2	0.2	0.18 (0.18)	0.07
4b	0.2	0.2	0.30 (0.3)	0.10
4c	0.2	0.3	0.25 (0.26)	0.09
4d	<0.01	0.03	0.03	<0.006
4e	<0.01	0.02	0.02	*d*
2-NG	0.1	0.12	0.14	0.04

[a] In argon-saturated aqueous solution, using $A(\lambda_{exc}) = 0.5$. [b] Absolute $\Phi(-CO_2)$ value, obtained by averages of the $\Delta\kappa/\Delta\kappa^{max}$ values and using 2-naphthylglyoxylic acid (2-NG) as reference, $\Phi(-CO_2) = 0.04$.[23] [c] Values in parentheses refer to saturation with oxygen. [d] No photodecarboxylation. [e] Value in brackets refers to acetonitrile-water (1:4, vol) mixture. [f] See text.

$k_3 = 7000$ M^{-1} s^{-1} have been reported for the photodecarboxylation of phenylglyoxylic acid[24] and 1- or 2-naphthylglyoxylic acids.[23] The pH range in alkaline aqueous solution is limited due to the slow hydrolysis of the phthalimide.[18] Inspection of **2a**/**2b**, **3c**, and **4e**, where decarboxylation is impossible, gave only small signals directly after the pulse, but not the above-mentioned characteristic features of CO_2 release and formation of bicarbonate. The primary part in these cases is probably due to photoionization as a side reaction followed by neutralization.

Quantum Yield of Decarboxylation. The $\Delta\kappa$ amplitude (at 1 ms after the pulse) under normalized conditions (I_L and A_{308}) is taken as a measure of the relative $\Phi(-CO_2)$ value (Figure 7). It is maximum for **3a**/**3b**, markedly smaller for **1, 2c, 4a**−**c**, and negligible for **4d** in the alkaline range using $\lambda_{exc} = 308$ or 248 nm (Table 3). Moreover, for **1, 2c**, and **4a**−**c**, the yield was found to be roughly the same in aqueous solution at pH 3.4−4 and 9−10, using the amplitudes and the equivalent conductivities of H^+ and OH^-. Thus, for these compounds there is no apparent effect of pH between 4 and 10 on $\Phi(-CO_2)$. For **4c** a pK_a value of 2 is estimated from small changes in the absorption spectra (a method which failed for **3b**). The positive and much smaller $\Delta\kappa$ signals for **3a**/**3b** at pH 3−5 are probably the consequence of a larger pK_a value.

The absolute $\Phi(-CO_2)$ values were obtained by using 2-naphthylglyoxylic acid as reference, $\Phi(-CO_2) = 0.04$.[23] In most cases we could not find any difference in oxygen- or argon-saturated aqueous solution (pH 4 or 9−10). For **3b** and **4b**, however, the $\Delta\kappa$ signal at pH 9−10 is significantly (ca. 30%) reduced on saturation by oxygen (Figure 7 and Table 3). The reason should be triplet quenching by oxygen. In the case of photolysis of **4b**, Φ_d should be equal to $\Phi(-CO_2)$ only if decarboxylation is quantitatively followed by cyclization. In the other extreme case, Φ_d is expected to be much smaller than $\Phi(-CO_2)$ since no significant spectral change is expected from decarboxylation without cyclization.

Discussion

Photoprocesses. The energy absorbed by **1**, **2a**−**c**, and **4a**−**e** in aqueous solution at room temperature is dissipated by internal conversion and/or by decarboxylation and subsequent cyclization. Fluorescence is extremely weak and intersystem crossing is relatively unimportant. The quantum yield of fluorescence of **5** as reference and of other *N*-alkylphthalimides in solution at room temperature is also smaller than $\Phi_f = 0.01$.[3,15] In contrast to the phthalimides mentioned above, the quantum yield of intersystem crossing of **5** is large and not specific for changes in solvent polarity.[10] Significantly lower triplet yields were determined for **3a**−**c** and even lower values for **1**, **2a**−**c**, and **4a**−**e** (Table 2). Photoinduced intramolecular charge separation between the thioether and the phthalimide moieties has been proposed to account for both decarboxylation and cyclization[1−8] which may be coupled processes. The cyclization products of **1**, **2**, and **4** are sulfur-containing heterocycles with five-, six-, and seven-membered ring systems.[1−8] Photoinduced charge separation has also been proposed to account for the cyclization products of *N*-(2-methyl-2-propenyl)phthalimides.[26]

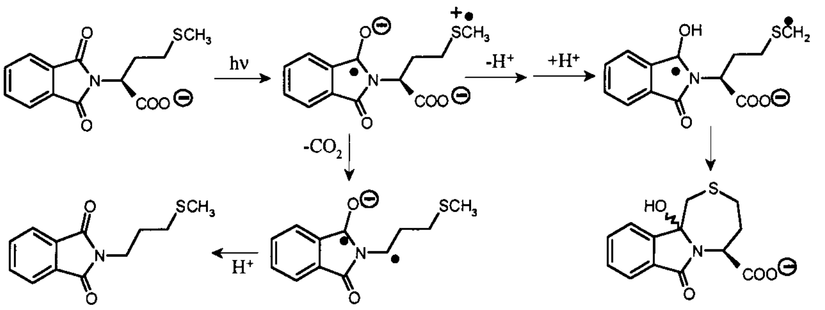
The OH radical induced decarboxylation of methionine, which can be taken as an analogue of the photochemistry of the *N*-phthaloylmethionine **1**, involves a sulfur radical cation and a longer lived dimeric sulfur radical cation with $\lambda_{max} = 480$ nm.[27] However, no transient, which could be attributed to a sulfur containing radical cation, was found for **1** under the applied conditions. Instead, the observed transient (Table 2) is most likely the lowest π,π triplet state, as already discussed for **1**, **2**, and the *N*-phthaloylvaline methyl ester.[10,11] Photodecarboxylation of aromatic carboxylic acids is known to involve the anion rather than the acid,[28] i.e., $\Phi(-CO_2)$ is larger above than below the pK_a. This was also found for several phthalimides in this work (Table 3). A similar pH dependence of Φ_d (Figure 3) is in line with this interpretation. In all cases examined OH^- production is instantaneous at pH 4 ($>5 \times 10^7$ s^{-1}) and somewhat slower at pH 8−10, $k = (0.5-1.5) \times 10^7$ s^{-1}.

Photoreactions with 3a−c. Owing to the absence of a sulfur atom for **3a** or **b** the intramolecular charge separation between the carboxyl and phthalimide moieties could be expected to be less efficient. This, however, is not the case.[6−9] The large Φ_d value (Table 1) mainly refers to production of **3′** (Scheme 1).[7] For **3a** we have proposed that the photocyclization is due to the fast intramolecular charge separation reaction in the spectroscopically nondetectable $^3n,\pi^*$ state in competition with population of the observable nonreactive $^3\pi,\pi^*$ state.[11] This competing process is more important than the above-discussed cases, as concluded from the substantial Φ_{isc} value (Table 2). On the other hand, $\Phi(-CO_2)$ is also quite substantial (Table 3).

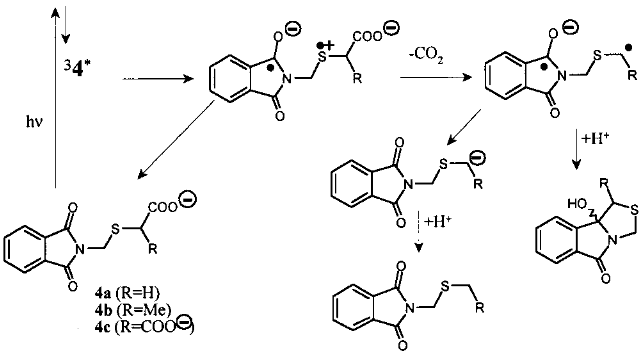
The possibility that decarboxylation of **3a/3b** in aqueous solution at pH 9−10 occurs via the observable $^3\pi,\pi^*$ state to a large extent has to be rejected since quenching by oxygen is efficient, $k_{ox} = 1.5 \times 10^9$ M^{-1} s^{-1} (Table 2), whereas $\Phi(-CO_2)$ is only 30% smaller in oxygen- than in argon-saturated solution (Figure 7 and Table 3). The presence of oxygen has also a marked but nevertheless rather small effect on Φ_d (Table 1). This is in contrast to nonaqueous solvents, where quenching of the observable triplet strongly reduces Φ_d.[11] For **3c** no decarboxylation is possible and alternative photochemical pathways, such as Norrish types I and II reactions, become relevant. The latter reaction seems to be important since Φ_d is not close to zero.

Photoreactions with 1 and 2. The photochemically stable *N*-methylphthalimide **5** shows high Φ_{isc} and k_{isc} values and very small Φ_f and τ_f values. The fluorescence properties of the more complicated photochemically reactive phthalimides are very similar. Thus, for **1** and **2a**−**c** in polar solvents,[3,11] a triplet route upon direct excitation at 248−308 nm is more likely than a singlet route. In the case of singlet photochemistry the rate constant for an intramolecular charge separation has to be much larger than k_{isc} for which $(0.1-1) \times 10^{10}$ s^{-1} is realistic.[22] On

SCHEME 2



SCHEME 3



the other hand, the yield of the observable triplet is rather small, but ΔA_{330} (as a measure of Φ_{isc}) increases on decreasing the temperature; this indicates a fast reaction competing with population of the observed triplet state which is suppressed at lower temperatures.[11] A conceivable explanation for the fast competing reaction is the involvement of ^{3}n,π* as an upper excited triplet state as precursor of cyclization.[11] The proposed mechanism of cyclization of **1** in aqueous solution via the ^{3}n,π* state and intramolecular charge separation between the thiomethyl and phthalimide moieties is illustrated in Scheme 2. The small quantum yield Φ_d (Table 1) and the larger $\Phi(-CO_2)$ value (Table 3) of **1** indicate that photodecarboxylation is more efficient than photocyclization (extreme case in eq 1). Decarboxylation competes with electron back transfer, both are probably faster than protonation of the ketyl radical part and thus cyclization is not effective.

For **2c** formation of a radical cation at the thiomethyl moiety in closer distance to the carboxyl group should have an enhancing effect on decarboxylation and subsequent cyclization. In fact, the larger Φ_d value of **2c** with respect to **1** and a comparable $\Phi(-CO_2)$ value indicate that the photochemical reactivity is higher. For **2c** the mechanism of decarboxylation and cyclization should be similar to that shown for **1** in Scheme 2. Ring closure is favored when protonation of the radical anion part is faster than back electron transfer. For **2a** and **b,** where no decarboxylation is possible, Φ_d is small, indicating that the cyclization is inefficient upon direct photolysis. This is in contrast to acetone-sensitized excitation[4,7] and the origin of the latter effect has been ascribed to intermolecular electron transfer.[11]

Photoreactions with 4. For **4a−e**, the Φ_{isc} and Φ_f values are also low at room temperature, but those for Φ_d and $\Phi(-CO_2)$ of **4a−c** are substantial (Tables 1−3). The proposed mechanism for decarboxylation and cyclization of **4a−c** in aqueous solution is as follows (Scheme 3). Intramolecular charge separation between the thiomethyl and phthalimide moieties in the ^{3}n,π* state may be favored by the closer distance between the respective radical ion positions. This should cause fast decarboxylation and subsequent protonation and ring closure. This mechanism corresponds with the α-silyl[29] or α-stannyl[30] thioether derivatives where trialkylsilyl or trialkylstannyl cations serve as leaving groups. The relatively large $\Phi(-CO_2)$ and Φ_d values of **4a−c** indicate that the ratio of rate constants for electron back transfer and decarboxylation is smaller than the above cases of **1** and **2**.

For **4d** decarboxylation was observed (inset b in Figure 8). In principle, the same mechanism could operate, but the reactivity is low as $\Phi(-CO_2)$ and Φ_d are rather small. This accounts for the interpretation than an increase in distance between the thioether moiety and the carboxylate anion reduces the effect of decarboxylation. In this case, direct photoinduced electron transfer involving the carboxylate anion might constitute an alternative channel. The remarkable drop in efficiency can be interpreted by the weaker donor properties of the carboxylate anion in comparison with the thioether group, indicating that the faster electron transfer involving the thioether group is followed by nonproductive back electron transfer. Although a "relay mechanism" with the sulfur atom as a primary hole generator and hole mediator can be postulated, this sequential process is unlikely because no reactivity was observed in the corresponding intermolecular experiment.[8]

For **4e** no decarboxylation is possible and electron back transfer is probably faster than protonation followed by cyclization. A reaction via the nonobservable ^{3}n,π* state is, because of its short lifetime, assumed not to be affected by oxygen. In fact, this was found in most cases. For **4b** under oxygen atmosphere, however, $\Phi(-CO_2)$ is ca. 30% reduced. This indicates some interaction of the two triplet states.

Conclusions

N-Phthaloyltranexamic acid (**3**) undergoes efficient photodecarboxylation and photocyclization in aqueous solution at pH > pK_a, indicating photoinduced electron transfer thereby oxidizing the carboxylate anion. The quantum yields Φ_d and $\Phi(-CO_2)$ for the sulfur-containing carboxylates are smaller and decrease in the order phthalimidomethylsulfanylacetic acids **4a−c, 2c**, and **1**. From the comparison of the quantum yields of fluorescence and intersystem crossing it follows that the triplet reactivity is traced as the dominant path. Owing to the low sensitivity toward oxygen we conclude that the higher excited n,π* triplet state is involved in the photoinduced electron-transfer reactions of the sulfur-containing compounds **4a−c, 2c**, and **1**, as well as the anion of **3** (at least in part). Time-resolved conductivity was shown to be a powerful tool for an analysis of the kinetics of electron transfer and the efficiency, $\Phi(-CO_2)$.

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