



$(P-P)S_2(OOCCH_3)_2 \sim$
 n by the expression (2)



AC catalysed by cationic
 or both Rh-monophosphi-
 Rh-carboxylate catalysts

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PHOTOCHEMICAL HYDROLYSIS OF SOME NITROPHENYL ACETATES

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Nitro substituent exhibits a *meta*-activating effect on the course of photochemical hydrolysis of phenyl acetates since UV photolysis of isomeric 4- and 3-nitrophenyl acetates in neutral aqueous solution leads to the formation of the corresponding phenols with quantum yields 0.002 and 0.006, respectively; 2-methoxy-4-nitro- and 2-methoxy-5-nitrophenyl acetates showed still greater difference in their photochemical reactivity (Φ_r 0.002 and 0.129, respectively). Quenching of the photohydrolysis of the latter compound with 2,4-hexadienoic acid indicates the participation of a triplet state with the effective lifetime of 0.15 μ s. The photoreaction is accelerated in acidic media which means that one of the early photochemical steps is the protonation of the excited state. No incorporation of ^{18}O into the product molecule was observed after the photolysis of 2-methoxy-5-nitrophenyl acetate in $H_2^{18}O$, which is an unambiguous evidence that the photoreaction proceeds as a light-induced hydrolysis of the ester bond.

In 1956 de Jongh¹ observed that a solution of 3-nitrophenyl phosphate accidentally exposed to sunlight took an intensely yellow coloration due to the formation of 3-nitrophenolate anion. Somewhat later it was shown on the basis of the photolysis in $H_2^{18}O$ that the photoreaction proceeds simultaneously as the hydrolysis of the ester bond as well as the nucleophilic aromatic substitution² (S_NAr^*) with hydroxide anion as a nucleophile, while only the P—O bond fission is observed in neutral solutions (water molecule as a nucleophile). In the S_NAr^* reactions, nitro group exhibits a pronounced substitution effect activating the aromatic nucleus almost exclusively in the *meta*-position³. With the exception of the first observations mentioned above^{1,2} almost all the experimental data concerning photochemical properties of nitrophenol derivatives are confined to their ethers and, moreover, there were no attempts to investigate the substitution effect of the nitro group in other types of photochemical reactions than nucleophilic photosubstitution (*e.g.*, photohydrolysis of the ester bond, electrophilic substitution). Only Sahini and coworkers⁴ have studied the photochemical behaviour of 3-nitrophenyl acetate and Wieland and coworkers⁵ described the photohydrolysis of 3-nitrophenyloxycarbonyl derivatives of amino acids in an attempt to use such compounds as photolabile protective groups in peptide synthesis.

It is the aim of the present study to compare the photochemical reactivity of various nitrophenyl acetates as to be able to assess the activation and orientation effects of the nitro group in this class of compounds and, on the other hand, to obtain some

information concerning the reaction mechanism (multiplicity and lifetime of reactive excited states, selectivity of the reaction).

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. UV spectra were recorded on a Varian Cary 219 apparatus; mass spectra were measured on an AEI MS 902 spectrometer (electron energy 70 eV, source temperature 150°C).

4-Nitrophenyl acetate (*I*), 3-nitrophenyl acetate (*II*), 2-methoxy-4-nitrophenyl acetate (*III*) and 2-methoxy-5-nitrophenyl acetate (*IV*) were prepared by 4-dimethylaminopyridine catalyzed acetylation⁶ of the corresponding phenols. Traces of oxygen were removed from the nitrogen gas (99.99%) in an absorption system described in our previous paper⁷. 2,4-Hexadienoic acid was crystallized three times from water, m.p. 113.5°C, ref.⁸ m.p. 112–113°C.

Preparative thin-layer chromatography was performed on silica gel plates (Woelm G-DC 8 × 5 cm, 1 mm thickness), elution with benzene-hexane-acetone 5 : 5 : 1. The high performance liquid chromatography was run on Separon SI C-18 (5 μm, Laboratorní přístroje, Praha) column in methanol-water (1 : 1), flow rate 0.50 ml min⁻¹, UV detection at 254 nm.

Preparative Photolyses

Solutions of acetates *I–IV* (0.05 mmol) in water with 5% of acetonitrile (25 ml) were bubbled with nitrogen and irradiated in a magnetically stirred photoreactor with external source of UV light, i.e., a 125 W medium pressure mercury lamp RVK-125 with Pyrex filter (2 mm thickness, 5 cm distance, 3 h irradiation time). The reaction mixture was extracted with ether (4 × 5 ml), ethereal extracts were dried with magnesium sulphate and the solvent was evaporated *in vacuo*. HPLC as well as TLC analysis revealed a single photoproduct in all cases (besides of small amount of unidentified polar polymers) which was isolated by preparative TLC. Chromatographic mobilities (HPLC, TLC) as well as mass spectra of the isolated products were identical with those of the authentic samples of the corresponding phenols *V–VIII*.

Determination of Quantum Yields

Monochromatic light of the wavelength 313 ± 5 nm was isolated from the spectrum of an Osram HBO-200 mercury lamp using a high intensity monochromator (Applied Photophysics M-300) and its intensity was determined by the method described elsewhere⁷. Solutions of nitrophenyl acetates *I–IV* (0.10–0.28 mmol l⁻¹, 3 ml) were irradiated at 25°C in a magnetically stirred quartz cuvette while a stream of argon was introduced into the irradiated solution. At regular time intervals (10–60 s) changes of optical density were determined with the accuracy of ± 0.0002 absorbance units at selected wavelengths (273 nm in the case of *I*, *II* 264 nm, *III* 276 nm, *IV* 313 nm) and the raw absorbance data were numerically evaluated according to a described procedure⁷. In the case of neutral and weakly acidic solutions (phosphate-citrate buffers, pH 2.2 to 7.0) no competitive ground-state hydrolysis was observed. For the determination of quantum yields in 0.6–6.0 mol l⁻¹ HClO₄ the rate of the photochemical hydrolysis was taken as a difference between the total reaction rate and the competitive ground-state reaction. The final conversion was kept below 20% and the empirically found reproducibility of the method was 10%.

Photolysis of the Acetate *IV* in H₂¹⁸O

2-Methoxy-5-nitrophenyl acetate (*IV*, 10.0 mg, 46.9 μmol) was dissolved in acetonitrile (1.00 ml)

an aliquot (10.0 μ l) of the stock solution was injected into a quartz cuvette containing 1.00 ml of water (25% ^{18}O). The solution was deoxygenated with argon and was irradiated with UV light (313 \pm 10 nm) of the intensity 10^{-8} mol photon s^{-1} for 60 min. HPLC analysis of the reaction mixture revealed approximately 50% conversion of the starting material and the formation of the single photoproduct *VIII*. The photolyzate was extracted with ether (3 \times 200 μ l), the aqueous layer was bubbled with argon for 15 min and was subsequently used for another identical experiment; the described procedure was repeated five times. Collected ethereal extracts were evaporated *in vacuo* and the obtained yellow oil was subjected to preparative TLC. The isolated phenol *VIII* (0.17 mg, 43%) was analyzed by mass spectrometry and the amount of ^{18}O incorporated into the product molecule was determined from the relative intensities at m/z 169 (M^+) and 171 ($\text{M} + 2^+$) in comparison with the authentic sample of unlabelled *VIII*.

Quantum-Chemical Calculations

CNDO/S-LCI calculations were performed using the standard parametrization⁹ with the involvement of 16×9 singly excited configurations. γ -Integrals were evaluated according to Mataga and Nishimoto¹⁰. Standard bond lengths were considered ($\text{C}_{\text{Ar}}-\text{C}_{\text{Ar}}$ 140 pm, $\text{C}_{\text{Ar}}-\text{N}_{\text{NO}_2}$ 148 pm, $\text{N}_{\text{NO}_2}-\text{O}_{\text{NO}_2}$ 121 pm, $\text{C}_{\text{Ar}}-\text{O}$ 136 pm, $\text{O}-\text{C}_{\text{CH}_3}$ 143 pm, $\text{O}-\text{C}_{\text{C=O}}$ 138 pm, $\text{C}_{\text{C=O}}-\text{O}_{\text{C=O}}$ 124 pm, $\text{C}_{\text{C=O}}-\text{C}_{\text{CH}_3}$ 150 pm, $\text{C}_{\text{Ar}}-\text{H}$ 108 pm, $\text{C}_{\text{CH}_3}-\text{H}$ 110 pm) and all bond angles were set equal to 120°. Geometry of the protonated molecules were taken according to Scheme 2 with bond length $\text{O}\cdots\text{H}^+$ 120 pm.

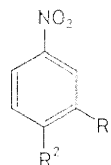
RESULTS AND DISCUSSION

Preparative photolyses of the nitrophenyl acetates *I-IV* gave the corresponding phenols *V-VIII* as sole photoproducts. From quantum yields collected in Table I it follows that 3-nitrophenyl acetate (*II*) exhibits about three times higher reactivity than the isomeric 4-nitrophenyl acetate (*I*), which indicates a *meta*-activating effect of the nitro substituent. This difference in photochemical reactivity is much enhanced by introducing a methoxyl into the *ortho*-position with respect to the acetoxy group, since the acetate *IV* is as much as three orders of magnitude more reactive in comparison with its isomer *III*.

TABLE I

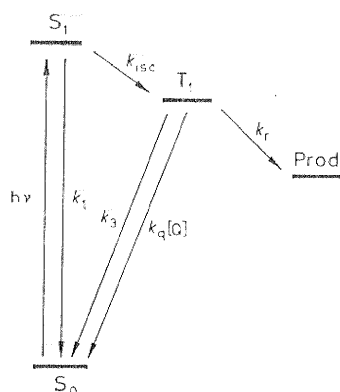
Quantum yields, Φ_r , of the photochemical hydrolysis of the acetates *I-IV* in aqueous solutions at pH 7.0 (0.066 mol l^{-1} phosphate buffer) with UV light (313 \pm 5 nm)

Substrate	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>
c_s , mmol l^{-1}	0.17	0.28	0.21	0.10
Photoproduct	<i>V</i>	<i>VI</i>	<i>VII</i>	<i>VIII</i>
Φ_r	0.002	0.006	0.002	0.129



- I, $R^1 = H$; $R^2 = OCOCH_3$ V, $R^1 = H$; $R^2 = OH$
 II, $R^1 = OCOCH_3$; $R^2 = H$ VI, $R^1 = OH$; $R^2 = H$
 III, $R^1 = OCH_3$; $R^2 = OCOCH_3$ VII, $R^1 = OCH_3$; $R^2 = OH$
 IV, $R^1 = OCOCH_3$; $R^2 = OCH_3$ VIII, $R^1 = OH$; $R^2 = OCH_3$

The quantum yield of photohydrolysis of IV is strongly dependent on the concentration of 2,4-hexadienoic acid as a triplet quencher (see Table II). The pronounced quenching effect can be interpreted as the involvement of a triplet state and it enables us to propose Scheme 1 for the mechanism of the photosolvolyis.



SCHEME 1

In the Scheme 1, k_1 (k_3) is the rate constant of the excited singlet (triplet) state monomolecular decay, k_{isc} stands for the rate constant of intersystem crossing, k_q is the

TABLE II

Quantum yield of photohydrolysis of acetate IV (0.10 mmol l^{-1}) in neutral aqueous solution (0.066-M phosphate buffer, pH 7.0), Φ_T , in dependence on the concentration of 2,4-hexadienoic acid. c_{HDA}

c_{HDA} , mmol l^{-1}	0.00	0.33	0.66	1.00	1.33
Φ_T	0.129	0.098	0.075	0.060	0.051

rate constant of the quenching process and k_r the pseudomonomolecular rate constant of the solvolysis. Applying the steady-state approximation we obtain for the dependence of the relative reciprocal quantum yield on the quencher concentration the equation (1),

$$\frac{\phi_0}{\phi} = 1 + \frac{k_q}{k_r + k_3} [Q]. \quad (1)$$

The coefficient at $[Q]$, often denoted as the Stern-Volmer constant K_{SV} , was calculated by least-squares analysis of the quenching data (see Fig. 1) and has the value of 1150 l mol^{-1} . Provided that the bimolecular quenching is diffusion-controlled¹¹ we can estimate the rate constant k_q from the viscosity of the solvent ($0.8 \cdot 10^{-3} \text{ Pa s}$) and from the absolute temperature (298 K) using an empirical formula¹¹, $k_q \approx 7.5 \cdot 10^9 \text{ l mol}^{-1} \text{ s}^{-1}$. Taking into account that $K_{SV} = k_q \tau_{\text{eff}}$ we can calculate the effective triplet lifetime, $\tau_{\text{eff}} = (k_r + k_3)^{-1} = 1.5 \cdot 10^{-7} \text{ s}$.

We have observed that the photochemical hydrolysis of *IV* is acid-catalyzed. The photoreaction is accelerated even in mildly acidic media (see Fig. 2) and the quantum yield increases up to very high concentrations of perchloric acid (see Fig. 3).

The curved shape of the dependence shown in Fig. 3 can possibly be interpreted in terms of a change in reaction mechanism in the highly acidic media, most probably due to the involvement of a second protonation site. For the interpretation of the acid catalysis itself, there are two hypotheses at hand, i.e., either the ground state

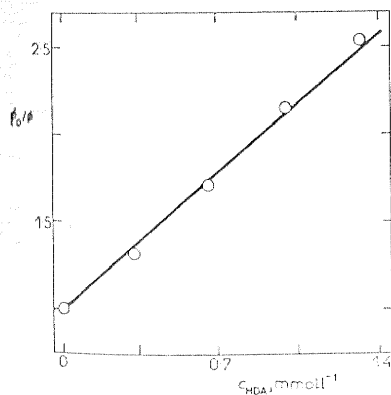


FIG. 1
Stern-Volmer plot for the quenching of the photohydrolysis of *IV* (0.10 mmol l^{-1}) in neutral aqueous solution by 2,4-hexadienoic acid (HDA)

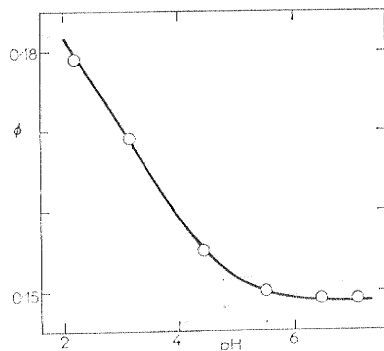


FIG. 2
Quantum yields, ϕ_0 , of the photohydrolysis of *IV* (0.10 mmol l^{-1}) in mildly acidic solutions (phosphate/citrate buffers)

and singlet (triplet) state monomer-system crossing, k_q is the

$10^9 \text{ l mol}^{-1} \text{ s}^{-1}$) in neutral aqueous solution
concentration of 2,4-hexadienoic

1.00 1.33

0.060 0.051

is protonated and the protonated species is photoexcited or, conversely, the protonation follows the excitation. The two possibilities are discussed below.

We have observed that the shape of the electronic absorption spectrum of *IV* is independent on the concentration of acid up to the point where it could not be measured due to the thermal hydrolysis (approx. 2M-HClO₄). On the other hand, electronic spectra of two hypothetical protonated forms of *IV* (see Scheme 2) calculated by the CNDO/S-LCI method differ considerably from the spectrum of unprotonated *IV*, while there is reasonable agreement between the experimental and calculated S_0-S_1 transition energy for the latter species (see the data in Table III).

TABLE III

Experimental and calculated (CNDO/S-LCI) excitation energies of the S_0-S_1 ($\pi\pi^*$) transition for the acetates *I-IV* and their protonated forms $I-H_a^+$ – $IV-H_a^+$ (protonation on the acetyl group) and $I-H_b^+$ – $IV-H_b^+$ (protonation on the nitro group)

Compound	Exp.	Calculated ^a		
		<i>b</i>	H _a ⁺	H _b ⁺
<i>I</i>	4.68	4.50	3.76	2.81
<i>II</i>	4.27	4.34	3.58	2.42
<i>III</i>	3.94	4.22	3.55	2.41
<i>IV</i>	4.23	4.34	3.46	2.56

^a eV; ^b unprotonated molecule.

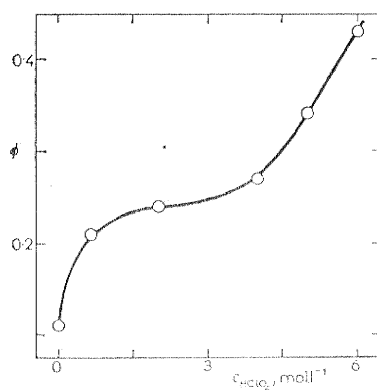


FIG. 3

Quantum yields, ϕ , of the photohydrolysis of *IV* (0.10 mmol l^{-1}) in strongly acidic solutions ($0.6-6.0 \text{ mol l}^{-1} \text{ HClO}_4$)

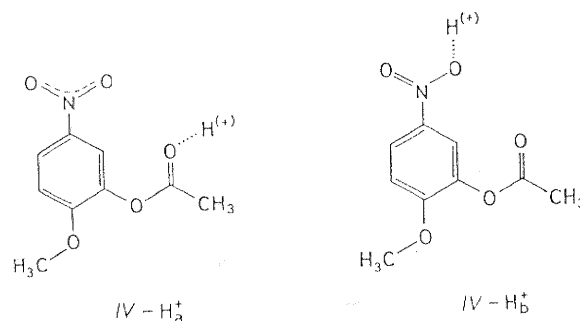
or, conversely, the photo-

absorption spectrum of *IV* at 313 nm, where it could not be assigned to the $S_0 \rightarrow S_1$ ($\pi\pi^*$) transition of *IV* (see Scheme 2) calculated from the spectrum of unprotonated *IV* (see the data in Table III).

of the $S_0 \rightarrow S_1$ ($\pi\pi^*$) transition (protonation on the acetyl group)

H^+
2.81
2.42
2.41
2.56

Φ_p of the photohydrolysis (mol l⁻¹) in strongly acidic solution (6.0 mol l⁻¹ HClO₄)



SCHEME 2

From the comparison of theoretical and experimental spectral data it follows that the protonation equilibrium is shifted almost completely to the side of the unprotonated *IV*, up to approximately 2M-HClO₄. On the contrary, the photolysis of *IV* (10^{-4} mol l⁻¹) is accelerated even at the concentration of 10^{-4} mol l⁻¹ H⁺, *i.e.*, under the conditions where the equilibrium concentration of a protonated form would be by a factor 10^{-8} lower than the equilibrium constant. As a corollary, the protonated form could not be identical with the light-absorbing species with respect to the inner filtration effect due to the parent unprotonated *IV* (molar absorption coefficient $1.010 \text{ m}^2 \text{ mol}^{-1}$ at 313 nm). Thus, the protonation of the substrate occurs in its electronically excited state.

In the photohydrolysis of acetate *IV* there are two possible pathways leading to the formation of phenol *VIII*, *i.e.*, the reaction could hypothetically occur either as a nucleophilic substitution on the phenyl ring carbon atom or as a hydrolysis of the ester bond. We have performed the photolysis of *IV* in H₂¹⁸O and have found that there was no incorporation of ¹⁸O into the product molecule; this is an unambiguous evidence that the photolysis of *IV* occurs exclusively as a hydrolysis of the ester bond, as in the case of the photoreaction of *meta*-nitrophenyl phosphate in neutral aqueous solution² mentioned above.

Having determined the selectivity of the photoreaction we have an important clue for a theoretical interpretation of the difference between the photochemical reactivity of various nitrophenyl acetates. Nevertheless, preliminary quantum-chemical calculations (based on the assumption of an attack of water molecule on the carbonyl carbon of the protonated excited substrate) were not able to interpret the difference in reactivity between *III* and *IV*.

In summary, we can conclude that the nitro group has a *meta*-activating effect on the course of the photochemical hydrolysis of nitrophenyl acetates which is especially pronounced in the case of isomeric acetates *III* and *IV*. The light-induced hydrolysis of *IV* occurs in such a way that, after absorption of a light quantum, the molecule

is protonated in one of the early photochemical steps. Then the protonated triplet state undergoes hydrolysis of the ester bond.

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