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ON THE REGIOSELECTIVITY OF THE NUCLEOPHILIC AROMATIC PHOTOSUBSTITUTIONS OF 4-NITROVERATROLE. A THREEFOLD MECHANISTIC PATHWAY.

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Abstract.- 4-Nitroveratrole (NVT) is photosubstituted with primary amines, piperidine and hydroxide ion. Primary amines and hydroxide ion cause replacement of the methoxy group in meta position with respect to the nitro group whereas piperidine photosubstitutes the methoxy group in para to the nitro group. Photoreactions with piperidine and hydroxide ion involve attack of the amine upon a triplet excited state of NVT. Mechanistic evidences indicate that the reaction with hydroxide ion is probably a $S_N2\ ^3Ar^*$ process whereas the reaction with piperidine involves a radical ion pair formed via electron transfer from the amine to a triplet excited state. Photoreactions with primary amines involve attack of the amine upon a singlet excited state of NVT ($S_N2\ ^1Ar^*$ process). These results are discussed and justified in the context of nucleophile ionization potential considerations and ground state donor-acceptor complex formation abilities.

INTRODUCTION

Nucleophilic Aromatic Photosubstitutions have been the object of intense research since their discovery in 1956.[1] In spite of the important effort done, mechanistic studies have been almost restricted to photohydrolysis reactions.[2] Recently Varma and coworkers have applied the Laser Flash Photolysis technique to the study of the photohydrolysis of several nitrophenyl ethers (3,5-dinitroanisole[3,4] and 3-nitroanisole[4]), proposing a general mechanistic scheme involving fast reaction between the nucleophile (hydroxide ion) and the nitrophenyl ethers triplet excited state which gives rise to a series of σ-complexes in the ground state.

Van Riel et al.[5] have pointed out the existence of three kinds of pathways leading to nucleophilic aromatic photosubstitutions: 1) direct displacement (S_N2Ar^*); 2) electron tranfer from the "nucleophile" to the aromatic substrate and 3) electron transfer from the aromatic compound to an acceptor followed by attack of the nucleophile on the aromatic radical-cation. In recent years several research groups have directed their attention to these reactions. In connection with our proposal of nitrophenyl ethers as photoactivatable moieties in photoaffinity labelling[6], we reported[7] in 1984 that the well known meta-orientation of the nitro group in intermolecular nucleophilic aromatic photosubstitutions (the reverse of the orientation in thermal reactions) only clearly holds for hydroxide ion as a nucleophile since when amines are used the regioselectivity depends upon the features of the nucleophile. The meta regioselectivity is observed for amines of high ionization potential, but it changes into para when amines of lower ionization potential are used. We have recently published[8] an explanation for these experimental results based on some qualitative mechanistic studies with 4-nitroanisole. Our evidences indicated that meta substitution is produced through a S_N2Ar^* reaction whereas para substitution arises from a radical ion-pair via electron transfer from the amine to a triplet excited state of the aromatic partner. This explanation agrees well with the general orientation rules for nucleophilic aromatic photosubstitution reactions proposed by Mutai et al.[9] and developed originally from their studies on photo-Smiles rearrangement reactions[10]. Almost simultaneously to the publication of our mechanistic proposal[8] a new example of change on regioselectivity with the ionization potential of the amine nucleophiles was reported[11] using 1-methoxy-4-nitronaphthalene as the aromatic substrate. Mechanistic studies on these reactions using flash photolysis and continuous irradiation techniques led to the proposal of an explanation of the reported experimental facts which was nearly identical to that simultaneously given by us.

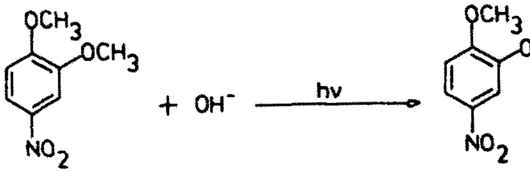
In the present paper we want to report the results and the conclusions of a mechanistic study on the reactions of 4-nitroveratrole (NVT) with primary amines, piperidine and hydroxide ion.

Herewith, a third previously non described (in intermolecular photosubstitutions) mechanistic pathway is proposed, namely a S_N2Ar* reaction through a singlet excited state. Its operativity is possibly due to the existence of a complex in the ground state. This pathway occurs in addition to the previously proposed S_N2Ar* and electron transfer mechanisms through the triplet excited state.

RESULTS.-

Photohydrolysis of 4-nitroveratrole

In agreement with the reported facts[1a,12] the irradiation (400W medium pressure Hg lamp, pyrex filter) for 2h of a solution of 400mg (2.19 mmole) of 4-nitroveratrole and 1.58g (0.034 mmole) of NaOH in 0.91 of THF-water (1:9) affords 2-methoxy-5-nitrophenol, 1, (96% isolated yield based on consumed starting material). No 2-methoxy-4-nitrophenol could be detected. Overall quantum yields for the production of 1 were measured at different nucleophile concentrations (Table 1). Quantum yield increases by increasing the nucleophile concentration and reaches a maximum at about 36-fold excess of nucleophile. This result is similar to that observed for the photohydrolysis of 3,5-dinitroanisole[3] for which a bimolecular mechanism has been proposed.



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The multiplicity of the reactive excited state was investigated using potassium sorbate as selective triplet quencher[13] (Table 2). There is a significant quenching effect which indicates the participation of a triplet excited state. This result agrees with those reported for the photohydrolysis of 3,5-dinitroanisole[3] and 3-nitroanisole[4]. The results of Tables 1 and 2 confirm the assignment of our reaction to the S_N2^3Ar* mechanistic class, as previously stated by Havinga et al.[5] Our quantum yields (in methanol-water 5:95) are smaller than those reported by Stratenous[12] for the same reaction carried out in THF-water (10:90). Moreover, our reaction shows an extreme sensitivity to the amount of methanol present in the solvent (Table 3) in contradiction to the well established fact[5] that S_N2^3Ar* reactions have a reduced sensitivity to solvent polarity. We attribute the results of table 3 to the operativity of a degenerate reaction: photosubstitution by methoxide ion, which reduces the photohydrolysis quantum yield.

Table 1.- Overall quantum yield of production of 1 in the photoreaction of NVT (1x10^{-3}M) with hydroxide ion in methanol/water (5:95 v.v) at different nucleophile concentrations.

$[OH^-]$	0.021	0.025	0.035	0.081	0.200	0.300	0.400	0.600
Φ^{334}	0.025	0.027	0.029	0.032	0.033	0.035	0.035	0.035

Table 2.- Overall quantum yield of production of 1 in the photoreaction of NVT (1x10^{-3}M) with hydroxide ion (0.3 M) in methanol/water (5:95 v.v) in the presence of different concentrations of potassium sorbate (Q).

$[Q]$	0	0.029	0.052	0.081	0.099	0.115	0.149
Φ^{334}	0.035	0.034	0.033	0.033	0.032	0.031	0.030

Table 3.- Overall quantum yield of production of 1 in the photoreaction of NVT ($1x10^{-3}$) with hydroxide ion (0.08 M) in different mixtures methanol/water.

Methanol/water (v:v)	25/75	22/78	20/80	10/90	5/95	1/99	water
Φ^{334}	0	0.002	0.013	0.017	0.033	0.059	0.069

Photoreactions of 4-nitroveratrole with primary amines

The preparative photoreaction between 4-nitroveratrole and excess methylamine in MeOH-water (20:80) (pH = 10, 4h irradiation with a 400W medium pressure Hg lamp and pyrex filter) gave two isomeric anilines: N-methyl-2-methoxy-5-nitroaniline[7,14], 2, (81% yield based on consumed starting material) and a small amount of N-methyl-2-methoxy-4-nitroaniline[7,14], 3. These isomeric products were fully characterized by spectroscopic methods.[15] The evolution of this reaction with time as shown in figure 1 features a clear isosbestic point.

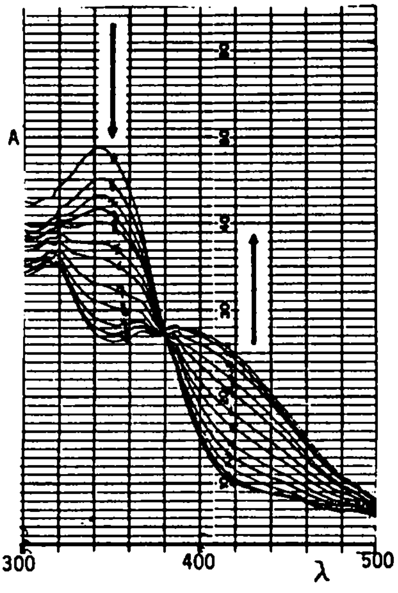
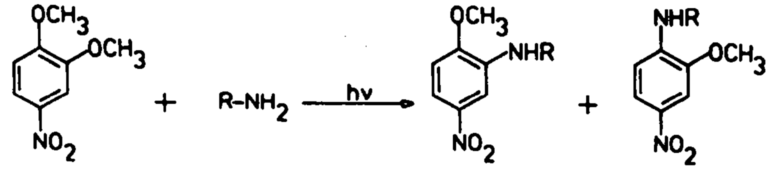


Fig. 1.- UV spectrum evolution with time in the reaction of NVT with methylamine.

The photoreaction between 4-nitroveratrole and n-hexylamine was carried out under similar conditions (uncontrolled pH) giving a 22% yield of N-(1-hexyl)-2-methoxy-5-nitroaniline, 4, and a minor amount of the isomer N-(1-hexyl)-2-methoxy-4-nitroaniline, 5, together with small amounts of photoreduction products. Products 4 and 5 were identified by spectroscopic methods. Thus, the UV spectra and the aromatic protons patterns in ^1H NMR are characteristic and different. The first assignment was made by simple comparison of the ^1H NMR spectra with those of of the N-methyl anilines 2 and 3. The use of homonuclear NOE experiments confirmed our first assignment. Moreover, isomer 5 was independently prepared by the thermal substitution reaction.



R= CH_3 (for 2 and 3)
R= C_6H_{13} (for 4 and 5)

2 (major)
4 (major)

3 (minor)
5 (minor)

Qualitative experiments. In Table 4 the relative yields (ϕ_{meta}/ϕ_{para}) of production of meta and para isomers for several photoreactions of 4-nitroveratrole with methyl and n-hexylamine are reported. The experiments with n-hexylamine have been previously reported and discussed.[8] It was preliminary concluded that the meta photosubstitution product, 4, is produced in a S_N2Ar^* reaction from singlet and perhaps partially from triplet excited states, whereas the para photosubstitution product, 5, arises from a radical ion pair via electron transfer from the amine to a triplet excited state. From Table 4 it can be deduced that the results with methylamine follow the same pattern. The sensitization of the production of 3 in front of 2 is noteworthy (reaction 7): even though it is small the result agrees with those obtained with triplet quenchers. Also interesting is the pH effect (reactions 1 and 10). A similar effect has been reported[16] for the photoreaction of 4-nitroveratrole with n-butylamine although no explanation was advanced. The main effect of the pH variation consists in the change of the free amine concentration, being this concentration higher at higher pH values. The observed result is in agreement with the variation of ϕ_{meta}/ϕ_{para} with the concentration of amine at uncontrolled pH (Table 5).

Table 4.- Effect of triplet quenchers, radical scavengers, solvents and pH on the photoreactions of NVT with methylamine and n-hexylamine[a] (pyrex filter).

Entry	Nucleophile[b]	Solution saturated with	Solvent	pH	Additive	ϕ_{meta}/ϕ_{para}
1	CH_3NH_2	Argon	CH_3OH/H_2O(20:80)	10[c]	---	4.4
2	$C_6H_{13}NH_2$	Argon	CH_3OH/H_2O(20:80)	d	---	4.2
3	$C_6H_{13}NH_2$	Air	CH_3OH/H_2O(20:80)	d	---	5.9
4	CH_3NH_2	Argon	CH_3OH/H_2O(20:80)	10[c]	Potassium sorbate	>30
5	$C_6H_{13}NH_2$	Air	CH_3OH/H_2O(20:80)	d	Potassium sorbate	>30
6	$C_6H_{13}NH_2$	Air	CH_3OH/H_2O(20:80)	d	1,3-cyclohexadiene	>30
7	CH_3NH_2	Argon	CH_3OH/H_2O(20:80)	10[c]	Benzophenone	2.8
8	$C_6H_{13}NH_2$	Air	CH_3OH/H_2O(20:80)	d	m-dinitrobenzene	>30
9	$C_6H_{13}NH_2$	Argon	CH_3OH/H_2O(20/80)	d	Methylviologen	>30
10	CH_3NH_2	Argon	CH_3OH/H_2O(20:80)	14	---	9.0
11	CH_3NH_2	Argon	i-PrOH/H_2O(95:5)	10[c]	---	>30
12	CH_3NH_2	Argon	CH_3OH/H_2O(75:25)	14	---	>30
13	$C_6H_{13}NH_2$	Air	i-PrOH	d	---	22
14	$C_6H_{13}NH_2$	Air	Hexane	d	---	e

a.- The reactions with n-hexylamine have been previously reported in ref.8. b.- Large excess of nucleophile. c.- After free base liberation from the hydrochloride pH 10 was achieved by addition of HClaq. d.- Uncontrolled pH. d.- Very complex mixture of products.

Table 5.- Variation of the ϕ_{meta}/ϕ_{para} ratio with the concentration of nucleophile in the photoreaction of NVT with n-hexylamine (Pyrex filter).

[Nu]/[NVT]	19/1	45/1	90/1	178/1	446/1
ϕ_{meta}/ϕ_{para}	1.81	1.82	3.03	4.20	5.75

Quantum yield measurements. We decided to carry out the quantitative measurements with n-hexylamine due to the fact that the volatility of methylamine would introduce large errors in its concentration values.

Overall quantum yields for the production of 4 were measured at different nucleophile concentrations (Table 6). Quantum yield increases by increasing n-hexylamine concentration. The multiplicity of the reactive excited state was investigated using potassium sorbate as selective triplet quencher (Table 7). The production of the meta isomer is independent of the triplet quencher concentration. This result suggests the involvement of a singlet as intermediate excited state for the production of the meta isomer. In all the quantum yield measurement experiments we have used a relatively narrow irradiation band ($\lambda \approx 334$nm)[29] to make sure that the quencher did not absorb light. Indeed, potassium sorbate has an UV absortion that goes over 300nm. This previously unnoticed quencher absortion was responsible for the mechanistic pathway (singlet or triplet) to the meta isomer being undefined in our preliminary note[8] where experiments were performed using only a pyrex filter ($\lambda > 290$nm).

Table 6.- Overall quantum yields of production of 4 in the photoreaction of NVT (1×10^{-3}) with n-hexylamine in methanol/water (20:80 v.v) at different nucleophile concentrations

$[C_6H_{13}NH_2]^a$	0.091	0.120	0.187	0.284	0.384	0.479
Φ^{334}	0.026	0.031	0.051	0.076	0.084	0.114

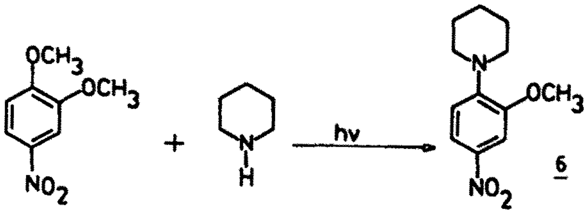
a.- Amine real concentrations once substracted the amount of ammonium cation produced by basic hydrolysis.

Table 7.- Overall quantum yields of production of 4 in the photoreaction of NVT (1×10^{-3}M) with n-hexylamine (0.3 M) in methanol/water (20:80 v.v) in the presence of different concentrations of potassium sorbate (Q).

[Q]	0	0.075	0.100	0.200	0.300	0.400
Φ^{334}	0.088	0.163	0.132	0.086	0.114	0.105

Photoreactions of 4-nitroveratrole with piperidine

The preparative photoreaction between 4-nitroveratrole and piperidine in MeOH-water (20:80) (4h irradiation with a 400W medium pressure Hg lamp and pyrex filter) afforded only the para photosubstitution product: N-(2-methoxy-4-nitrophenyl)piperidine, 6, (25% yield based on consumed starting material). No meta photosubstitution product was detected. Product 6 was characterized by spectroscopic methods as previously described for 5. At the temperature at which the photoreaction was carried out (room temperature) no thermal reaction took place.



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When the photoreaction was carried out in isopropanol the yield of photosubstitution product dropped to zero. However, a glc analysis of the reaction mixture showed a complete conversion of the starting material. We attribute this to competitive photoreduction processes. It is well known[17,18,19] that the two accepted mechanisms for photoreduction of aromatic nitrocompounds involve hydrogen atom abstraction by the nitroaromatic triplet state or by a radical anion derived from it. This abstraction is much more favoured in isopropanol than in methanol.

The reaction in methanol-water (20:80) and in the presence of m-dinitrobenzene was completely quenched (m-dinitrobenzene does not interact with NVT lowest triplet state[20]), thus supporting the operativity of an electron transfer step in the pathway leading to the para photosubstitution product.

Quantum yield measurements. Overall quantum yields for the production of 6 were measured at different nucleophile concentrations (Table 8). Quantum yields increase by increasing the nucleophile concentration. The multiplicity of the reactive excited state was investigated using potassium sorbate as selective triplet quencher (Table 9). There is a significant quenching effect due to the potassium sorbate which indicates the involvement of a triplet excited state.

Table 8.- Overall quantum yields of production of 6 in the photoreaction of NVT ($1x10^{-3}M$) with piperidine in methanol/water (20:80 v.v) at different nucleophile concentrations.

[Piperidine]^a	0.185	0.281	0.378	0.476	0.966
Φ^{334}	0.007	0.011	0.016	0.025	0.046

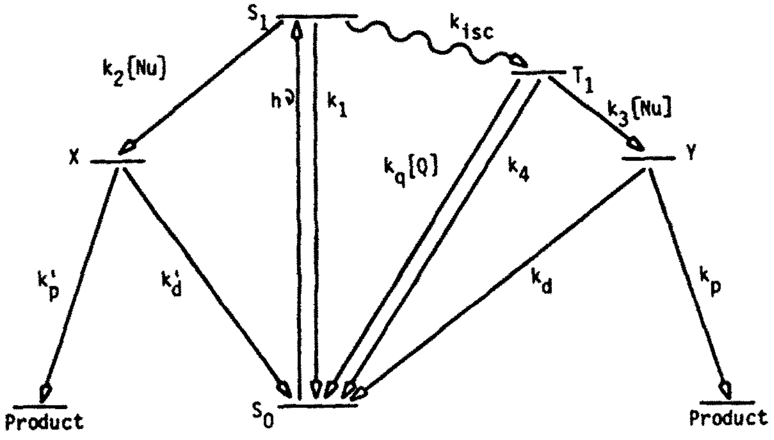
a.- Amine real concentrations once substracted the amount of ammonium cation produced by basic hydrolysis.

Table 9.- Overall quantum yields of production of 6 in the photoreaction of NVT ($1x10^{-3}M$) with piperidine (0.5 M) in methanol/water (20:80 v.v) in the presence of different concentrations of potassium sorbate (Q).

[Q]	0	0.01	0.02	0.06	0.10	0.30
Φ^{334}	0.026	0.009	0.005	0.002	0.001	0.001

DISCUSSION.-

On the basis of the above results and those previously reported by us[8] we suggest the overall kinetic scheme of Scheme 1 for the reactions considered in the present work.



SCHEME 1

The photohydrolysis of 4-nitroveratrole occurs through a triplet excited state to a complex Y, possibly in the ground state surface, and finally to the meta photosubstitution product in which seems to be a typical S_N2^3Ar* reaction.[5] The application of the steady-state approximation to the right part of the scheme in the absence of quenchers leads to the equation 1:

$$\Phi = \Phi_{isc} \cdot \frac{k_p}{k_p + k_d} \cdot \frac{k_3[Nu]}{k_4 + k_3[Nu]} \qquad \text{eq. 1}$$

and from eq. 1:

$$\frac{1}{\Phi} = \frac{1}{\Phi_{isc}} \cdot \frac{k_p + k_d}{k_p} \cdot \left(1 + \frac{k_4}{k_3\ Nu}\right) \qquad \text{eq. 2}$$

Therefore, if the scheme applies and the photohydrolysis product comes from a single origin a linear relationship between Φ^{-1} and $[Nu]^{-1}$ should be observed. Indeed, this is the case, the relationship being represented in Figure 2A. A regresion analysis of the dependence of Φ^{-1} upon $[OH^-]^{-1}$ using the values of Table 1 gave a linear equation (c.c. 0.985): $\Phi^{-1} = (28.1 \pm 0.4) + (0.23 \pm 0.02)[OH^-]^{-1}$. From eq. 2 we have that k_4/k_3 equals the slope to intercept ratio, therefore: $k_4/k_3 \simeq 8.2 \times 10^{-3}$.

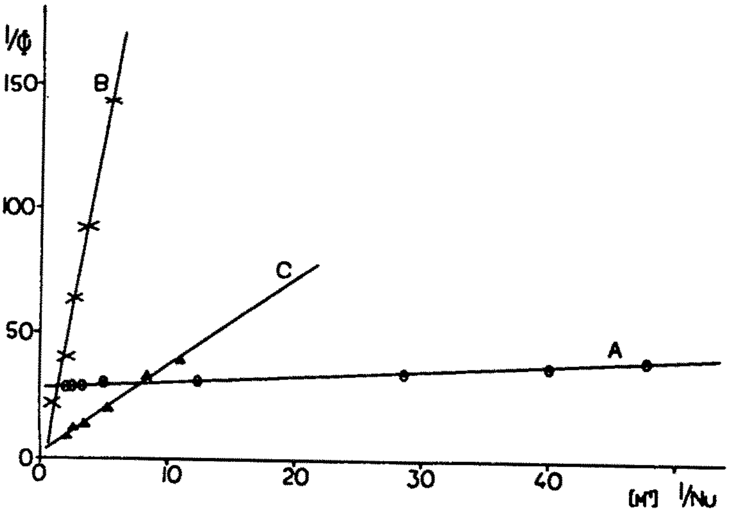


Fig. 2.- Plot of the inverse quantum yield of production of the main photosubstitution product *vs.* inverse nucleophile concentrations. (A) Photohydrolysis of NVT (*meta* isomer, 1, data from Table 1). (B) Photoreaction of NVT with piperidine (*para* isomer, 6, data from Table 8). (C) Photoreaction of NVT with n-hexylamine (*meta* isomer, 4, data from Table 6).

According to the Stern-Volmer analysis the dependence of the relative reciprocal quantum yield on the quencher concentration is given by equation 3:

$$\frac{\Phi_o}{\Phi} = 1 + \frac{k_q}{k_3\ Nu + k_4}[Q] \qquad \text{eq. 3}$$

Using the values of Table 2 the figure 3 is obtained and a least squares fit gave the following equation (c.c. 0.990): $\Phi_o/\Phi = (0.995 \pm 0.006) + (0.999 \pm 0.063)[Q]$. Therefore, $k_q/k_3[Nu] \simeq 1$ and considering[20] $[Nu] = 0.3M$ and $k_q \simeq 0.6 \times 10^9$ (See also ref. 4 for a discussion on the low k_p value of some aromatic nitrocompounds), the value $k_3 \simeq 1.9 \times 10^9\ mol^{-1}\ s^{-1}$ can be determined. Since k_4/k_3 is now known, the value $k_4 \simeq 1.5 \times 10^7\ s^{-1}$ arises. This value represents a $\tau \simeq 6.4\ 10^{-6}$ s for the triplet state in our experiments in the absence of nucleophile and quencher. The decay rate constant for the 4-nitroveratrole triplet state has been measured[20] in acetonitrile-water (20:80) and dioxane-water (20:80) being $k'_4 = 0.5\ 10^6$. This discrepancy can be attributed to the fact that in our cases k_4 includes $k_{MeO^-}[MeO^-]$. The concentration of MeO^- in a solution 0.3M in hydroxide ion in methanol-water (5:95) is 3.5×10^{-5}M. From these values an estimation of k_{MeO} can be deduced, $k_{MeO} \simeq 4.4 \times 10^9\ M^{-1} s^{-1}$, in the difussion control limit but of the same order than k_{OH} (k_4 in our Scheme).

From the interception of the linear equation of Φ^{-1} *vs* $[OH^-]^{-1}$ (eq. 2) an estimation of the efficiency of product production once the triplet has interacted with the nucleophile $(k_p/(k_p+k_d))$ can be deduced. We have measured the Φ_{ISC} for NVT in methanol to be ≥ 0.3 (see the Experimental part). From Figure 2A: $(k_p+k_d)/k_p)(\Phi_{ISC})^{-1} = 28.1$ and $k_p/(k_p+k_d) = 0.12$. Considering the relative high efficiency of the nucleophile-triplet productive interaction ($k_3/k_4 = 122$) we can say that the relatively low quantum yields observed in this photoreaction are due to the low efficiency in the other branching points.

A parallel analysis considering the data for the reaction of piperidine (Tables 8 and 9) could not be performed because data in Table 8 (Figure 2B) are not good enough to get confident equation parameters (least square analysis). Furthermore in Figure 4 a curvature of the graphic of Φ_o/Φ vs $[Q]$ can be observed at high quencher concentrations, probably due to the contribution of the thermal process once Φ gets very small. Therefore we can only treat our data in a qualitative manner. From Tables 8 and 9 and Figures 2B and 4 we can state that the para photosubstitution product in this reaction is of single origin and it comes from triplet excited state. From Table 9 at low quencher concentrations (4 first points) an estimation of $(k_Q/(k_4+k_3\ \mathrm{Nu}\ )) = 226 \pm 6$ is obtained (least square analysis, cc.0.999), what implies that piperidine interacts (productively) in a much less efficient manner with the NVT lower triplet excited state than hydroxide ion does.

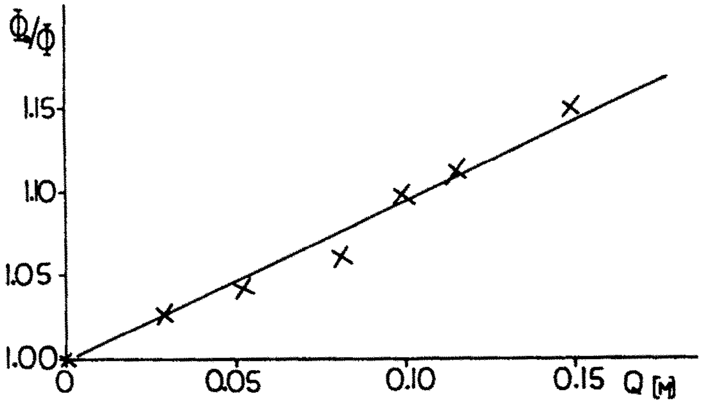


Fig. 3.- Plot of the relative inverse quantum yield of production of the meta photosubstituted product, 1, vs. quencher concentrations (potassium sorbate) in the photohydrolysis of NVT (Data from Table 3).

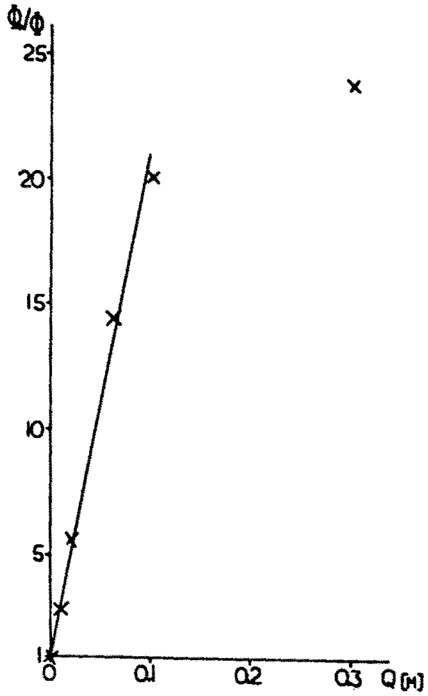


Fig. 4.- Plot of the relative inverse quantum yield of production of the para photosubstituted product 6 in the photoreaction of NVT with piperidine (Data from Table 9).

Qualitative experiments, reaction regioselectivity, and parallel experiments carried out with n-hexylamine (vide infra) lead us to the conclusion that the productive interaction between piperidine and NVT triplet excited state is carried out through single electron transfer, being Y (Scheme 1) in the present case a radical ion pair that can collapse to a sigma complex (precursor of the photosubstitution product), or diffuse away giving rise to photoreduction products or starting material. Recently exciplexes have been postulated as intermediates previous to the electron transfer step[21] in a related process.

Qualitative experiments[8] already indicated that the production of the *meta*-photosubstitution isomer in the reaction of NVT with n-hexylamine is much less sensitive to the presence of triplet quenchers than the production of the *para*-isomer. Our present data confirm that preliminar result for primary amines and the data in Table 7 indicate that the *meta* isomer must come from a singlet excited state. We can now apply the steady-state approximation to the left side of the Scheme 1 obtaining equation 4:

$$\Phi = \frac{k'_p}{k'_p+k'_d} \; \frac{k_2[Nu]}{k_{isc}+k_1+k_2[Nu]} \qquad \text{eq. 4}$$

and from eq.4:

$$\frac{1}{\Phi} = \frac{k'_p+k'_d}{k'_p}\left(1 + \frac{k_1+k_{isc}}{k_2[Nu]}\right) \qquad \text{eq. 5}$$

Representation of Φ^{-1} *vs* $[Nu]^{-1}$ for the production of *4* (*meta* isomer) in the reaction of NVT with n-hexylamine is shown in Figure 2C. Least square analysis of data from Table 6, produces a good strait line (cc. 0.995) with empirical formulae: $\Phi^{-1} = (2.0\pm1.0) + (3.41\pm0.16)[Nu]^{-1}$. From it $(k_1+k_{isc})/k_2 \approx 1.7$. Lifetimes of 3,5-dinitroanisole[22] and 2-nitronaphthalene[23,24] have been measured by picosecond laser flash photolysis in several aqueous solvents being the values $1.2\text{x}10^{-11}$s and $1.6\text{x}10^{-11}$s respectively. The corresponding lifetime for 3-nitroanisole has been studied only in acetonitrile and trifluoroethanol being the value[22] $7\text{x}10^{-12}$s in both cases. Due to the extremely rapid deactivation of the singlet excited state no big differences are expected in different solvents. Assuming a similar limiting value for 4-nitroveratrole $k_1+k_{isc} \geqslant 6\text{x}10^{10}s^{-1}$, $k_2 \approx 3.5\text{x}10^{10}M^{-1}s^{-1}$ is obtained. This value is well above the diffusion control limit in our solvent. This high value suggest a preorganization in the ground state previous to excitation. Amines and nitroaromatics can interact in the ground state giving a loose donor-acceptor complex (no changes in the NVT U.V. spectrum are observed when the amine is added), that on excitation produces reaction (primary amines) or deactivation and intersystem crossing (secondary amines). It is well known that tertiary amines quench the fluorescence of aromatics by electron transfer and fast back electron transfer leading to faster non radiative decay and intersystem crossing. Recently bimolecular quenching constants exceeding the theoretical diffusion control limit have been reported[25]. Secondary amines may behave similarly with respect to NVT singlet excited state. A point that support this interpretation is the fact that hydroxide ion does not react via singlet excited state. The reaction is very similar in its general features but it goes via the triplet excited state. No complex must be present in the ground state in this case and therefore hydroxide ion is unable to interact with the singlet excited state that decays or gives intersistem crossing to fast.

Analysis of the equation obtained from Figure 2C (Table 6) shows that the efficiency in the substitution reaction once *X* is reached (Scheme 1) is rather high, $k'_p/(k'_p+k'_d)= 0.5$. Calculated values for k_2 and efficiency from *X* should be considered as lower limits due to the fact that we do not exactly know the concentration of the ground-state donor-acceptor complex between the amine and 4-nitroveratrole that on excitation gives rise to photosubstitution.

The variation of the ratio ϕ_{meta}/ϕ_{para} with the concentration of nucleophile (Table 5) and the variation (Table 4) of this ratio with the pH of the solution (the pH will control the amount of free amine in solution) also suggest the involvement of different excited states in the production of both photosubstitution products. Steady -state approximation, applied to Scheme 1 leads without considering the relative product efficiency from *X* and from *Y*, to equation 6.

$$\frac{\phi_{meta}}{\phi_{para}} \propto \frac{k_2k_4}{k_3k_{isc}} + \frac{k_2}{k_{isc}}[Nu] \qquad \text{eq. 6}$$

Therefore we should observe a linear relationship between ϕ_{meta}/ϕ_{para} and $[Nu]$.Table 5 results show that such a relationship seems to exist. A good straight line is not obtained because the used conversion was too high and no corrections were performed for the internal filter effect. It must be remarked that in case both photoproducts would have come from the same excited state, a non dependance of the quantum yields ratio on the nucleophile concentration would have been found (providing there is no other further step in the two pathways where the nucleophile acts in a different way).

Qualitative experiments reported in Table 4, indicate that methylamine behaves similarly to n-hexylamine, and therefore we think the Scheme proposed for n-hexylamine is general for the production of meta photosubstitution product when the nucleophile is a primary amine. From this Table 4 a parallelism is observed with respect to the production of the para isomer between those reactions and the reactions with secondary amines. We also believe the Scheme proposed for the piperidine photoreaction is general for the production of the para-isomer. This general Scheme agrees with the explanation given in the literature[9] for the observed change of regioselectivity in photo-Smiles reactions upon change of the amine type. In our case, and probably due to the fact we are dealing with intermolecular reactions, the electron transfer occurs to the triplet excited state.

CONCLUDING REMARKS.-

The photochemistry of methoxynitroaromatic compounds with nucleophiles has received renewed attention recently. A competition between S_N2Ar^* mechanism and electron transfer has been established recently in different cases[8,9,10,11]. Our work shows that this competition exists in the reaction of NVT with hydroxide ion (main $S_N2^3Ar^*$) and secondary amines (main electron transfer to the triplet excited state), but we have also demonstrated the existence of another previously non considered pathway for intermolecular reactions, namely $S_N2^1Ar^*$ photosubstutution on the singlet excited state, specialy feasible for primary amine nucleophiles. Future mechanistic studies should consider this third pathway that must be operative in some other reactions of nitrophenyl ethers. Thus, it has been reported[26] that m-nitroanisole reacts with liquid ammonia giving m-nitroaniline in a good S_N2Ar^* reaction but that on sensitization a different product, 2-methoxy-4-nitroaniline is obtained. This could be in agreement with our results, the unsensitized reaction being possibly $S_N2^1Ar^*$ and the sensitized one a reaction through electron transfer from the amine to the triplet excited state of m-nitroanisole.

Our results indicate that nucleophile ionization potential determine the reaction being of S_N2Ar^* or electron transfer class. The differenciation between $S_N2^3Ar^*$ and $S_N2^1Ar^*$ seems to be related with the donor-acceptor complex formation ability in the ground state. Finally, photosubstitution through electron transfer compites with photoreduction in intermolecular reactions.

EXPERIMENTAL.-

General information.

All melting points are uncorrected. PNMR and CNMR spectra were recorded at 80 and 20 MHz on a Brucker WP80SY spectrometer using TMS as internal standard. IR spectra were recorded on a Perkin--Elmer 1310 spectrometer. U.V. spectra were recorded on a Perkin-Elmer 550 UV/Vis spectrophotometer. Mass spectra were recorded on a Hewlett-Packard 5985B mass spectrometer. The GC analyses were performed on a HP-5890A Gass Cromatograph using a HP-Crosslinked dimethylsilicone Gum 12m x 0.2mm x 0.33 m film thickness capillary column. Quantum yield measurements were performed on a Applied Photophysics QYR15 merry-go-round apparatus. 4-Nitroveratrole was prepared by nitration of veratrole[27].

Preparative reactions.

Reaction mixtures were irradiated in a 1l pyrex inmersion well reactor. A 400W medium pressure Hg lamp was used as light source. The solutions were irradiated for 4h. Photohydrolysis of 4-nitroveratrole (0.400 g, 2.19 mmol) in 900 ml of a solution 0.044 M of NaOH in THF/Water (1:9 v:v) afforded 2-methoxy-4-nitrophenol[5,28], 1, (96% yield based on the consumed starting material). Photoreaction between 4-nitroveratrole (0.233 g, 1.27 mmol) and methylamine (0.93 mols) in methanol/water (2:8 v:v) afforded 0.187 g of N-methyl-2-methoxy-5-nitroaniline[14], 2, (81% yield , based on the amount of consumed starting material).

N-(1-hexyl)-2-methoxy-5-nitroaniline, 4.- Irradiation of a solution of 0.69 g (3.8 mmol) of 4-nitroveratrole and n-hexylamine (3.78 mmol) in 700 ml of isopropanol afforded as a major product 4, (0.206 g, 22% yield), m.p. 34-36°C isolated by column chromatography through acid alumina using hexane as a eluent. IR (KBr): 3420, 1580, 1510, 1330 cm^{-1}. PNMR ($CDCl_3$): 0.9(t,3H), 1.3-1.8(m,8H), 3.2(dd,2H), 3.9(s,3H), 6.7(d,J=8.7Hz,1H), 7.4(d,J=2.5Hz,1H), 7.6(dd,J=8.7Hz,J=2.5Hz,1H). Irradiation at 3.9 (OMe) gives NOE enhancement (14.4%) at 6.7. CNMR($CDCl_3$): 13.85, 22.48, 26.74, 29.13, 31.51, 43.40, 55.91, 103.41, 107.81, 112.60, 138.72, 142.64, 151.41. UV (EtOH), $_{max}$ (nm): 203(log 3741), 263(log 4.050), 308(log 3.416), 378(log 3.276), 397(log 3.329). MS: m/e(%), 252(M,38), 181(100), 135(16), 43(11), 41(23). Calculated for $C_{13}H_{20}N_2O_3$: C,61.88; H,7.99; N,11.10. Found: C,61.80; H,7.96; N,11.12.

N-(1-hexyl)-2-methoxy-4-nitroaniline, 5.- A solution of 1.05 g (5.76 mmol) of NVT and 20 ml (151 mmol) of n-hexylamine in 70 ml of methanol was heated to 130°C in a sealed reactor for 4 days. After conventional work up and a column chromatography through acid alumina using benzene as eluent a mixture of NVT and 5, was obtained. N-(1-hexyl)-2-methoxy-4-nitroaniline, 5, was further purified as hydrochloride. Liberation of the free base afforded 0.275 g of 5, (20% yield), m.p. 67-68°C. IR (KBr): 3390, 1585, 1525, 1490, 1310 cm^{-1}. PNMR ($CDCl_3$): 0.9(t,3H), 1.2-1.8(m,8H), 3.2(dd,2H), 3.9(s,3H), 5.0(1H), 6.4(d,J=8.7Hz,1H), 7.6(d,J=2.5Hz,1H), 7.9(dd,J=8.7Hz,J=2.5Hz,1H). Irradiation at 3.9 (OMe) gives NOE enhancement (20.9%) at 7.6. CNMR ($CDCl_3$): 13.78, 22.41, 26.60, 29.03, 31.40, 42.97, 55.76, 104.64, 106.3, 119.84, 136.81, 144.42, 145.03. UV (EtOH), $_{max}$ (nm) : 207(log 3.839), 265(log 3.479), 400(log 4.098). MS: m/e(%), 252(M,27), 182(10), 181(100), 135(16). Calculated for $C_{13}H_{20}N_2O_3$: C,61.88; H,7.99; N,11.10. Found: C,61.66; H,8.15; N,11.10.

N-(2-methoxy-4-nitrophenyl)piperidine, 6.- Irradiation of a solution of 0.657 g (3.6 mmol) of NVT and 16.79 g (197 mmol) of piperidine in a mixture of 140 ml of methanol and 560 ml of water afforded after conventional work up and purification through an acid alumina column chromatography, using hexane as a eluent, 0.208 g (25% yield based on consumed starting material) of N-(2-methoxy--4-nitrophenyl)piperidine, 6, m.p. 74-75°C. IR (KBr): 3070, 2980, 2920, 1570, 1480, 1430, 1370, 1330 cm^{-1}. PNMR ($CDCl_3$): 1.7(6H), 3.2(4H), 3.95(s,3H), 6.85(d,J=8.7Hz,1H), 7.7(d,J=2.5Hz,1H), 7.9(dd,J=8.7Hz,J=2.5Hz,1H). Irradiation at 3.95 (OMe) gives NOE enhancement (17%) at 7.7. CNMR ($CDCl_3$): 24.24, 25.94, 51.32, 55.85, 106.78, 116.51, 117.82, 141.40, 148.57, 151.14. UV (EtOH) $_{max}$ (nm): 207(log 4.228), 388(4.055). MS: m/e(%), 236(M,100), 235(92), 189(15), 175(14), 150(14), 91(17), 78(17), 63(14), 41(21). Calculated for $C_{12}H_{16}N_2O_3$: C,61.00; H,6.83; N,11.86. Found: C,61.03; H,6.80; N,11.80.

Qualitative experiments and semipreparative reactions.-

Reaction mixtures were irradiated in a 100 ml pyrex inmersion well reactor. A 125W high pressure Hg lamp was used as light source. The solutions were irradiated for 1h. The amounts of photoproducts and unchanged starting material were determined by G.C. analysis.

Quantum yield measurements.-

Quantum yields for the photoproducts were measured using a merry-go-round apparatus. The irradiation source was a 250W medium pressure Hg lamp. The wavelenghth of excitation (334 nm) was selected using an appropiate filter solution[29a]. The amounts of photoproducts were determined by G.C. analysis as well as by UV absorbtion spectroscopy when possible. Actinometry was performed using potassium ferrioxalate[30], and conversion was kept around 5% in all the cases. Care was taken that > 98% of the light were absorbed by the sample and the actinometer. No precautions were taken with the presence of oxygen[11,31]. All the values are the result of five measurements eliminating the two extrems and averaging the other three.

Triplet quantum yield Φ_{isc} of NVT was determined by means of the comparison between the sensitized E-Z isomerization of E-3-phenyl-1-hydroxy-2-propene, and E,E-2,4-hexadienoic acid (sorbic acid) by benzophenone (Φ_{isc}=1) and NVT[32], in the absence of oxygen. A simple window glass (standard)[29b] filter ($\lambda > 310$nm) was used in this case to assure that both NVT (λ_{max} 350 nm) and benzophenone (λ_{max} 366 nm) were excited without parallel excitation of the substrate (especially, sorbic acid absorbtion reaches 300 nm). Values in between 0.27 and 0.34 were obtained in several experiments. For this method to be valid the rate constant for the decay of the unperturbed triplet state of the NVT must be neglegible in front of the rate constant of energy transfer between NVT in its triplet state and substrate. Results reported and discussed in the present work suggest that this is just the case.

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REFERENCES.-

1.- (a) J.Cornelisse, E.Havinga, Chem. Rev., 1975, 75, 353. (b) E.Havinga, J.Cornelisse, Pure Appl. Chem., 1976, 47, 1. (c) J.Cornelisse, G.Lodder, E.Havinga, Rev. Chem. Intermed., 1979, 2, 231.

2.- J.Cornelisse, G.P.De Gunst, E.Havinga, Adv. Phys. Org. Chem., 1975, 11, 225.

3.- C.A.G.O.Varma, J.J.Tamminga, J.Cornelisse, J.C.S. Faraday Trans. 2, 1982, 78, 265.

4.- P.H.M. van Zeijl, L.M.J. van Eijk, C.A.G.O.Varma, J.Photochem., 1985, 29, 415.

5.- H.C.H.A. van Riel, G.Lodder, E.Havinga, J. Am. Chem. Soc., 1981, 103, 7257.

6.- A.Castelló, J.Cervelló, J.Marquet, M.Moreno-Mañas, X.Sirera, Tetrahedron, 1986, 42, 4073.

7.- J.Cervelló, M.Figueredo, J.Marquet, M.Moreno-Mañas, J.Bertrán, J.M.Lluch, Tetrahedron Lett., 1984, 25, 4147.

8.- A.Cantos, J.Marquet, M.Moreno-Mañas, Tetrahedron Lett., 1987, 28, 4191.

9.- (a) K.Mutai, R.Nakagaki, H.Takeda, Bull. Chem. Soc. Jpn., 1985, 58, 2066. (b) K.Mutai, R.Nakagaki, Bull. Chem. Soc. Jpn., 1985, 58, 3663.

10. (a K. Mutai, K.Kobayashi, K.Yokoyama, Tetrahedron, 1984, 40, 1755. (b) K.Mutai, K.Yokoyama, S.Kanno, K.Kobayashi, Bull. Chem. Soc. Jpn., 1982, 55, 1112.

11. N.J.Bunce, S.R.Cater, J.C.Scaiano, L.J.Johnston, J. Org. Chem, 1987, 52, 4214.

12. J.L.Stratenus, Thesis, Leiden 1966.

13. A.A.Lamola, Photochem. Photobiol., 1968, 8, 601.

14. M.E.Kronenberg, A.van der Heyden, E.Havinga, Rec. Trav. Chim. Pays-Bas, 1967, 86, 254.

15. F.Sanchez-Ferrando, Magn. Reson. Chem., 1985, 23, 185.

16. P.Kuzmic, L.Pavlicová, J.Velek, M.Soucek, Coll. Czech. Chem. Commun., 1986, 51, 1665.

17. N.Levy, M.D.Cohen, J.C.S. Perkin 2, 1979, 553.

18. A.Cu, A.C.Testa, J. Am. Chem. Soc., 1974, 96, 6698.

19. J.Marquet, M.Moreno-Mañas, A.Vallribera, A.Virgili, J.Bertrán, A.González-Lafont, J.M.Lluch, Tetrahedron, 1987, 43, 351.

20. L.M.J.van Eijk, J.Marquet, C.A.G.O.Varma, in preparation (laser flash photolysis experiments).

21. N.C.Yang, W.Chiang, J.R.Langan, Tetrahedron Lett., 1984, 25, 2855.

22. C.A.G.O.Varma, F.L.Plantenga, A.H.Huizer, J.P.Zwart, Ph.Bergwerf, J.P.M.van der Ploeg, J.Photochem., 1984, 24, 133.

23. G.R.Fleming, A.E.W.Knight, J.M.Morris, R.J.Robbins, G.W.Robinson, Chem. Phys. Lett., 1977, 51, 399.

24. H.Othani, T.Kobayashi, D.Suzuki, S.Nagakura, Bull. Chem. Soc. Jpn., 1974, 53, 43.

25. N.C.Yang, Z.Lu, Tetrahedon Lett., 1984, 25, 475.

26. A.van Vliet, M.E.Kronenberg, J.Cornelisse, E.Havinga, Tetrahedron, 1970, 26, 1061.

27. M.H.Vermeulen, Rec. Trav. Chim. Pays-Bas, 1906, 25, 12.

28. D.Cardwell, R.J.Robinson, J. Chem. Soc., 1915, 107, 255.

29. "Photochemistry" by J.C.Calvert, J.N.Pitts, Jr.. Ed. J.Wiley and sons Inc. 1966. (a) p. 733, (b) p. 748.

30. C.G.Hatchard, C.A.Parker, Proc. Roy. Soc. (London), 1953, A220, 104.

31. J.den Heijer, T.Spee, G.P.de Gunst, J.Cornelisse, Tetrahedron Lett., 1973, 1261.

32. A.A.Lamola, G.S.Hammond, J. Chem. Phys., 1965, 43, 2129.