

THE PHOTOSUBSTITUTION OF 2-FLUORO-4-NITROANISOLE WITH n-HEXYLAMINE.
EVIDENCE OF TWO DIFFERENT TRIPLET EXCITED STATES IN A DUAL MECHANISTIC PATHWAY.

ROSER PLEIXATS and JORGE MARQUET*

Department of Chemistry, Universitat Autònoma de Barcelona.

08193 Bellaterra, Barcelona, Spain.

(Received in UK 7 November 1989)

Abstract.- The photoreaction of 2-fluoro-4-nitroanisole with n-hexylamine gives rise to fluoride (major) and methoxy (minor) substitution. A continuous irradiation mechanistic study indicates that the first is produced through a S_N2Ar^* mechanism that involves a $\pi-\pi^*$ triplet excited state whereas the second is a consequence of n- π^* triplet excited state chemistry via an electron transfer mechanism.

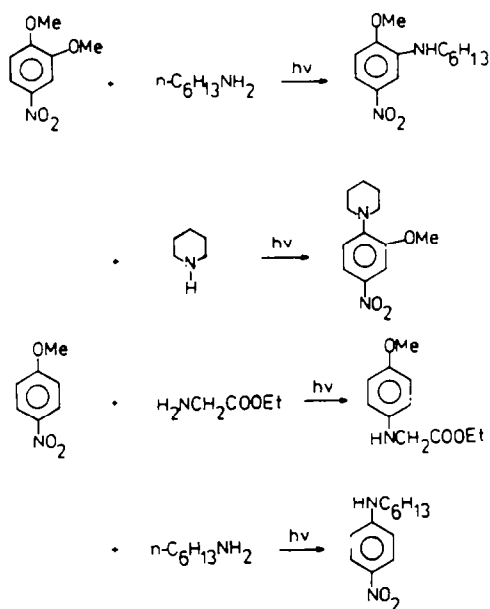
INTRODUCTION

Nucleophilic Aromatic Photosubstitutions have been the object of intense research since their discovery in 1956¹. In spite of the important effort done, mechanistic studies had been for years almost restricted to photohydrolysis reactions^{2,3,4}. Many reported experimental facts have remained unexplained until recently, specially in cases when nucleophiles others than OH^- were used.

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 transfer 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 reactions³⁻¹². In the course of our investigation on the photosubstitution of 4-nitroveratrole and 4-nitroanisole with amines (Scheme 1), we found¹³ that the regioselectivity of these reactions depends on the ionization potential of the nucleophile. A mechanistic borderline between S_N2Ar^* reactions (for high ionization potential amines) and electron transfer from the amine to the substrate triplet excited state (for low ionization potential amines) was proposed on the basis of mechanistic continuous irradiation¹⁴⁻¹⁶ and laser flash photolysis¹⁷ experiments. Some other related regioselectivity changes have been reported for photo-Smiles reactions^{6,7} and for the photosubstitution of 1-methoxy-1-nitronaphthalene with nucleophiles¹². The explanations given are related to ours.

It is well established that triplet $\pi-\pi^*$ and n- π^* states lie close enough in energy in nitrophenyl derivatives¹⁸ including nitrophenyl ethers so that both states are populated, the $\pi-\pi^*$ state usually being of lower energy in polar (hydrogen bond forming) media¹⁹. Heterolytic nucleophilic aromatic photosubstitution (S_N2Ar^*) is associated with the $\pi-\pi^*$ state whereas photoreduction resulting from electron²⁰ or hydrogen atom²¹ transfer is

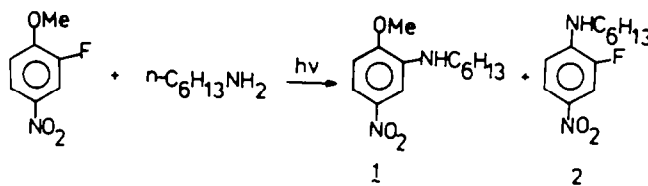
associated with the $n-\pi^*$ state²². Wubbels has suggested²³ that the electron transfer pathway to para photosubstitution in nitrophenyl ethers (Scheme 1) is the result of $n-\pi^*$ photochemistry, but as far as we know no experimental data support this proposal.



Scheme 1

Lately we have directed our attention to fluoronitrophenyl ethers^{24,25} as photoactive compounds with interesting possibilities as photoprobes in biochemistry. No mechanistic studies of the photoreactions of this kind of compounds have been reported being the previous examples of their reactivity very scarce^{26,27}. These compounds show a high and broad photoreactivity in front of different nucleophiles. In addition, meta (fluorine) and para (methoxy) photosubstitution is observed with nucleophiles of relatively low ionization potential²⁵. Interestingly the photoreaction between n -hexylamine and 2-fluoro-4-nitroanisole produces both amine photosubstitution products (Scheme 2) in amounts large enough to permit a simultaneous study of the involved mechanistic paths. Previous mechanistic studies on the nucleophilic aromatic photosubstitution of 4-nitroveratrole^{14,15} and 4-nitroanisole¹⁶ relied on the use of different nucleophiles to achieve enough production of the different final photoproducts (Scheme 1), being difficult to tackle the problem of the involvement of more than one triplet excited state. The present paper reports a continuous irradiation based mechanistic study on the photosubstitution of 2-fluoro-4-nitroanisole with n -hexylamine which constitutes another example supporting previous interpretations (in related substrates) about the involvement of different mechanistic paths

leading to different photoproducts. Evidence is also presented about the involvement of two different triplet excited states in the $S_N2^3Ar^*$ and "electron transfer"¹⁴⁻¹⁶ mechanisms.



Scheme 2

RESULTS

The studied process is indicated in Scheme 2 and the preparative details have been reported elsewhere²⁵.

Qualitative Experiments.- In Table I the effects of triplet quenchers (potassium sorbate) and radical scavengers (*m*-dinitrobenzene) in the production of *N*-hexyl-2-methoxy-5-nitroaniline, 1, (*meta* photoproduct) and *N*-hexyl-2-fluoro-4-nitroaniline, 2, (*para* photoproduct) in the photoreaction of 2-fluoro-4-nitroanisole with *n*-hexylamine (Scheme 2) are described. Consideration of Table I results by themselves and by comparison with related ones previously described by us¹⁴⁻¹⁶ lead to the conclusion that *meta* (fluoride) photosubstitution is the result of a normal $S_N2^3Ar^*$ reaction whereas the *para* (methoxy)

Table I.- Effect of triplet quenchers and radical scavengers on the photoreaction of 2-fluoro-4-nitroanisole with *n*-hexylamine^a.

Exp.	Product	Additives	$(1 - (\frac{\xi}{\xi_{blank}})) \times 100^b$
1	<u>1</u>	Potassium Sorbate ^c	50
2	<u>2</u>	Potassium Sorbate ^c	88
3	<u>1</u>	<i>m</i> -Dinitrobenzene ^d	11
4	<u>2</u>	<i>m</i> -Dinitrobenzene ^d	91

a) General conditions: 125 W Hg high pressure lamp, MeOH/H₂O(20:80), 9m. To ensure the different additives were not absorbing, a filter prepared with triacetic acid lactone (0.1M) in *t*-butanol ($\lambda > 340\text{nm}$) was used. Each reaction was carried out in parallel to a blank (using a standard solvent mixture, MeOH/H₂O:20/80, and in the absence of additives). No precautions were taken to avoid oxygen. b) Photosubstitution production percentage of decrease referred to the blank reaction. The ξ/ξ_{blank} value corresponds to the normalized integration ratio of the substitution product gas chromatographic peaks in the compared photoreactions, using the integration of a fixed amount of internal reference. The values result from five measurements, eliminating the higher and lower ones and averaging the remaining three values. The products were identified by comparison with authentic samples. 2-fluoro-4-nitroanisole ($5.8 \times 10^{-3}\text{M}$), *n*-hexylamine ($6.0 \times 10^{-4}\text{M}$). c) $5.0 \times 10^{-4}\text{M}$. d) $9.8 \times 10^{-3}\text{M}$.

photosubstitution occurs through single electron transfer from the amine to the substrate excited triplet state. The 11% variation observed in the production of 1 in the presence of *m*-dinitrobenzene (experiment 3) is within the accepted error range specially if one considers the corresponding observed variation for the production of 2 (91%).

Quantum yield measurements.- Overall quantum yields for the production of 1 (meta) and 2 (para) were measured at different nucleophile concentrations (Table II). Quantum yields increase by increasing the nucleophile concentration in both cases. The multiplicity of the reactive excited states was investigated using potassium sorbate as selective triplet quencher (Table III). There is a significant quenching effect due to potassium sorbate in both cases which indicates the involvement of triplet excited states in the production of both photoproducts of scheme 2.

Table II.- Overall quantum yield of production of 1 (meta) and 2 (para) in the photoreaction of 2-fluoro-4-nitroanisole ($1.52 \times 10^{-3} M$) with *n*-hexylamine in methanol/water (20:80) at different nucleophile concentrations.

$[C_6H_{13}NH_2]$	0.076	0.097	0.151	0.227	0.379	0.520
Φ_{meta}	0.026	0.031	0.039	0.045	0.050	0.051
Φ_{para}	0.0023	0.0032	0.0050	0.0077	0.0084	0.0114

Table III.- Overall quantum yield of production of 1 (meta) and 2 (para) in the photoreaction of 2-fluoro-4-nitroanisole ($5.31 \times 10^{-3} M$) with *n*-hexylamine (0.379M) in methanol/water (20:80) in the presence of different concentrations of potassium sorbate [Q].

[Q]	0	0.0215	0.0329	0.0539	0.0739
$\Phi_{meta} \times 10^2$	5.0	4.39	4.07	3.61	
$\Phi_{para} \times 10^2$	0.84	0.61	0.53		0.37

KINETIC DISCUSSION.

The study of the mechanism of production of both photosubstitution products (Scheme 2) with a single nucleophile offers interesting possibilities. The results of Tables I and III indicate the involvement of triplet excited states as intermediates in the production of both photoproducts 1 and 2. Thus, if we consider the operativity of a single excited state for both photoreactions (Scheme 3), the kinetic equations to consider are:

$$\Phi_{\text{meta}} = \Phi_{\text{isc}} \times \frac{k_p}{k_p + k_d} \times \frac{k_3 [\text{Nu}]}{k_4 + (k_3 + k_5) [\text{Nu}]} \quad \text{eq. 1}$$

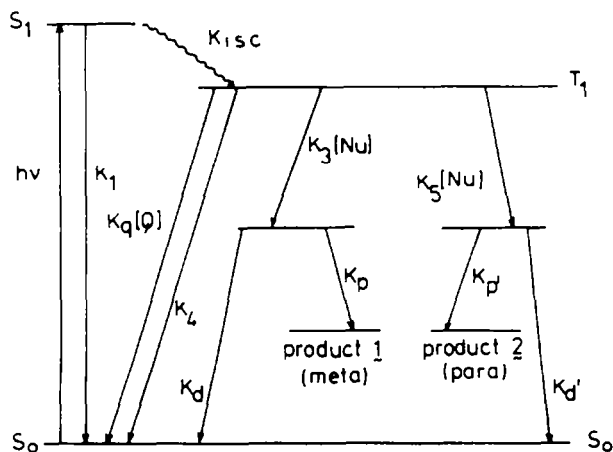
$$\Phi_{\text{para}} = \Phi_{\text{isc}} \times \frac{k_{p'}}{k_{p'} + k_{d'}} \times \frac{k_5 [\text{Nu}]}{k_4 + (k_3 + k_5) [\text{Nu}]} \quad \text{eq. 2}$$

From them:

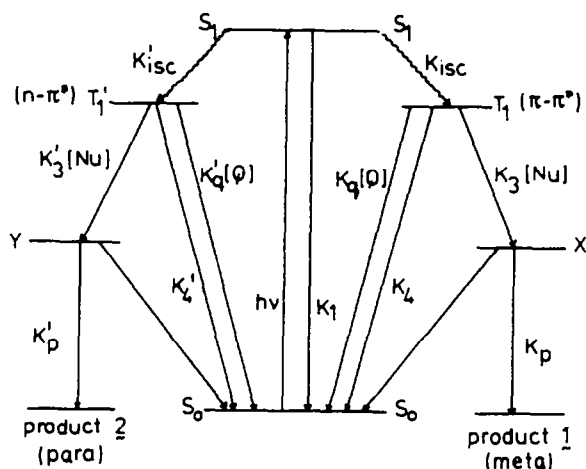
$$\frac{1}{\Phi_{\text{meta}}} = \frac{1}{\Phi_{\text{isc}}} \times \frac{k_p + k_d}{k_p} \times \left(\frac{k_3 + k_5}{k_3} + \frac{k_4}{k_3 [\text{Nu}]} \right) \quad \text{eq. 3}$$

$$\frac{1}{\Phi_{\text{para}}} = \frac{1}{\Phi_{\text{isc}}} \times \frac{k_{p'} + k_{d'}}{k_{p'}} \times \left(\frac{k_3 + k_5}{k_5} + \frac{k_4}{k_5 [\text{Nu}]} \right) \quad \text{eq. 4}$$

From eq. 3 and 4 we have that if the Scheme 3 applies the slope to intercept ratio must be equal in both cases with a value of $k_4/(k_3+k_5)$. Analysis of the data reported in Table II (Figure 1) indicates that even though there is a linear relationship between Φ^{-1} and $[\text{Nu}]^{-1}$ in both cases (which indicates a single origin for each photoproduct), the slope to intercept ratio differ enough (0.11 for 1 vs. 1.5 for 2, vide infra) to have to consider more than one triplet excited state.



Scheme 3



Scheme 4

All this considered we propose the kinetic scheme described in Scheme 4 and we attribute $\pi-\pi^*$ (T_1) character to one triplet excited state and a $n-\pi^*$ character to the other (T_1'). The scheme is somewhat oversimplified since k_4 and k_4' include the decay rate constants of any of the considered triplet excited states via the other one, and k_{isc} and k_{isc}' include the production of any considered triplet excited state via the other. In any case Scheme 4 allow us to analyze the relative properties of both triplet excited states. In this case the general kinetic equation will be:

$$\frac{1}{\Phi} = \frac{1}{\Phi_{isc}} \times \frac{k_p + k_d}{k_p} \times \left(1 + \frac{k_4}{k_3 [Nu]} \right) \quad \text{eq. 5}$$

The parameters involved depend on which photoproduct is studied. Thus, the relationship between Φ^{-1} and $[Nu]^{-1}$ in the case of 1 corresponds to a straight line represented in Figure 1A. A regression analysis using the values of Table 2 gave a linear equation (cc. 0.995):

$$\Phi^{-1} = (15.4 \pm 0.7) + (1.68 \pm 0.09)[Nu]^{-1}$$

From eq. 5 we have that k_4/k_3 equals the slope to intercept ratio, therefore $k_4/k_3 \approx 0.11$ in this case.

A parallel analysis in the case of 2 leads to the straight line represented in Figure 1B and from the values of Table 2 to the linear equation (cc. 0.989):

$$\Phi^{-1} = (19.7 \pm 16.0) + (29.8 \pm 2.2)[Nu]^{-1}$$

In this case $k_4'/k_3' \approx 1.5$. The smaller quantum yield values in the case of 2 make it difficult to obtain good kinetic parameters and this is observed in the relatively high standard errors of the intercept value. Nevertheless the slope to intercept ratio differ

enough for 1 and 2, even considering the error range, as to have to postulate two triplet excited states to explain the experimental facts.

According to the Stern-Volmer analysis the dependence of the relative reciprocal quantum yield on the quencher concentration is given by equation 6:

$$\frac{\Phi_0}{\Phi} = 1 + \frac{k_q [Q]}{k_4 + k_3 [Nu]} \quad \text{eq. 6}$$

Using the values of Table III for the production of 1 and 2, the figures 2A and 2B are obtained and least squares fits lead to the following equations:

$$\Phi_0/\Phi_{\text{meta}} = (0.99 \pm 0.01) + (7.2 \pm 0.3)[Q] \quad (\text{cc. } 0.998)$$

$$\Phi_0/\Phi_{\text{para}} = (1.007 \pm 0.007) + (17.1 \pm 0.2)[Q] \quad (\text{cc. } 0.9999)$$

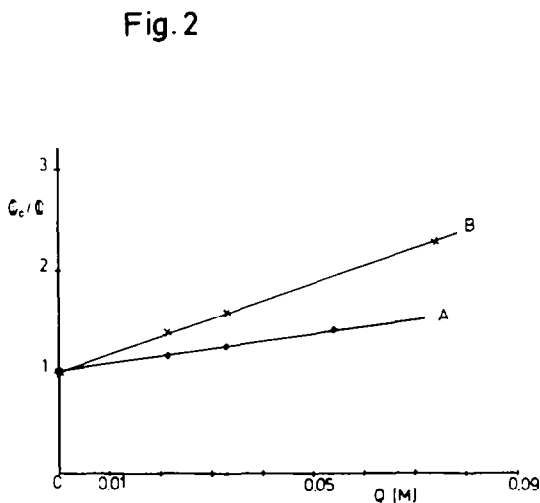
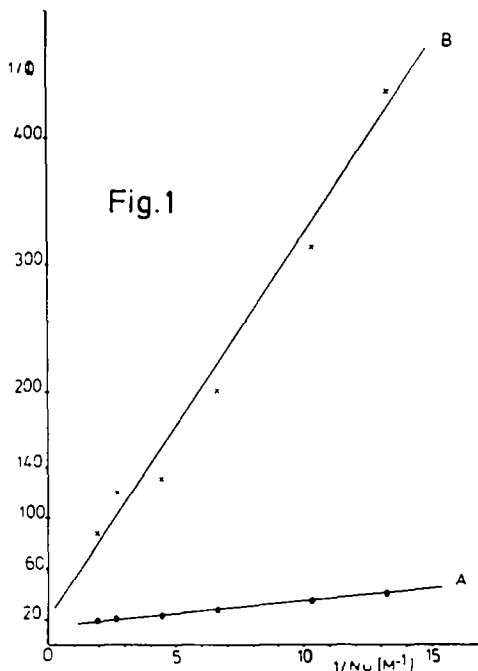
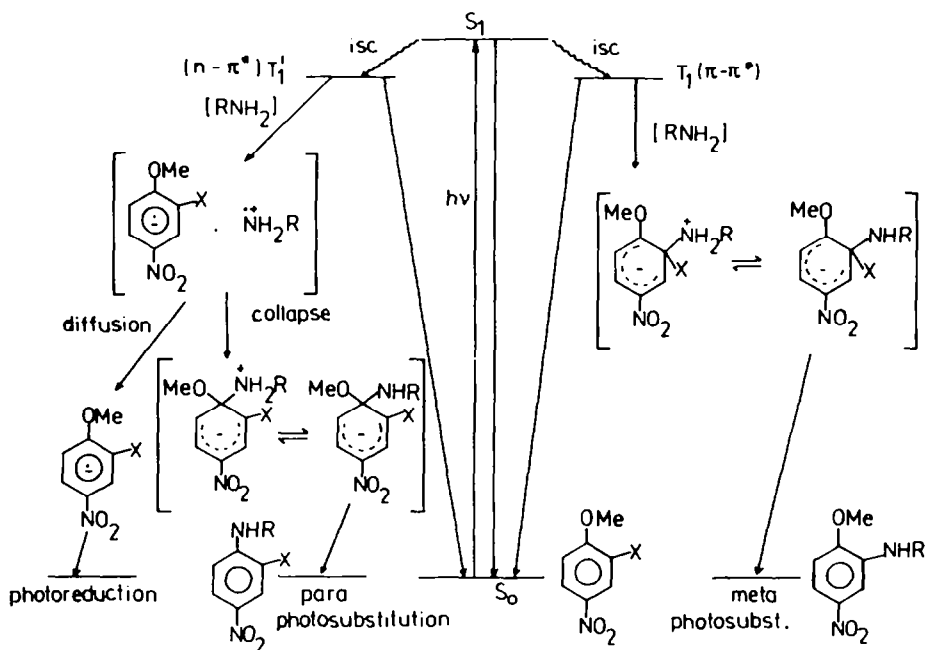


Figure 1.- Plots of the inverse quantum yield of production of 1 (A) and 2 (B) vs. inverse nucleophile concentrations. Data from Table II.

Figure 2.- Plots of the relative inverse quantum yields of production of 1 (A) and 2 (B) vs. quencher concentrations (potassium sorbate). Data from Table III.

These results confirm the protagonism of two triplet excited states. The analysis of the described results considering k_q equal in both cases (we can use $k_q \approx 10^9 \text{ M}^{-1}\text{s}^{-1}$ for

comparisons) leads to $k_4 \approx 3.1 \times 10^7 \text{ s}^{-1}$ and $k_4' \approx 4.6 \times 10^7 \text{ s}^{-1}$, which indicates a similar lifetime for both excited triplet states. On the other hand $k_3 \approx 2.8 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ and $k_3' \approx 3.1 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ which indicates that the interaction between the nucleophile and the triplet excited state leading to product 1 (meta substitution) is faster than the corresponding interaction with the triplet excited state leading to product 2 (para photosubstitution) by one power of ten. It must be remembered here that the values corresponding to the production of 2 should be taken with some precaution due to the relative high standard error in the intercept of the k^{-1} vs. $[\text{Nu}]^{-1}$ representation.



Scheme 5

The use of a single nucleophile overcomes the undefinition of previous related works^{15,16} about the involvement of more than one triplet excited state, mainly due to the different properties of the nucleophiles required to achieve the change in mechanistic pathway. Here we attribute T_1 (Scheme 4) to the $\pi-\pi^*$ triplet excited state responsible for the S_N2Ar^* reaction (meta photosubstitution). In solvents such as water and alcohols this state is stabilized by hydrogen bonding becoming in several studied nitrophenyl ethers the lowest triplet excited state¹⁹ thus making the direct photosubstitution the main process. We

also attribute T_1' to the $n-\pi^*$ triplet excited state responsible for the "electron transfer and collapse of the radical ion pair" photosubstitution pathway¹⁴⁻¹⁷. As commented previously, the $n-\pi^*$ triplet excited state of nitrophenyl derivatives is also considered responsible for the photoreductions observed in this type of compounds, and an electron transfer mechanism has been proposed²⁰ in the presence of electron donors. We attribute the almost complete absence of photoreduction in the photoreaction of 2-fluoro-4-nitroanisole with *n*-hexylamine to the small volume of the fluorine substituent. After electron transfer from the amine to the $n-\pi^*$ excited triplet state of the nitrophenyl ether has been completed, a competition is established between back electron transfer (leading to the ground state, collapse (after isc) of the formed radical-ion pair (leading to photosubstitution) and diffusion apart (leading to photoreduction), the result depending, at least in part, on the relative geometry of the radical-ion pair and therefore on the volume of the substituents. We have reported previously²⁸ that 4-nitrocatechol ethers other than methyl ethers do not give rise to photosubstitution through the "electron transfer" mechanism, supporting the given explanation.

In Scheme 5 a general picture of the different possibilities for the photoreactions of nitrophenyl ethers with nucleophiles via triplet excited states based on the present and previous¹⁴⁻¹⁷ results is shown. The relative importance of the $n-\pi^*$ and $\pi-\pi^*$ pathways will depend on the nature of the nitrophenyl ether substrate, the ionization potential of the nucleophile and the used solvent.

EXPERIMENTAL

General.— Uv spectra were recorded on a Hewlett-Packard 8452A diode array spectrophotometer. The GC analyses were performed on a HP-5890A Gas Chromatograph using a HP-Crosslinked Dimethylsilicone Gum 12m x 0.2mm x 0.33m film thickness capillary column. Quantum yield measurements were performed on a Applied Photophysics QYR15 merry-go-round apparatus. The wavelength of excitation was selected using a Jobin Ivon monochromator. The preparative details about the reaction of 2-fluoro-4-nitroaniline and *n*-hexylamine, and the complete description of photoproducts 1 and 2 are reported in reference 25.

Qualitative Experiments and Semipreparative Reactions (Table I). Reaction mixtures were irradiated using a 125W high pressure Hg lamp as a light source. To ensure the different additives were not absorbing, a filter prepared with triacetic acid lactone (0.1M) in *t*-butanol ($\lambda > 340$ nm) was used. The amounts of photoproducts were determined by gas chromatography analysis using an internal reference. All the values result from five measurements, eliminating the higher and lower ones and averaging the remaining three. The photoproducts were identified by comparison with authentic samples.

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 wavelength of excitation (366 nm) was selected using a monochromator. The amounts of photoproducts were determined by GC analysis (internal reference). Actinometry was performed using potassium ferrioxalate²⁹, and conversion was kept around 5% in all 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. All the values result from five measurements, eliminating the higher and lower ones and averaging the remaining three.

ACKNOWLEDGEMENTS

We wish to thank Professor M. Moreno-Mañas for stimulating discussions and Dr. A. Cantos for valuable technical help. Financial support from DGICYT ("Ministerio de Educación y Ciencia" of Spain) through project n° PB87-0032 is gratefully acknowledged.

REFERENCES

- (1) a) Cornelisse, J.; Havinga, E. Chem. Rev. 1975, 75, 353. b) Havinga, E.; Cornelisse, J. Pure Appl. Chem. 1976, 47, 1. c) Cornelisse, J.; Lodder, G.; Havinga, E. Rev. Chem. Intermed. 1979, 2, 231.
- (2) Cornelisse, J.; De Gunst, G.P.; Havinga, E.; Adv. Phys. Org. Chem. 1975, 11, 225.
- (3) Varma, C.A.G.O.; Tamminga, J.J.; Cornelisse, J. J.C.S. Faraday Trans. 2, 1982, 78, 225.
- (4) Van Zeijl, P.H.M.; van Eijk, L.M.J.; Varma, C.A.G.O. J. Photochem. 1985, 29, 415.
- (5) Van Riel, H.C.H.A.; Lodder, G.; Havinga, E. J. Am. Chem. Soc. 1981, 103, 7257.
- (6) Mutai, K.; Yokoyama, K.; Kamno, S.; Kobayashi, K. Bull. Chem. Soc. Jpn. 1982, 55, 1112.
- (7) Mutai, K.; Kobayashi, K.; Yokoyama, K. Tetrahedron 1984, 40, 1755.
- (8) Wubbels, G.G. Acc. Chem. Res. 1983, 16, 285.
- (9) Wubbels, G.G.; Susens, D.P.; Coughlin, E.B. J. Am. Chem. Soc. 1988, 110, 2538.
- (10) Wubbels, G.G.; Snyder, E.J.; Coughlin, E.B. J. Am. Chem. Soc. 1988, 110, 2543.
- (11) Wubbels, G.G.; Severson, B.R.; Sanders, H. J. Am. Chem. Soc. 1989, 111, 1018.
- (12) Bunce, N.J.; Cater, S.R.; Scaiano, J.C.; Johnston, L.J. J. Org. Chem. 1987, 52, 4214.
- (13) Cervelló, J.; Figueredo, M.; Marquet, J.; Moreno-Mañas, M.; Bertrán, J.; Lluch, J.M. Tetrahedron Lett. 1984, 25, 4147.
- (14) Cantos, A.; Marquet, J.; Moreno-Mañas, M. Tetrahedron Lett. 1987, 28, 4191.
- (15) Cantos, A.; Marquet, J.; Moreno-Mañas, M.; Castelló, A. Tetrahedron 1988, 44, 2607.
- (16) Cantos, A.; Marquet, J.; Moreno-Mañas, M. Tetrahedron Lett. 1989, 30, 2423.
- (17) Van Eijk, A.M.J.; Huizer, A.H.; Varma, C.A.G.O.; Marquet, J. J. Am. Chem. Soc. 1989, 111, 88.
- (18) Gonzalez-Lafont, A.; Lluch, J.M.; Bertrán, J.; Marquet, J. Spectrochim. Acta. 1988, 44A, 1427.
- (19) Varma, C.A.G.O.; Plantenga, F.L.; Huizer, A.H.; Zwart, J.P.; Bergwerf, Ph.; Van der Ploeg, J.P.M. J. Photochem. 1984, 24, 133.
- (20) Gu, A.; Testa, A.C. J. Am. Chem. Soc. 1974, 96, 6698.
- (21) Levy, N.; Cohen, M.D. J.C.S. Perkin 2, 1979, 553.
- (22) Petersen, W.C.; Letsinger, R.L. Tetrahedron Lett. 1971, 2197.
- (23) Wubbels, G.G.; Halverson, A.M.; Oxman, J.D.; De Bruin, Van H. J. Org. Chem. 1985, 50, 4499.
- (24) Figueredo, M.; Marquet, J.; Moreno-Mañas, M.; Pleixats, R. Tetrahedron Lett. 1989, 30, 2427.
- (25) Pleixats, R.; Figueredo, M.; Marquet, J.; Moreno-Mañas, M.; Cantos, A. Tetrahedron, in press.
- (26) Brasen, P.; Lammers, J.G.; Cornelisse, J.; Lugtenburg, J.; Havinga, E. Tetrahedron Lett. 1972, 685.
- (27) Lammers, J.G.; Lugtenburg, J. Tetrahedron Lett. 1973, 1777.
- (28) Castelló, A.; Marquet, J.; Moreno-Mañas, M.; Sirera, X. Tetrahedron Lett. 1985, 26, 2489.
- (29) Calvert, J.G.; Pitts, J.N. in Photochemistry, Wiley, New York 1966, p. 784.