Photochemical Methoxide Exchange in Some Nitromethoxybenzenes. The Role of the Nitro Group in S_N2 Ar* Reactions[†]

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Abstract: Photoinduced methoxide exchange has been measured for *o*-, *m*-, and *p*-nitro[^{14}C]methoxybenzene as well as for the [^{14}C]methoxy-labeled 4-nitroveratroles. In these reactions (of the $S_N2\ ^3Ar^*$ type), where the substituting and leaving groups are the same, the origin of the meta activation found cannot be otherwise than in the steps leading to the symmetrical σ complex. Next to considerations on the basis of charge distributions of the excited aromatic compounds and of electron densities in the HOMO and LUMO, a rationalization for the regioselectivity and activation is offered on the basis of the energy gap between the ground-state and the excited-state surfaces. Since the level of the ground-state σ complex corresponding to meta substitution as compared to that for ortho/para substitution is highest in energy and since the trajectory from the (triplet) excited state leading to the σ complex for meta substitution is lowest in energy, the energy gap between the excited-state and ground-state hypersurface is considerably smaller for the geometry that leads to the meta σ complex and thus to meta substitution. Meta direction and activation of photosubstitutions will therefore be outspoken in the case of a substituent that gives difficult or no substitution at the meta position in the ground state and brings with it low triplet energy. The NO_2 group conforms nicely to these criteria.

For the numerous examples of nucleophilic aromatic photosubstitution reactions[1] that have been collected since their discovery in 1956,[2] three major mechanisms have emerged[3] (Scheme I). In contrast to the third type of reaction,[4] which has no requirement for activation by other substituents, the first two types of reaction show strong and opposite substituent effects.

Scheme I

$$ArX^* \xrightarrow{Y^-} [ArXY]^- \xrightarrow{-X^-} ArY \quad S_N2\ Ar^*$$

$$ArX^* \xrightarrow{-e^-} [ArX]^{+\cdot} \xrightarrow{Y^-} ArY \text{ or } Ar(-H)XY \quad S_{R^+N}1\ Ar^*$$

$$ArX \xrightarrow{h\nu,\ e^-} [ArX]^{-\cdot} \xrightarrow{-X^-} [Ar]\cdot \xrightarrow{Y^-} \rightarrow ArY \quad S_{R^-N}1\ Ar^*$$

In the $S_{R^+N}1$ Ar* type of reaction electron-donating substituents show an activating and ortho/para-directing influence. This at first sight puzzling activation could be understood from the finding that the decisive step of the reaction consists of the transfer of an electron from the (triplet) excited aromatic compound to the (waterrich) medium, yielding a solvated electron and a radical cation. This process is promoted by electron-donating substituents. The radical cation then reacts with the nucleophile, accounting for the regioselectivity.[5]

On the other hand, if in the S_N2 Ar* type of reaction an electron-withdrawing group—a nitro group in particular—is attached to the aromatic nucleus a strong activating and meta-directing influence results. The reason for this behavior has been discussed by several authors.[6] However a detailed explanation of the remarkably strong influence of the nitro group in particular could not easily be given. The activating and directing influence of the nitro group can be caused by factors at various stages of the reaction.

The earlier hypothesis that the nucleophilic photosubstitution of nitro compounds proceeds via an intermediate σ complex[7] could recently be proven for the case of the photohydrolysis of 3,5-dinitroanisole.[8] The decay of such a σ intermediate then can lead to the starting material or to the product. The ratio of the rate constants of these two processes may vary depending on the substitution pattern and the conditions and may bring about a directing influence of the nitro group. The ratio of the rate of elimination of the hydroxide ion and the methoxide ion from the σ complex of *m*-nitroanisole formed in photohydrolysis in aqueous alkaline solution is found to vary with a change of pressure on the solution. An increase in pressure decreases the quantum yield of the reaction.[9] The selectivity of the nitro group can however also be controlled by factors in the formation of the σ complex. In order to assess the importance of both these factors, we studied nucleophilic aromatic photosubstitution reactions where the nucleophilic agent and the leaving group are identical. This was accomplished by labeling the leaving group with ^{14}C. In this way the two modes of decay of the σ complex are the same,[10] thereby eliminating this decay as a cause of selectivity. A possibily occurring effect by the nitro group then has to be attributed to the formation of the σ complex.

Moreover one has to be sure that the S_N2 Ar* mechanism prevails. A number of the nitro aromatic compounds that were studied in the past also contain electron-donating substituents (in ortho and para positions), and their photoreactions were carried out in a waterrich polar medium. These factors favor the occurrence of the $S_{R^+N}1$ Ar* reaction. Part of the problems in earlier interpretations stem from the fact that compounds compared did not necessarily react according to the same mechanism.

In this paper we wish to report the symmetrical exchange reactions of the isomeric [*methoxy*-^{14}C]nitroanisoles and [*methoxy*-^{14}C]-4-nitroveratroles with sodium methoxide in methanol upon irradiation and some related studies of these systems to

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[†] Dedicated to George S. Hammond on the occasion of his 60th birthday.

(1) (a) Cornelisse, J.; Havinga, E. *Chem. Rev.* **1975**, *75*, 353. (b) Döpp, D. O. *Top. Curr. Chem.* **1975**, *55*, 49.

(2) Havinga, E.; de Jongh, R. O.; Dorst, W. *Recl. Trav. Chim. Pays-Bas* **1956**, *75*, 378.

(3) Havinga, E.; Cornelisse, J. *Pure Appl. Chem.* **1976**, *47*, 1.

(4) (a) Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* **1973**, *38*, 1407. (b) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.

(5) den Heyer, J.; Shadid, O. B.; Cornelisse, J.; Havinga, E. *Tetrahedron* **1977**, *33*, 779.

(6) (a) Grinter, R.; Heilbronner, E. *Helv. Chim. Acta* **1962**, *45*, 2496. (b) Havinga, E.; de Jongh, R. O. *Bull. Soc. Chim. Belg.* **1962**, *71*, 803. (c) Zimmerman, H. E.; Sandel, V. R. *J. Am. Chem. Soc.* **1963**, *85*, 915. (d) Zimmerman, H. E.; Somasekhara, S. *Ibid.* **1963**, *85*, 922. (e) Discussion of paper: Havinga, E. In "Reactivity of the Photoexcited Organic Molecule"; Wiley: New York, 1967; p 201; in particular: Hammond, G. S., p 223. (f) Mulder, J. J. C. In Havinga E.; de Jongh, R. O.; Kronenberg, M. E. *Helv. Chim. Acta* **1967**, *50*, 2550; In Havinga, E.; Kronenberg, M. E. *Pure Appl. Chem.* **1968**, *16*, 137. (g) Mulder, J. J. C. Thesis, Leiden, 1970. (h) Dauben, W. G.; Salem, L.; Turro, N. J. *Acc. Chem. Res.* **1975**, *8*, 41.

(7) (a) Havinga, E. "Reactivity of the Photoexcited Organic Molecule"; Wiley: New York, 1967; p 201. (b) Barltrop, J. A.; Bunce, N. J.; Thomson, A. *J. Chem. Soc. C* **1967**, 1142. (c) McCain, J. H.; Letsinger, R. L. *J. Am. Chem. Soc.* **1967**, *91*, 6425. (d) Havinga, E.; Kronenberg, M. E. *Pure Appl. Chem.* **1968**, *16*, 137.

(8) Tamminga, J. J. Thesis, Leiden, 1979.

(9) Aomi, H.; Sasaki, M.; Osugi, J. *Rev. Phys. Chem. Jpn.* **1977**, *47*, 111.

(10) In this paper except for a secundary ^{12}C/^{14}C kinetic isotope effect, which is negligible.

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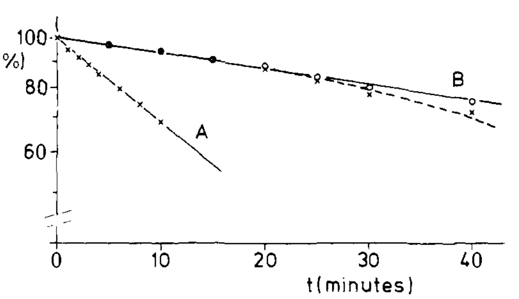
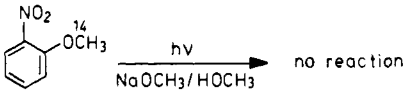


Figure 1. Relative specific activities of **2** (A) and **3** (B) (5×10^{-3} M) as a function of time on irradiation (λ = 313 nm) with $NaOCH_3$ (0.25 M) in MeOH: ×, uncorrected for concurrent reduction and nitrosubstitution; ○, corrected.

ascertain the proposed mechanism.[11]

Results

Symmetrical Exchange Reactions of the Nitroanisoles. [*Methoxy*-^{14}C]-*o*-nitroanisole (**1**), [*methoxy*-^{14}C]-*m*-nitroanisole (**2**), and [*methoxy*-^{14}C]-*p*-nitroanisole (**3**) were irradiated under identical conditions in the presence of sodium methoxide in methanol ([aromatic compound] = 5×10^{-3} M, [$NaOCH_3$] = 0.25 M, λ_{exc} = 313 nm, nondeoxygenated solutions, room temperature) (eq 1–3). Within experimental error no reaction of 1 could be detected. Irradiation of **2** afforded the exchange of the methoxy group with a quantum yield of $\phi = 0.08$. Furthermore a very small amount of the reduction product *m*-nitrosoanisole was isolated. The irradiation of **3** does not result in a clean exchange reaction. Besides slow exchange ($\phi = 0.012$) one also observes reduction to *p*-nitrosoanisole ($\phi = 0.01$) and substitution of the nitro group to form 1,4-dimethoxybenzene ($\phi = 0.002$). The first-order behavior of the exchange of **2** and **3** as representative examples of the observed kinetics is shown in Figure 1. In the case of **3** the exchange data have to be corrected for the concurrent formation of 4-nitrosoanisole and 1,4-dimethoxybenzene. The photobehavior of **1**, **2**, and **3** in methoxide–methanol solution differs from that of these compounds in hydroxide–water solution. On irradiation in aqueous alkaline solution **1** gives 2-nitrophenol and 2-methoxyphenol in a ratio of 10:1,[12] **2** gives 3-nitrophenol with a quantum yield of $\phi = 0.22$,[13] and **3** gives 4-nitrophenol and 4-methoxyphenol in a ratio of 1:4 ($\phi_{total} = 0.085$).[14] No nitroso products are found. The formation of reduction products in methoxide–methanol is not surprising. Photoreduction of aromatic nitro compounds is well-known to occur easily in alcoholic solutions.[15] The presence of alkoxide ions accelerates the reduction.[15] The reaction proceeds via the triplet state and H abstraction or radical anion formation.[16] Noteworthy is the difference in photosubsitution behavior of **3** and especially **1** in the two solvent systems (see Discussion).



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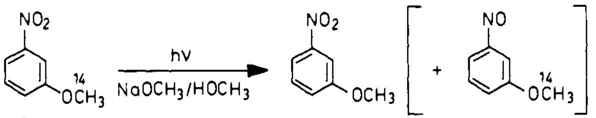
(1)



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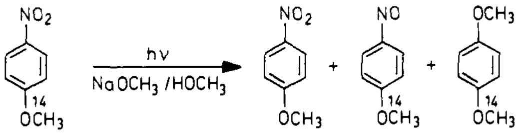
(2)



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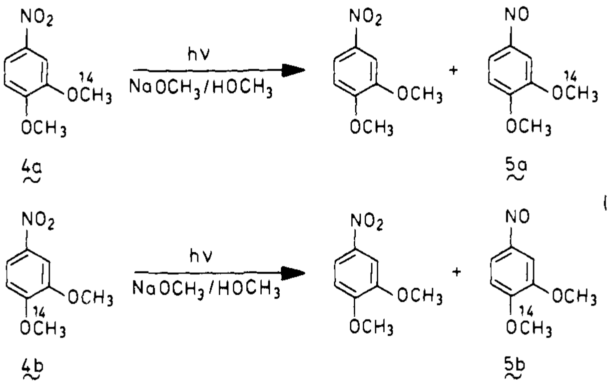
(3)

Table I. Quantum Yields of the Photohydrolysis of *m*-Nitroanisole (2×10^{-4} M) in Various Solvent Systems (λ_{exc} = 313 nm)

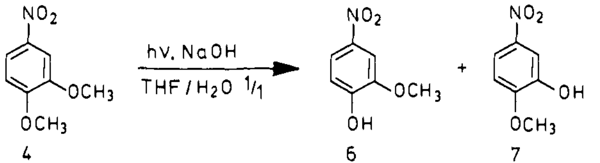
system	ϕ	system	ϕ
10^{-2} M NaOH in water	0.22	10^{-2} M NaOH in *tert*-butyl alcohol + 5% water	0.03
10^{-2} M NaOH in *tert*-butyl alcohol + 10% water	0.23	10^{-2} M NaOH in *tert*-butyl alcohol	0.01
10^{-2} M NaOH in *tert*-butyl alcohol + 7.5% water	0.19		

Symmetrical Exchange Reactions of the 4-Nitroveratroles. A difference in quantum yields of the symmetrical exchange reactions of **1**, **2**, and **3** could possibly originate from a difference in the lifetimes of the three different reacting species. To avoid this complication we studied the photochemical symmetrical exchange reactions of [2-*methoxy*-^{14}C]-4-nitroveratrole (**4a**) and [1-*methoxy*-^{14}C]-4-nitroveratrole (**4b**) in methanol. For both compounds the reaction conditions were the same: [4-nitroveratrole] = 5×10^{-3} M, [$NaOCH_3$] = 0.1 M, λ_{exc} = 313 nm, nondeoxygenated solutions, room temperature (eq 4). The quantum yield for the exchange of the methoxy group was found to be 0.21 for the meta position and 0.016 for the para position. The photochemical reduction leading to 4-nitrosoveratrole (**5**) has a quantum yield of 0.01. No indications were found for the formation of 1,2,4-trimethoxybenzene. The photochemical hydrolysis of **4** has been reported to give only substitution at the meta position with a quantum yield of $\phi = 0.09$.[17] The UV analysis used could not assay for substitution at the para position if that occurred for less than 5%. Therefore a more accurate ratio of the hydrolysis at the para vs. meta position was determined. GC analysis of the reaction mixture of the irradiation (λ = 313 nm) of a solution of 4-nitroveratrole (5×10^{-3} M) and sodium hydroxide (0.1 M) in tetrahydrofuran–water (1:1) shows (at 60% conversion) 1:370 as the ratio of the products 4-nitroguaiacol (**6**) and 5-nitroguaiacol (**7**) (eq 5).



4a 5a 4b 5b

(4)



4 6 7

(5)

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[11] (a) An extensive presentation is given in: van Riel, H. C. H. A. Thesis, Leiden, 1977. (b) A review (in part) is offered in: Cornelisse, J.; Lodder, G.; Havinga, E. *Rev. Chem. Intermed.* **1979**, *2*, 231.

[12] de Vries, S. Thesis, Leiden, 1970.

[13] (a) de Jongh, R. O.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1966**, *85*, 275. (b) den Heyer, J.; Spee, T.; de Groot, G. P.; Cornelisse, J. *Tetrahedron Lett.* **1973**, 1261.

[14] (a) Letsinger, R. L.; Ramsay, O. B.; McCain, J. H. *J. Am. Chem. Soc.* **1965**, *87*, 2945. (b) de Vries, S.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1965**, *84*, 601.

[15] Frolov, A. N.; Kuznetsova, N. A. El'tsov, A. V.; Rtishchev, N. I. *J. Org. Chem. USSR* (*Engl. Transl.*) **1973**, *9*, 988 and references therein.

[16] (a) Muszkat, K. A.; Weinstein, M. *J. Chem. Soc. Perkin Trans. 2* **1976**, 1072. (b) Wong, S. K.; Wan, J. K. S. *Can. J. Chem.* **1973**, *51*, 753.

[17] Stratenus, J. L. Thesis, Leiden, 1966.

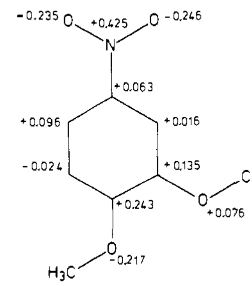
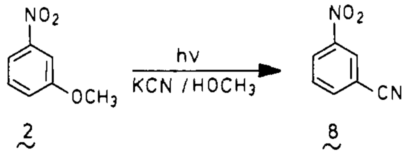


Figure 2. Charge distribution in the radical cation of 4-nitroveratrole computed by INDO.

Mechanism. In order to distinguish between several possible mechanisms for the subsitution reactions discussed here we applied various probes for the key compounds.

Solvent Dependence. From the study of compounds that react according to the $S_{R^+N}1$ Ar* mechanism it is well-known that that mechanism is promoted by polar media.[5] The photohydrolysis of *m*-nitroanisole was therefore studied in a series of *tert*-butyl alcohol–water systems. The observed quantum yields are given in Table I. Only at very high percentages of *tert*-butyl alcohol is a decrease in the quantum yield found.

Dependence on Nucleophilic System. The photocyanation of *m*-nitroanisole in methanol was studied to obtain additional information on the role of the nucleophilic system (nucleophile in a particular solvent). A solution of *m*-nitroanisole (2.2 × 10^{-4} M) and potassium cyanide (2.5 × 10^{-2} M) in methanol yields *m*-nitrobenzonitrile (**8**) as the sole product upon irradiation (λ_{exc} = 313 nm) (eq 6). The quantum yield is 0.16.



(6)

Electrolyses. In order to assert that the photoreactions studied do not involve radical anion or radical cation type mechanisms, we performed a number of electrolysis experiments: anodic oxidation of *m*-nitroanisole (3 × 10^{-4} M) in the presence of sodium hydroxide (0.1 M) in water–2% methanol does not yield the subsitution product meta nitrophenolate ion; anodic oxidation of 4-nitroveratrole (**4**) (2.5 × 10^{-4} M) in the presence of sodium hydroxide (0.1 M) in water does not yield 5-nitroguaiacol (**7**) as a product; anodic oxidation of [2-*methoxy*-^{14}C]-4-nitroveratrole (**4a**) (5 × 10^{-3} M) in the presence of sodium methoxide (0.1 M) in methanol does not show an exchange at the meta position; cathodic reduction of [2-*methoxy*-^{14}C]-4-nitroveratrole (**4a**) (5 × 10^{-3} M) in the presence of sodium methoxide (0.1 M) in methanol yields 4-nitrosoveratrole (**5**) as the reduction product (no exchange reaction was observed).

Discussion

The present study was embarked on to arrive at a better understanding of the meta-directing influence of a nitro group in aromatic photosubsitution reactions of the S_N2 Ar* type. First of all, however, one has to be sure that the reactions studied are of this category and do not proceed via a radical anion or a radical cation type mechanism. In this respect the following results are of importance. (1) The ease of formation of a radical cation upon irradiation strongly depends on the dielectric constant of the solvent.[5] Den Heijer reported a significant decrease of the quantum yield of the photocyanation of 4-fluoroanisole in water when 20% *tert*-butyl alcohol was added.[5] In the photohydrolysis of *m*-nitroanisole we could not detect a decrease of the quantum yield even when the solvent mixture consisted of 90% *tert*-butyl alcohol and 10% water. (2) Under electrolysis conditions where it could be assumed that radical cations had been formed the compounds did not show substitution or exchange at the meta position with respect to the nitro group. (3) The reduction of 4-nitroveratrole indicated the formation of the radical anion in the cathodic reduction. Again, no exchange could be detected at the meta position. (4) The charge distributions in the radical cations of the molecules studied should give an indication of the reactivity of the various positions if radical cations were involved. 4-Nitroveratrole is a molecule that is very suitable to check this as it is substituted at the meta as well as the para position with respect to the nitro group. Figure 2 shows the charge distribution in the radical cation of 4-nitroveratrole, as computed by INDO. This charge distribution does not account for a highly reactive meta position. On the contrary in the radical cation the para position carries the highest positive charge. (5) One should expect that the rates of reactions of radical cations show a similar dependence on nucleophilic systems as observed by Ritchie for cations.[18] He reported the correlation

$$\log (k_n/k_{H_2O}) = N_+$$

Herein k_n is the rate constant for the reaction of a cation in a nucleophilic system, k_{H_2O} is the rate constant for the reaction of the same cation in water, and N_+ has a value that is characteristic for the nucleophilic system n and independent of the cation. In Table II the quantum yields of the photoreactions of *m*-nitroanisole with OH^- (H_2O), CN^- (CH_3OH), and CH_3O^- (CH_3OH) are listed along with the N_+ values. It is obvious that there is no parallelism at all between the reported N_+ values and the observed quantum yields, thus making the involvement of a radical cation most unlikely.

Table II. Quantum Yields of Photoreactions of *m*-Nitroanisole (λ = 313 nm) in Different Nucleophilic Systems

nucleophilic system	ϕ	N_+
OH^- (H_2O)	0.22	4.5
CN^- (CH_3OH)	0.16	5.9
CH_3O^- (CH_3OH)	0.08	7.5

From the above results we can safely conclude that aromatic photosubstitution reactions, featuring NO_2-induced meta substitution, do not proceed by way of photoionization (or radical anion formation). The S_N2 Ar* mechanism seems to be operating.

The situation for *p*- and especially *o*-nitroanisole is less clear. In view of the different behavior in water and in methanol solutions it is possible that these compounds contrary to *m*-nitroanisole react via a different mechanism in the two solvents. Indications for a difference in mechanistic behavior of *o*- and *p*-nitroanisole and *m*-nitroanisole are also found in the photocyanation in water of these compounds. Photocyanation and anodic cyanation of the ortho and para compound give the same products in the same ratio. This is not the case with the meta compound.[19] On the other hand flash photolysis of water solutions of *o*- and *p*-nitroanisole shows just as in the case of the meta compound only triplet formation and no absorptions due to radical cations or/and solvated electrons,[19] as with $S_{R^+N}1$ Ar* reactions.[5] The lack of reactivity of *o*-nitroanisole in a S_N2 Ar* type reaction may be ascribed to steric hindrance. If the nitro group is not in the plane of the ring, its influence is diminished. The lack of reactivity of 3-nitro-4-*tert*-butylanisole has been explained similarly.[20]

Adopting the S_N2 Ar* mechanism, which for the present study is the S_N2 ^{3}Ar* mechanism, as both classical[13b,21] and flash photolysis studies[8,11b] have shown that methoxy nitro aromatic compounds react via the triplet state, how can one account for the high reactivity at the meta position?[22] The results obtained with symmetrical exchange reactions enable to determine if the meta activation results from different decay processes of a possibly

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[18] Ritchie, C. D. *Acc. Chem. Res.* **1972**, *5*, 348.

[19] den Heyer, J. Thesis, Leiden, 1977.

[20] Nijhoff, D. F.; Havinga, E. *Tetrahedron Lett.* **1965**, 4199.

[21] (a) Letsinger, R. L.; Steller, K. E. *Tetrahedron Lett.* **1969**, 1401. (b) Beijersbergen van Henegouwen, G. M. J.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1970**, *89*, 907. (c) de Gunst, G. P.; Havinga, E. *Tetrahedron* **1973**, *29*, 2167.

[22] We are well aware of the fact that high quantum yields do not necessarily imply high reactivitiy. Generally data on lifetimes are not yet available.

Table III. Quantum Yields of the Photochemical Symmetrical Methoxide Exchange and Photohydrolysis of Some Nitromethoxybenzenes

compd	ϕ(methoxide exchange)[a]	ϕ(photohydrolysis)[a]
m-nitroanisole	0.08	0.22[b]
p-nitroanisole	0.012	0.01[c]
4-nitroveratrole (meta position)	0.21	0.09[d]
4-nitroveratrole (para position)	0.016	0.0002

[a] Wavelength of excitation, λ = 313 nm. [b] Reference 13a. [c] Reference 12 and 14b. [d] Reference 17.

formed intermediate complex or whether it originates in an earlier stage of the reaction. This is done by comparing the selectivity in substitution reactions (hydrolysis) and in symmetrical exchange reactions (methoxide exchange) of nitroanisoles and 4-nitroveratrole. The quantum yields for these reactions are presented in Table III.

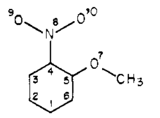
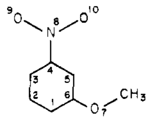
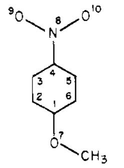
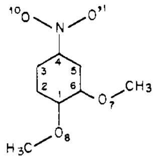
The results in Table III show that the meta-directing influence of the nitro group is smaller in the symmetrical exchange reactions than in the photohydrolyses but that it is a significant effect in all cases. Although there might be some contribution to the meta-directing effect from the decay process of a possible intermediate σ complex, the main cause has to be found at an earlier stage of the reaction.

Three theoretical approaches have been explored to investigate the interaction of a nucleophile with an excited aromatic (triplet) molecule, leading to the formation of a σ complex. (a) In the first approach the charge distribution in the excited state is used as a static reactivity index for the rate of reaction of the nucleophile with the excited aromatic molecule at different positions. See ref 6. (b) In the second approach the electron density in the HOMO and the electron density in the LUMO of the molecule are used in combination as a reactivity index for the rate of reaction of the nucleophile at different positions. This method had been proposed by Epiotis.[23] (c) In the third approach the energy difference between the excited-state surface and the ground-state surface is used as a dynamic reactivity index, this difference being the important factor which governs the ease of formation of a ground-state σ complex from the excited (triplet) state and the nucleophile.

The first two methods may account for the regioselectivity of the reactions and the third one for both regioselectivity and reactivity.

Approach a. The charge distributions of the isomeric nitroanisoles and 4-nitroveratrole have been calculated in the ground state and the lowest triplet state. The results of these computations are given in Table IV.

Table IV. The Charge Distribution of *o*-, *m*-, and *p*-Nitroanisole and 4-Nitroveratrole in the Ground State (S_0^A) and the Lowest State (T_1^{tot} and T_1^A)[a]

		S_0^A	T_1^{tot}	T_1^A
	1	+0.043	+0.022	+0.010
	2	−0.015	−0.017	0.000
	3	+0.037	+0.005	−0.006
	4	−0.014	−0.019	+0.046
	5	+0.189	+0.157	+0.146
	6	−0.051	−0.051	−0.035
	7	−0.190	−0.199	−0.204
	8	+0.489	+0.163	+0.178
	9	−0.344	−0.130	−0.141
	10	−0.330	−0.116	−0.133
	1	−0.029	−0.050	−0.062
	2	+0.023	+0.023	+0.037
	3	0.000	−0.032	−0.043
	4	+0.048	+0.047	+0.105
	5	−0.028	−0.061	−0.070
	6	+0.173	+0.173	+0.185
	7	−0.208	−0.208	−0.213
	8	+0.480	+0.157	+0.173
	9	−0.336	−0.131	−0.137
	10	−0.335	−0.128	−0.137
	1	+0.192	+0.173	+0.160
	2	−0.041	−0.042	−0.026
	3	+0.038	+0.005	−0.005
	4	−0.009	+0.006	+0.068
	5	+0.038	+0.005	−0.005
	6	−0.050	−0.051	−0.034
	7	−0.208	−0.213	−0.214
	8	+0.484	+0.159	+0.172
	9	−0.340	−0.130	−0.140
	10	−0.341	−0.131	−0.140
	1	+0.143	+0.122	+0.110
	2	−0.032	−0.033	−0.016
	3	+0.016	−0.018	−0.028
	4	+0.028	+0.024	+0.088
	5	−0.013	−0.044	−0.055
	6	+0.131	+0.130	+0.145
	7	−0.206	−0.206	−0.209
	8	−0.204	−0.209	−0.211
	9	+0.483	+0.157	+0.172
	10	−0.338	−0.127	−0.138
	11	−0.337	−0.125	−0.137

[a] The charge densities S_0^A and T_1^A are CNDO/2 calculated values. The charge density in the lowest triplet state is also calculated (T_1^{tot}) by the PPP-SCF-CI method and corrected for the σ-electron contribution. The difference between the CNDO/2 and PPP calculated charge densities for the various positions of the aromatic molecule in the S_0 state has been taken as this contribution. The results of the two methods are in good agreement.

Table V. The Electron Densities in the HOMO and LUMO of *m*- and *p*-Nitroanisole and 4-Nitroveratrole on the Carbon Atoms Bonded to a Substituent, Calculated by CNDO/2[a]

	C-NO$_2$		C-OCH$_3$		
molecule	HOMO*	LUMO	HOMO*	LUMO	positn of substitutn
4-nitroveratrole					2
m	0.09	0.15	0.14	0.01	
p	0.09	0.15	0.12	0.18	
m-nitroanisole	0.03	0.16	0.17	0.02	1
p-nitroanisole	0.24	0.14	0.17	0.18	1 and 4

[a] Data for the highest occupied molecular orbital of π character.

Analysis of these data leads to the following observations. (1) For the nitroanisoles as well as for 4-nitroveratrole there exists a qualitative correlation between the observed reactivities and the charge densities at the carbon atoms involved in the substitution in the lowest triplet state. Positions with larger positive charge show higher reactivity. (2) The carbon atoms carrying a nitro substituent have substantial positive charge densities in the lowest triplet state of these molecules. This could be the reason that in some photoreactions substitution of the nitro group occurs (this work and ref 1). However according to our experimental results this substitution only occurs with *p*-nitroanisole and not with the other nitroanisoles or with 4-nitroveratrole, a selectivity that is not rationalized by the charge density calculations.[24] (3) The calculations show a shift of electron density from the NO$_2$ group into the ring. This presents some difficulty in understanding why with aromatic compounds in the triplet state the NO$_2$ substituent effects such a large reactivity increase of the ring atoms vs. nucleophiles. Evidently the static reactivity index, charge density, may give an indication about the observed selectivities but is unsatisfactory with respect to explaining some essential features of the S$_N$2 ^{3}Ar* type reaction.

Approach b. Based on his treatment of qualitative potential energy surfaces in terms of the linear combination of fragment

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[23] (a) Epiotis, N. D. "Theory of Organic Reactions"; Springer-Verlag: New York, 1978. (b) *Ibid.* p 276. (c) Epiotis, N. D.; Shaik, S. *J. Am. Chem. Soc.* **1978**, *100*, 29.

[24] A reviewer pointed out that the argument is not valid any more if the nitro group in *p*-nitroanisole is displaced via a mechanism different from S$_N$2 Ar*. In our opinion the S$_{R+N}$ Ar* is not likely to occur in view of the influence of the solvent polarity.

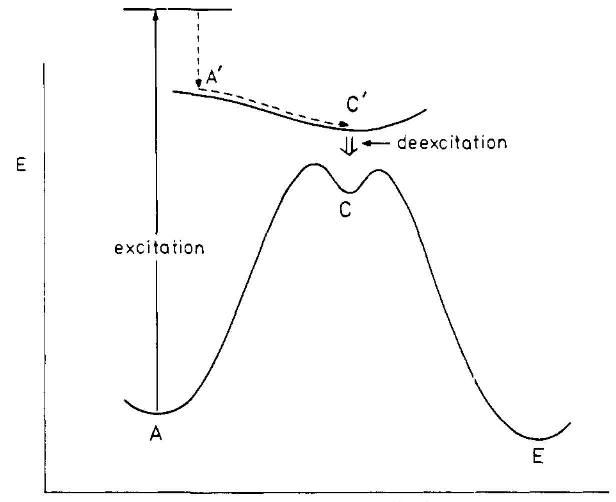

Figure 3. The possible course of an S_N2 Ar* reaction. Two-dimensional representation of a reaction pathway along multidimensional energy surfaces.

configurations approach, Epiotis[23] has put forward the hypothesis that a photochemical nucleophilic aromatic subsitution will occur in a manner which involves attack of the site of the aromatic molecule having the highest HOMO electron density and, simultaneously, the smallest LUMO electron density.

The electron densities at the carbon atoms bonded to a substituent have been calculated by CNDO/2 for *m*- and *p*-nitroanisole and 4-nitroveratrole.[25] Epiotis has computed comparable electron densities for the isomeric nitrophenols.[23b] The results are given in Table V.

There is a good correlation between the regioselectivity predicted and the actual regioselectivity. The reactivity index proposed by Epiotis seems to give a good indication of the directing effects in nucleophilic aromatic photosubstitution reactions of the S_N2 Ar* type.

Approach c. The course of a photochemical reaction is governed by both the shape of the potential energy surface of the excited state and the shape of the potential energy surface of the ground state.[26] A representation of the trajectories on these energy surfaces corresponding to a nucleophilic aromatic substitution of the S_N2 Ar* type is given in Figure 3.

The ground-state potential energy relationships have been thoroughly studied in thermal nucleophilic aromatic substitution reactions[27] and need no further discussion here. Interaction of the nucleophile with the vibrationally relaxed electronically excited aromatic molecule (A^1) possibly leads to the formation of an encounter complex or of an exciplex (C^1)[28,29] which can either decompose into its components or convert into the σ complex on the ground-state surface (C). The reaction then may proceed to yield product (E) or revert to starting material (A). The transition probability $C^1 \rightarrow C$ is related to the width of the energy gap. Data on radiationless transitions show that a decrease in the energy difference results in an exponential increase in the corresponding rate constants.[31] So the formation of a ground-state σ complex is favored when its energy content is high and/or when the excited state has a low-energy content.

Table VI. Differences in Reaction Energies ($\Delta\Delta E$) (kcal/mol) and Differences in Energy Content of the Lowest "Triplet States" ($\Delta E_\sigma{}^*$) for the Reactions under Discussion

reaction	$\Delta\Delta E$	$\Delta E_\sigma{}^*$
methoxy exchange of 4-nitroveratrole meta vs. para	16.57	−14.12
hydrolysis of 4-nitroveratrole meta vs. para	17.40	
methoxy exchange of nitroanisoles meta vs. para	15.35	−14.17
hydrolysis of nitroanisoles meta vs. para	16.17	

This in a straightforward manner qualitatively rationalizes the predominance of meta substitution in the photoinduced process on the basis of the high-energy level of the σ complex corresponding to meta subsitution in ground-state chemistry. For a somewhat more detailed discussion the energy contents of the starting materials and the σ complexes relevant for the photohydrolysis and photoexchange reactions of the nitroanisoles and 4-nitroveratrole were calculated by using the CNDO/2 method. From these data $\Delta\Delta E$ is obtained. $\Delta\Delta E = \Delta E_{\text{meta}} - \Delta E_{\text{para}}$ represents the difference in reaction energies of formation in the ground state of the σ complexes for meta and para subsitution. Also the energy contents of the lowest triple state of the σ complexes formed in the symmetrical exchange reactions were calculated to get some indication of the energy level of the excited-state surface. The triplet of the σ complex thus is used as a "model" for the encounter complex or exciplex formed from the nitro compound in its triplet and the nucleophile. From these data $\Delta E_\sigma{}^*$ is obtained. $\Delta E\sigma^* = E\sigma^*_{\text{meta}} - E\sigma^*_{\text{para}}$ equals the difference in energy content of the lowest triplet state of the σ complex formed from the aromatic compound in its lowest triplet and the nucleophile in meta and para substitution, respectively. The results are given in Table VI.

The results of the calculations are in suggestive, be it of course qualitative, agreement with the relative reactivities found in the photoreactions. (1) The photochemically more reactive meta-substituted compound in the ground state always has a 15–18 kcal/mol larger energy content than the corresponding para-substituted compound ($\Delta\Delta E$ values). (2) Comparing the methoxy exchange of *m*- and *p*-nitroanisole and 4-nitroveratrole as well as the hydrolysis of these compounds, the largest selectivity in both of these reaction types is found where the largest values of $\Delta\Delta E$ are calculated. (3) The selectivity of the photosubsitution reaction decreases by making the reaction symmetrical; in line with this experimental result the $\Delta\Delta E$ value for the methoxy exchange is lower than for the hydrolysis for both sets of compounds. (4) The difference in energy content of a meta and para σ complex in the lowest triplet state has a sign opposite to the one in the ground state: the lowest triplet state of the meta complex has the lowest energy content, indicating a small energy gap between the excited-state surface and the ground-state surface and a facile crossing.

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(25) Ferrier, S. J. H. Thesis, Leiden, to be submitted for publication.

(26) This now common mode of description in course of time developed through the contributions of many authors, i.e.: (a) Olson, A. R.; *Trans. Faraday Soc.* **1931**, *27*, 69. (b) Mulliken, R. S. *Phys. Rev.* **1932**, *41*, 751. (c) Longuet-Higgins, H. C.; Abrahamson, E. W. *J. Am. Chem. Soc.* **1965**, *87*, 2045. (d) Hoffmann, R.; Woodward, R. B. *Ibid.* **1965**, *87*, 2046. (e) Hammond, G. S. In "Reactivitiy of the Photoexcited Organic Molecule"; Wiley: New York, 1967, p 119 and in discussions in this volume; Hammond, G. S. *Adv. Photochem.* **1969**, *7*, 373. (f) Havinga, E. In "Reactivity of the Photoexcited Organic Molecule"; Wiley: New York 1967; p 201. (g) van der Lugt, W. Th. A. M.; Oosterhoff, L. J. *J. Am. Chem. Soc.* **1969**, *91*, 6042. (h) Zimmerman, H. E. *Angew. Chem.* **1969**, *81*, 45. (i) Förster, Th. *Pure Appl. Chem.* **1970**, *24*, 443. (k) Dougherty, R. C. *J. Am. Chem. Soc.* **1971**, *93*, 7187. (l) Michl, J. *Top. Curr. Chem.* **1974**, *46*, 1. (m) Salem, L. *J. Am. Chem. Soc.* **1974**, *96*, 3486. (n) Santiago, C.; McAlduff, E. J.; Houk, K. N.; Snow, R. A.; Paquette, L. A. *J. Am. Chem. Soc.* **1978**, *100*, 6149. (o) Turro, N. J. "Modern Molecular Photochemistry"; Benjamin-Cummings: Menlo Park, Calif., 1978.

(27) (a) Foster, R.; Fyfe, C. A. *Rev. Pure App. Chem.* **1966**, *16*, 61. (b) Crampton, M. R. *Adv. Phys. Org. Chem.* **1969**, *7*, 211. (c) Strauss, M. J. *Chem. Rev.* **1970**, *70*, 667.

(28) In a flash photolysis study of 3,5-dinitroanisole and the nucleophile OH^- Tamminga[8] established the occurrence of a charge-transfer complex (exciplex) as an intermediate preceeding the formation of the σ complex.

(29) This "aromate–nucleophile complex" can be formed in its triplet from the triplet excited aromatic compound and the nucleophile via a simple electron-transfer reaction along a single adiabatic surface.[30]

(30) Dauben, W, G.; Salem, L.; Turro, N. J. *Acc. Chem. Res.* **1975**, *8*, 41.

(31) (a) Zener, C. *Proc. R. Soc. London, Ser. A* **1932**, *137*, 696. (b) Landau, L. *Phys. Z. Sowjetunion* **1932**, *2*, 46. (c) Henry, B. R.; Siebrand, W. "Organic Molecular Photophysics"; Wiley: New York, 1973; Vol. I, p 155.

Most important, the strong activating influence of a nitro group can be explained along the same lines. Introduction of a nitro group in a benzene or an anisole molecule gives an appreciable lowering of the energy of the lowest triplet state (E_T(benzene) = 85 kcal/mol, E_T(anisole) = 80 kcal/mol, E_T(nitrobenzene) = 60 kcal/mol, E_T(*p*-nitroanisole) = 60 kcal/mol,[32] E_T(*m*-nitroanisole) = ~60 kcal/mol[8] (weak phosphorescence in methylcyclohexane–isopentane)). So the energy of the excited-state surface is substantially lowered, thus decreasing the energy gap between that surface and the ground-state surface and thereby activating the photosubstitution reactions.

Conclusion

The picture given under approach c smoothly rationalizes the phenomena of activation and of meta direction by the nitro group in $S_N2\ {}^3Ar^*$ reactions. The ease of formation of the ground-state σ complex from the excited-state surface is the decisive factor in the reaction. The energy contents of the ground-state surface as well as of the excited-state surface govern the reactivity and selectivity of the nitro compounds.

This picture is easily expanded to a general description with predictive power for S_N2 Ar* reactions: nucleophilic aromatic substitution reactions will occur efficiently under irradiation when they do not occur thermally or at a very low rate because of their high activation energy and when the excited-state surface is of low energy, i.e., when the energy gap between the ground-state and the excited-state surface is small. In benzene derivatives with a donor and an acceptor subsitutent usually the meta compound has a lower triplet energy than the para compound.[33] This favors meta direction and activation by an electron-withdrawing subsituent as a general phenomenon. When however the energy gap between the excited-state and the ground-state surface remains large, there is no facile crossing. For example a cyano group in the ground state has an effect similar to that of the nitro group, so ground-state surfaces will be comparable, but introduction of the cyano group in anisole, contrary to the nitro group, does not decrease the energy of the triplet state to a large extent (E_T(*m*-cyanoanisole) = 72 kcal/mol, E_T(*p*-cyanoanisole) = 75 kcal/mol).[34] Methoxide exchange in *m*- and *p*-cyanoanisole and 4-cyanoveratrole shows low reactivity and low selectivity.[25] The intermediacy of a σ complex in the reaction means that in the case of a nonsymmetrical substitution the thermal decomposition of the asymmetrical σ complex is another factor which governs the product formation. The higher the energy content of a σ complex with respect to the product the easier this product will be formed. On this basis it is possible to understand observed "leaving group effects".[1] It also explains the "merging resonance stabilization"[1,3] found in some photosubstitution reactions. Using the same method as described earlier to calculate the difference in reaction energies between starting material and σ complex, it is also possible to calculate $\Delta\Delta E$ between σ complex and products. This additional information then results in a more complete understanding of the course and mechanism of the nucleophilic aromatic photosubstitution reaction of the S_N2 Ar* type.

Experimental Section

General Information. Melting points were determined on a Büchi Schmelzpunktbestimmungsapparat. Ultraviolet spectra were recorded on a Cary 14 or Cary 15 spectrophotometer. Optical densities at fixed wavelengths were obtained with a Zeiss PMQ II spectrophotometer. A Perkin-Elmer EPS-3T was used to measure transmissions. Infrared spectra were recorded on a Beckman IR-10 spectrophotometer, proton magnetic resonance spectra recorded on a JEOL JNM-MH-60 (minimar) or on a JEOL JNM-PS-100 spectrometer, and mass spectra recorded on a GEC AEI-MS 902 mass spectrometer and on a GEC AEI-MS 20 mass spectrometer, coupled with a Hewlett-Packard 5750 gas chromatograph. GLC analyses were performed on a Becker Multigraph-F 410 gas chromatograph equipped with a flame ionization detector employing one of the following columns: 3m × 1/8in. 20% SE-30 on Chromosorb WAW, 45-60 M; 2m × 1/4in. 10% SE-30 on Gaschrom Q, 80-100 M or 2m × 1/8in. 20% Carbowax 20 M TPA on Chromosorb WAW, 45-60 M. Preparative GC separations were performed on a Varian Aerograph 920, equipped with a thermal conductivity detector, using a 6m × 3/8in. 20% SE-30, Chromosorb WAW, 45–60 M column. Radioactivities were measured with a Packard Tricarb 3310 liquid scintillation counter. Efficiencies were determined by using the channel ratio method. Electrolysis experiments were conducted in a U-shaped tube. On one side a Pt electrode was immersed in a solution containing only the nucleophile, and on the other side a Pt electrode (gauze) was immersed in the reaction mixture. The arms of the tube were separated by a glass frit.

Materials. The [^{14}C]methoxy-labeled compounds **1**–**5** were all prepared from the corresponding phenols by methylation with [^{14}C]methyl iodide (The Radiochemical Centre, Amersham) according to the method of Claisen.[35] The phenols were refluxed in acetone with a twofold excess of radioactive methyliodide and an excess potassium carbonate. The methoxy compounds were purified by repeated crystallization from methanol or by destillation (in the case of **1**). The products were diluted with the inactive compounds to get the desired specific activity (~10^5 dpm/mmol). 4-Nitroguaiacol was prepared from 4-nitroveratrole by alkaline hydrolysis with potassium hydroxide in water.[36] 5-Nitroguaiacol was prepared by a modification of its synthesis by Cardwell.[37] 4-Nitroveratrole was hydrolysed in a concentrated hydrogen bromide solution. Hydrogen bromide was added several times during the reaction. The product was purified by column chromatography (silica gel, benzene) and crystallization from water. 4-Nitroveratrole was prepared by nitration of veratrole.[38] All compounds described were characterized and identified by melting point and IR, NMR, and mass spectrometry.

Irradiation Procudures. Two methods have been used to carry out the irradiations. (**a**) Reaction mixtures were irradiated in a cylindrical reactor (content 100 mL). A quartz glass inner tube was filled with water or a filter solution, and a lamp was immersed in the center of the apparatus. A Hanau TNK 6/20 was used as a light source for irradiations at 254 nm, a Hanau Q81 combined with various filter solutions at other wavelengths. (**b**) Reaction mixtures were irradiated in a spectrophotometer cuvette, using a Philips HP 125-W lamp as the light source. The wavelength of excitation was selected by using an appropriate filter solution. In both methods the mixtures were stirred and if necessary cooled to make sure that the temperature of the solution was 15–20 °C.

Kinetics. The chemical changes of the aromatic compounds in the irradiation were monitored by measuring the optical densities of the system at several wavelengths and by GLC analysis. The change in the radioactivity of the aromatic compound as a function of time of irradiation was determined by two different procedures. (**a**) A 1.0-mL aliquot of the reaction mixture was added to 10.0 mL of water and 10.0 mL of a scintillator solution (PPO and dimethyl-POPOP in toluene or Insta-Fluor, Packard). The organic layer was washed with water and dried, and the radioactivity (A) was determined. The change in A reflects the change in the specific activity (α) of the compound irradiated. (**b**) A 1-mL aliquot was added to 2 mL of water and 2 mL of chloroform. The reaction product was obtained pure from the organic layer by preparative gas chromatography. This product was dissolved in methanol. The optical density (D) and the radioactivity (A) of this solution were determined. The change in the specific activity of the compound measured is reflected by the change in A/D. Under the conditions of the irradiations no thermal exchange occurs. The exchange reactions show first-order kinetics (cf. Figure 1). If in the irradiation in addition to the exchange product a chemically different product is formed, the specific activities have to be corrected for the decrease of starting material and the fraction of the incident light not absorbed by the starting material. From the change of the (corrected) specific activities as a function of irradiation time the rate of exchange can be calculated. The quantum yields of the exchange and the other reactions have been determined by comparison with the photohydrolysis of *m*-nitroanisole. This is a well-defined reaction with known quantum yields at various wavelengths. The photohydrolysis was performed under the same conditions as the reaction to be determined. From the measured rates of hydrolysis (v_H) and for example exchange (v_E) and the known quantum yield for the hydrolysis (ϕ_H), the quantum yield for the exchange reaction (ϕ_E) is calculated by $\phi_E = (v_E/v_H)\phi_H$. The rates v_E and v_H have been corrected to 100% light absorption.

Acknowledgment. We wish to thank Professors J. Cornelisse and J. J. C. Mulder for stimulating discussions and Dr. E. J. J. Groenen for valuable assistance with the quantum mechanical calculations.

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[32] Brinen, J. S.; Singh, B. *J. Am. Chem. Soc.* **1971**, *93*, 6623.

[33] Wagner, P. J. *Pure Appl. Chem.* **1977**, *49*, 259.

[34] Lui, Y. H.; McGlynn, S. P. *J. Mol. Spectrosc.* **1975**, *55*, 163.

[35] Claisen, L.; Eisleb. O. *Justus Liebigs Ann. Chem.* **1913**, *401*, 29.

[36] Pollecoff, F.; Robinson, R. *J. Chem. Soc.* **1918**, *113*, 64.

[37] Cardwell, D.; Robinson, R. *J. Chem. Soc.* **1915**, *107*, 255.

[38] Vermeulen, M. H. *Recl. Trav. Chim. Pays-Bas* **1906**, *25*, 12.