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SOME PROBLEMS IN AROMATIC PHOTOSUBSTITUTION

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INTRODUCTION

In this paper we wish to summarize results in the field of (heterolytic) aromatic photosubstitution and especially bring into focus a few problems that arise from recent investigations. To this end the following plan is adopted: (A) Review and interpretation of results as available 1–2 years ago. A few fundamental problems will be indicated. (B) Presentation of some new reactions that in at least one respect seem to differ from those discussed under (A). (C) Summary of present situation and of problems for discussion.

(A) REVIEW OF EARLIER WORK

Interest in aromatic photosubstitution reactions was sparked by the observation of R. O. de Jongh that nitrophenyl esters and ethers, which are very stable in aqueous solution in the dark, undergo a strikingly smooth hydrolysis upon irradiation with light that is absorbed by the aromatic system[1]. A feature that contributed to our decision to investigate the reactions more extensively, was the fact that the *meta* compounds were more reactive than the *ortho* and *para* isomers, in contradistinction to the rules of classical ground state chemistry[1, 2]. Before discussing the characteristics of these processes some examples are given of additional reactions discovered during the period 1956–1966 (*Figures 1–6*)[2–5]. From these figures one gets the impression that a large variety of heterolytic aromatic substitutions may be effected by irradiation provided one chooses the right, mostly mild conditions. Of course, this opens interesting possibilities for the synthetic chemist!

As a general characteristic of this category A one may notice that not only these reactions show the rather outspoken specificity, but that the orientation rules are entirely different from the classical *ortho/para* activation; there is generally governing a specific *meta*, or *meta/ortho* activation (desactivation). In this context may also be mentioned reactions studied by Zimmerman *et al.* like the solvolysis of substituted benzylacetates and the photohydrolysis of trifluoromethylbenzenes discovered by Heilbronner and Seiler, where the *meta* compounds with electron donating substituents react more readily than the *ortho* and especially the *para* isomers[6,7].

Now here arises one of the first problems, which constitutes a general difficulty in photochemistry: the efficiency of a reaction, as measured by its quantum yield is the result of a competition between several processes, the chemical conversion leading to product and the desactivations of the excited

molecules. Thus, when we compare the photoreactions of two different compounds, say *m*- and *p*-nitroanisoles, then the fact that the *meta* compound reacts much better than the *para* may be due to a greater reactivity in the excited state of the *meta* compound. It may also be due, however, to a shorter lifetime of the excited *para* isomer, not allowing efficient bimolecular reaction.
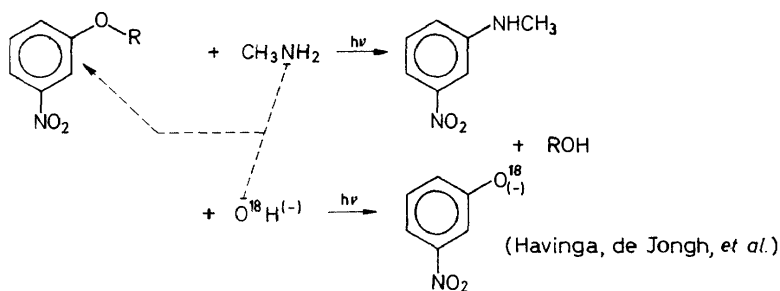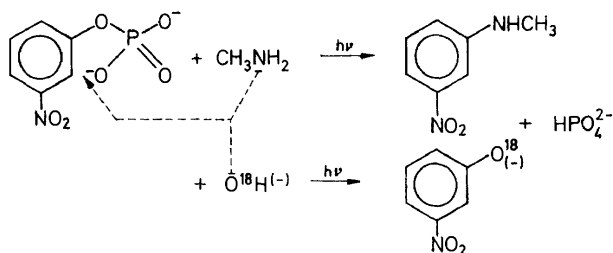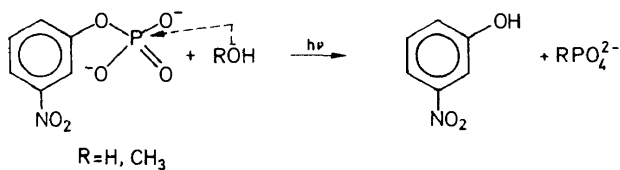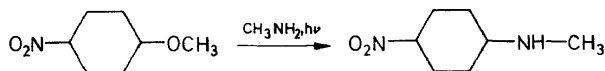
Figure 1. Photohydrolysis and photoamination of nitrophenyl esters and ethers[1, 2]

We stand on somewhat firmer ground if we compare the rates of reaction (quantum yields) of two positions in one and the same molecule, thus eliminating the factor "lifetime of the excited state". If we do so in this
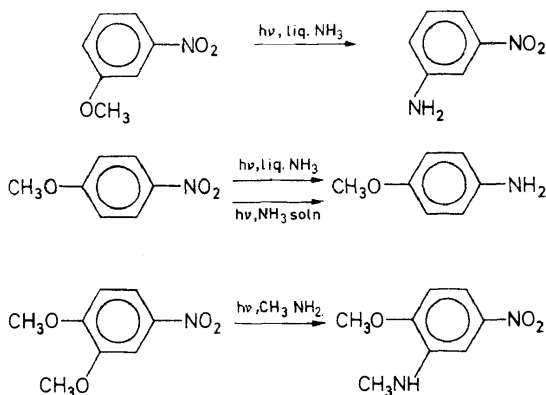
Figure 2. Photoamination of nitrophenyl ethers[2, 9]
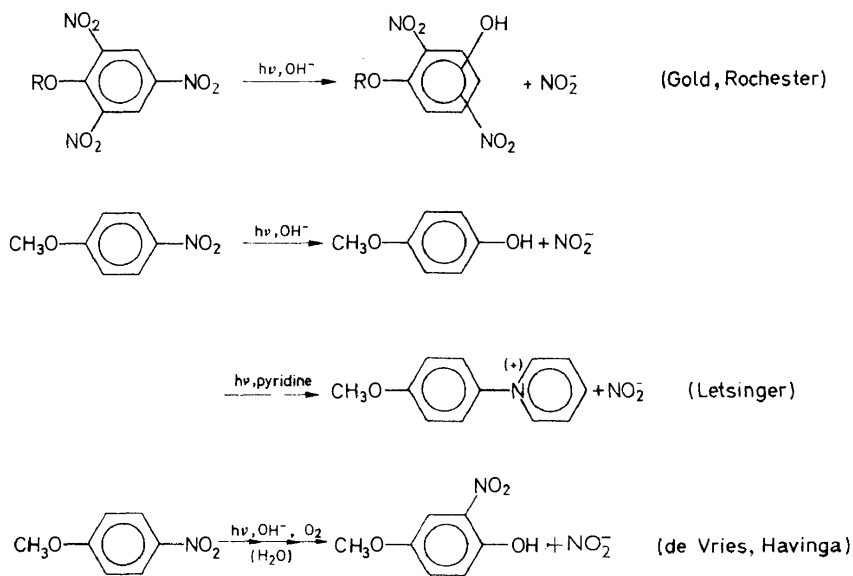
Figure 3.
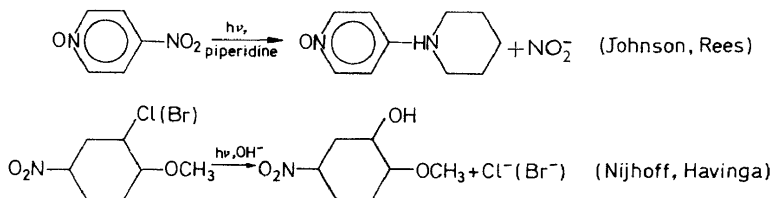
Figures 3 and 4. Nucleophilic photosubstitution of the aromatic nitro group and of aromatic halogen[3, 2d, 2g]

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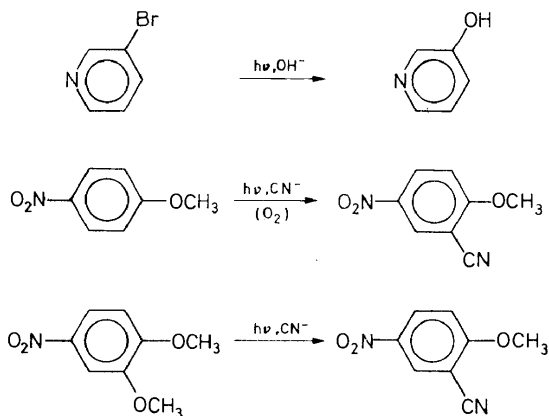
Figure 5. Photohydrolysis of 3-bromopyridine[2h]; photocyanation[4]

Figure 6. Photodeuteration of monosubstituted benzenes[5]

S=NO$_2$,CN

(Zimmerman, Zimmerman, Somasekhara)

(Zimmerman, Sandel)

Figure 7. Photohydrolysis of phenyltrityl ethers and of benzyl derivatives[6]

class of aromatic photosubstitutions we then observe the *meta* activation by a nitrosubstituent in the case of nucleophilic reaction[8] and the *ortho/meta* activations by electron donors such as alkyl- and methoxy-groupings for electrophilic substitutions, (photodeuteration)[5] (*Figures 8* and *9*).
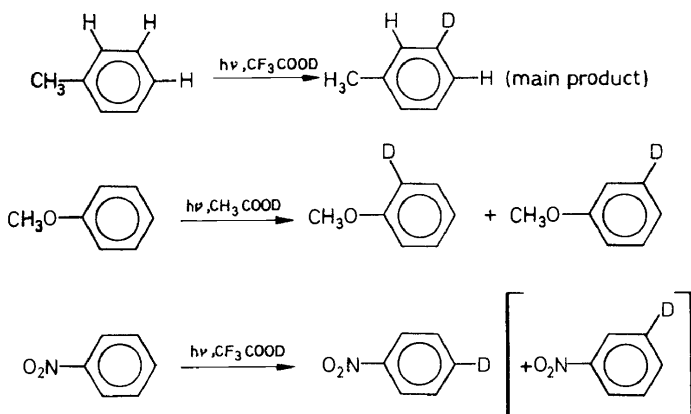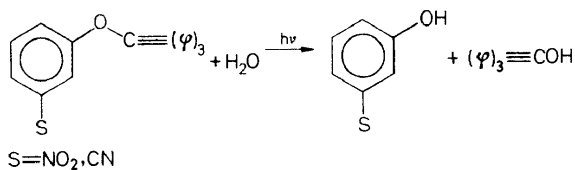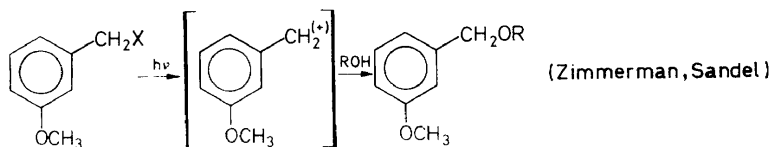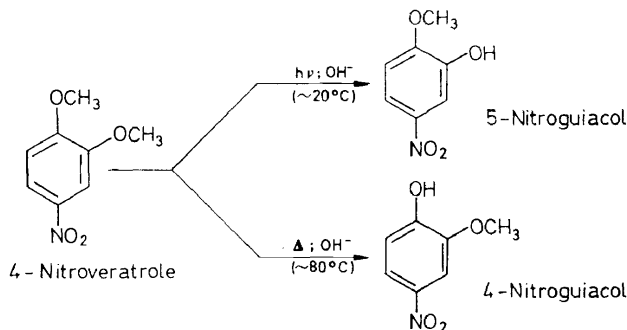

Figure 8. Comparison of photoreactivities at *meta* and *para* positions[8]
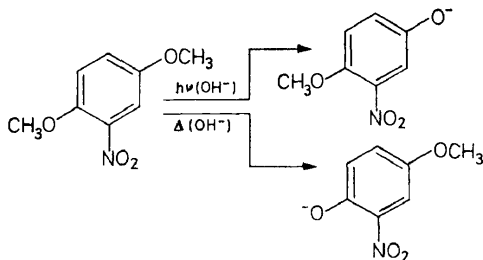
Figure 9. Comparison of photoreactivities at *meta* and *ortho* positions[8]

We may therefore with some justification state that there is *meta* or *meta/ortho* activation in this category of reactions. Let us now try to arrive at a simplified mechanistic picture of this group of reactions that comprises *inter alia* photohydrolysis, photoamination and photocyanation of nitrophenyl and naphthyl ethers as nucleophilic substitutions, and the photodeuteration of alkylbenzenes and alkoxybenzenes as electrophilic substitution. These generally are very clean reactions with good quantum yields. The reactions are practically temperature independent, first order in light intensity and zero order in the aromatic compound as is to be expected for normal photoreactions. Quantum yield is the same for light absorbed in the first $\pi-\pi^*$ and the second $\pi-\pi^*$ band (*Figure 10*). No indications of the occurrence of triplet states or free radicals were found. $n-\pi^*$ Excitation does not—or only slightly—contribute to the reaction; the quantum yield goes down at wavelengths over 350 mμ, where $n-\pi^*$ absorption occurs.

All this leads to the conclusion that we can best describe the reactions as starting from a low vibrational level of the "first excited singlet" ($\pi \to \pi^*$ or sometimes $n \to \pi^*$). This is in agreement with the fact that chloride and, in particular, bromide ions, known to catalyse the $S_1 \to T_1$ transformation,

strongly diminish the quantum yields of these reactions when present in significantly high concentrations (~ -1 molar, cf. below).

Suggestive data are gained from the study of the influence of the concentration of the reagent. The reagent has to be present in rather high concentrations (10^{-3} to 10^{-2} molar or higher) in order to obtain a substantial quantum yield. This is consistent with the idea of a bimolecular reaction in which one of the partners has a short-lived excited state. The quantum yield increases with increasing concentration, levelling off at concentrations of 0·1–1 molar towards a constant and maximum value (mostly in between 0·1 and 0·5) (*Figure 11*). This suggests a competition between the (spontaneous)
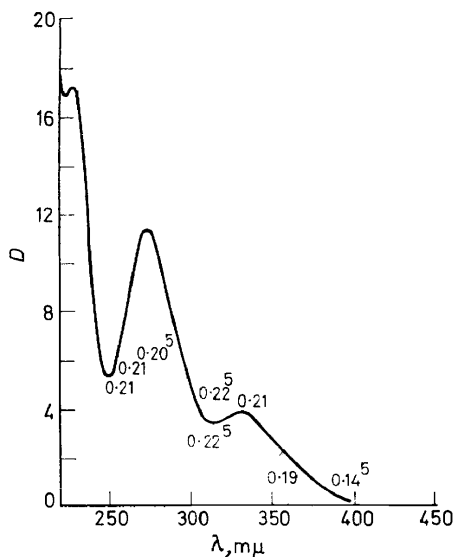

Figure 10. Quantum yields at various wavelengths for the photohydrolysis of *m*-nitroanisole in 0·01 N NaOH
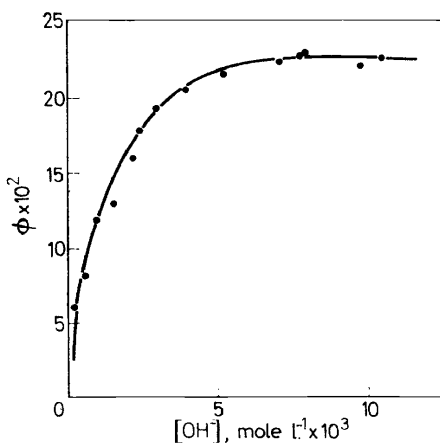

Figure 11. Quantum yield (ϕ) as a function of the concentration of substituting reagent (OH$^-$) in the case of the photohydrolysis of *m*-nitroanisole

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desactivations (fluorescence, internal conversion) of the excited molecules and their encounters with the reaction partner. However, even if the latter is present in such a high concentration that the spontaneous desactivation can compete no longer, the quantum yield remains significantly below 1. This means that encounters between excited molecule and reaction partner lead to reaction for a certain percentage and to quenching for the remaining percentage.

In order to rationalize all experimental data we may set up a scheme† that includes our knowledge of the mechanism of aromatic substitution in the ground state (*Figure 12*). As a useful example we choose the deuteron/proton
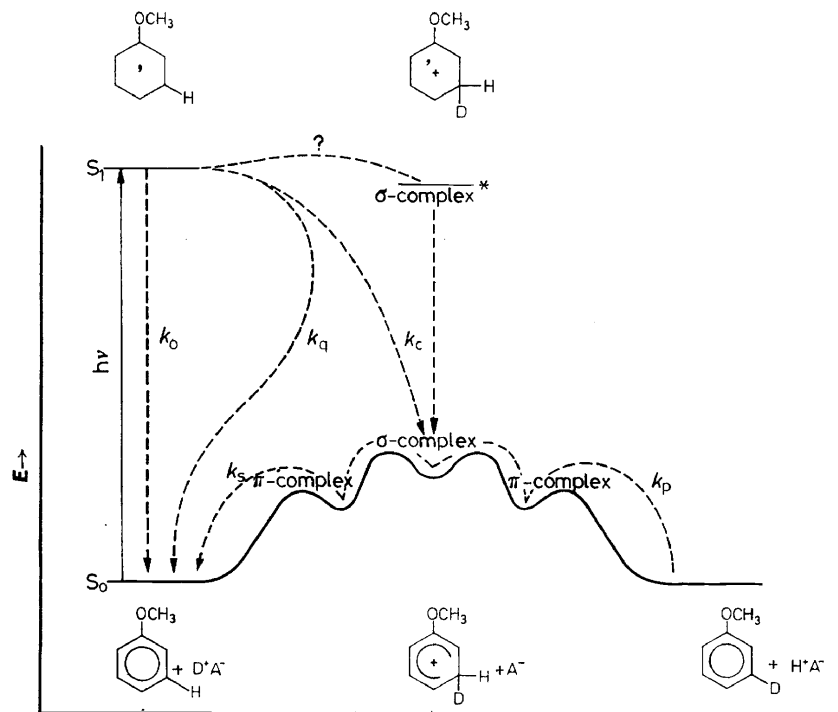
Figure 12. Possible energy relationships and reaction paths in the photodeuteration of anisole

exchange, because this reaction is fairly simple and symmetrical. In the ground state reaction curve the intermediate σ-complex is accounted for, whilst also the (probably not essential) presence of π-complexes is indicated.

Starting from the S_1 state a molecule may (i) become desactivated by fluorescence or internal conversion (k_0); (ii) encounter a CF_3COOD molecule and become quenched[a] (k_q), or react[b] (k_c).

It seems improbable that this reaction (ii[b]) of the molecules in the S_1 state would require non-negligible activation energy and proceed, e.g. towards an excited product or an excited σ-complex at a higher level than

† It seems worthwhile to emphasize that a two-dimensional representation for a photo-reaction of a molecule of even moderate complexity can be extremely deceptive.

that of S_1 + CF$_3$COOD. This would ask for longer lifetime than an S_1 state can have (10^{-8}–10^{-9} sec). Let us assume, therefore, that the system goes either to a relatively low lying excited σ-complex (if existent) and then very rapidly to the ground state σ-complex or that (more probably) it cascades down directly to the σ-complex in the ground state. The conversion to the ground state σ-complex may be a rather probable process, since the corresponding energy gap is relatively small. In this latter case one could consider the reaction as a kind of internal conversion from the excited S_1 state to the ground state σ-complex. (We would not at this stage differentiate for the mechanism of the σ-complex formation between a direct attack of the substituting reagent and a process wherein the initial stage electron transfer between aromatic and reagent takes place, followed by combination of the radicals formed.) From the σ-complex the system comes further down to product (k_p) or returns to the starting situation (k_s) along pathways normally trodden in ground state substitution reactions. It is easy to derive that this mechanism leads to the following relation between the reciprocal values of the quantum yield and the concentration of the reagent R.

$$\frac{1}{\phi} = \frac{k_s + k_p}{k_p} \times \frac{k_0}{k_c[R]} + \frac{k_s + k_p}{k_p} \times \frac{k_q + k_c}{k_c}$$

Such a linear relationship between $1/\phi$ and $1/[R]$ has been found to exist in all cases investigated (*Figures 13, 14*). It is in agreement with the picture

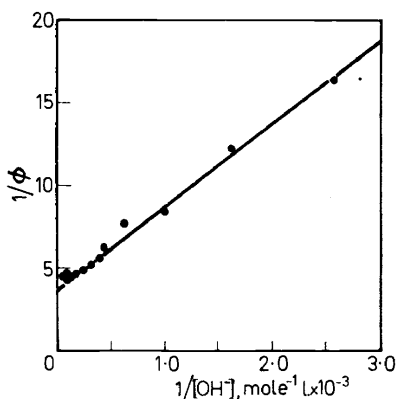*Figure 13.* Linear relationship of $1/\phi$ *versus* $1/[OH^-]$ for reaction of *Figure 10*

developed for the reaction path, but of course constitutes no proof of it. As a further attractive feature one may remark that the results are reasonable from a quantitative point of view.

For the alkaline hydrolysis of *m*-nitroanisole the following values were found:

$$\frac{1}{\phi} = 0.005 \frac{1}{[OH^-]} + 3.6$$

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At a concentration of $\sim 10^{-3}$ mole [OH$^-$], desactivation and product formation are in balance. The not unreasonable assumption $k_q \simeq k_c$ and $k_s \simeq k_p$, fits the equations found, together with $k_0/k_c = 2 \cdot 5 \times 10^{-3}$ mole/l. Whether this picture be right or wrong, it has the advantage of pointing to a definite problem. Even if one compares the quantum yields for reactions
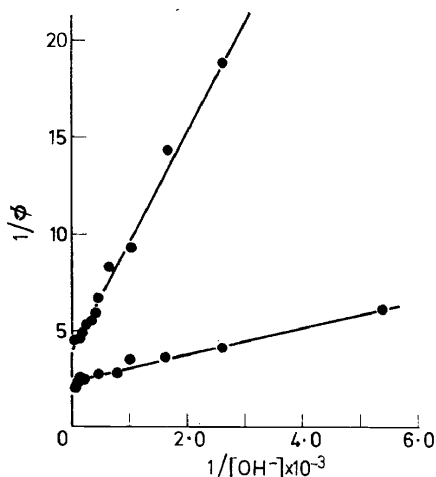
Figure 14. $1/\phi$ *versus* $1/$[OH$^-$] for photohydrolysis; *m*-nitroanisole (upper curve) and 3,5-dinitroanisole (lower curve)

at different positions in one and the same excited molecule and thus eliminates the problem of different lifetimes one cannot be certain that reliable information about the relative reactivities at the carbon atoms of the aromatic is obtained. Although k_0 can be eliminated it is not simple to deduce values for k_c from the equations. In the next example of the photodeuteration of anisole with CF$_3$COOD in tetrahydrofuran the situation seems rather

Figure 15. $1/\phi$ *versus* $1/$[CF$_3$COOD] for the photodeuteration of anisole; *ortho* position lower curve, *meta* position upper curve, *para* position no reaction)

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favourable. The equations for *ortho* and *meta* substitution (*para* substitution does not occur!) are:

$$\frac{1}{\phi^o} = \frac{k_o}{k_c^o[CF_3COOD]} \times \frac{k_s^o + k_p^o}{k_p^o} + \frac{k_q + k_c^m + k_c^o}{k_c^o} \times \frac{k_s^o + k_p^o}{k_p^o}$$

$$= \frac{0.64}{[CF_3COOD]} + 8.$$

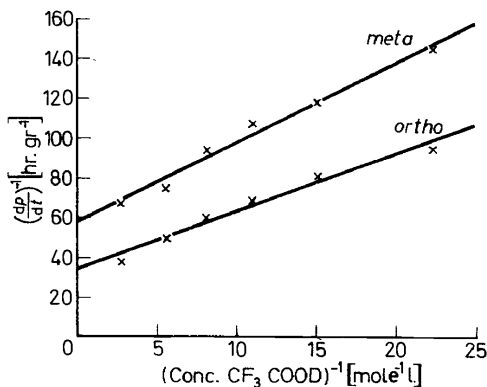$$\frac{1}{\phi^m} = \frac{k_o}{k_c^m[CF_3COOD]} \times \frac{k_s^m + k_p^m}{k_p^m} + \frac{k_q + k_c^m + k_c^o}{k_c^m} \times \frac{k_s^m + k_p^m}{k_p^m}$$

$$= \frac{1.0}{[CF_3COOD]} + 14.$$

For a substitution by deuterium it seems likely that

$$\frac{k_p^o}{k_s^o + k_p^o} \simeq \frac{k_p^m}{k_s^m + k_p^m}$$

This gives us from the intercepts: $k_c^o/k_c^m = 1.7$. Furthermore, assuming an isotope effect of the order $k_p^o/k_s^o \simeq k_p^m/k_s^m \simeq 4 : k_o/k_c^o \simeq 0.5$ mole/l. and $k_o/k_c^m \simeq 0.8$ mole/l. This gives the value 1.6 for k_c^o/k_c^m, in agreement with the value 1.7 derived from the intercepts.
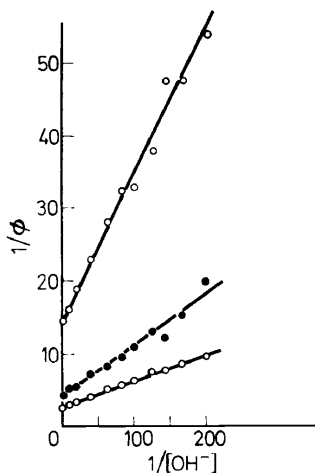
Figure 16. $1/\phi$ *versus* $1/[OH^-]$ for the photohydrolysis of 2-bromo-4-nitroanisole [lower curve: disappearance of starting material; middle curve: substitution of bromine atom; upper curve: substitution of methoxy group]

The ratios of the intercepts and the slopes have proved consistent also in the other systems studied. As a third example we would mention the alkaline photohydrolysis of 2-bromo-4-nitroanisole[2g]. For the substitution of the bromine substituent one obtains: $1/\phi = 0.075 \times 1/[OH] + 4.0$; for the replacement of the methoxy group: $1/\phi = 0.21 \times 1/[OH^-] + 14.$

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To round off this survey it may be remarked that the reaction pattern observed in this category of nucleophilic and electrophilic substitution reactions does not show much relation to the calculated localization energies in the S_1 state. In some cases there is a striking correspondence to the electron densities as calculated by the Pariser–Parr–Pople method†. The photo-deuteration of anisole and the photohydrolysis of nitroveratrole are examples that clearly show this relationship (*Figures 15, 17* and *18*). This feature seems understandable on the basis of the experience that very fast substitution reactions in the ground state also are governed by the charge density.
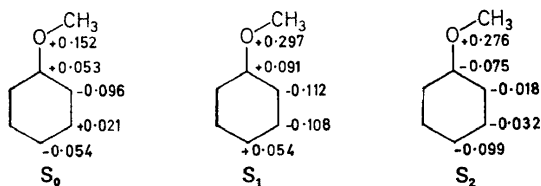
Figure 17. Calculated charge densities of anisole in S_0, S_1 and S_2
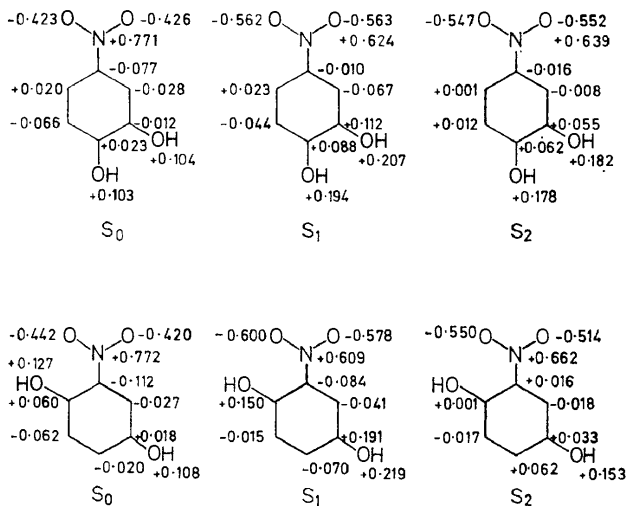
Figure 18. Calculated charge densities of 4-nitrocatechol and nitrohydroquinone in S_0, S_1 and S_2

Evidently, with these very fast photosubstitutions, it is the electrical attraction between the charges at the ring carbon atoms and the reagent that in the first phase of the interaction determine at which position the reagent will approach the aromatic ring and subsequently will react to form the

† The calculations were carried out by Drs. J. J. C. Mulder of the Department of Theoretical Organic Chemistry (Head: Prof. Dr. L. J. Oosterhoff). The calculations were rounded off by taking into account configuration interaction of all singly excited states.

σ-complex. Of course, in the related alternative rationlization of initial electron transfer between the exited aromate and the substituting reagent the importance of the charge distribution can be understood equally well.

(B) SOME NEW REACTIONS

During the last two years another category of photosubstitution reactions has been discovered. The reactions occur under the influence of light and not in the dark but they seem to follow the *ortho/para* orientation rule of ground state chemistry. *Figure 19* gives some examples of this category that comprises photoamination in liquid ammonia of nitrobenzene, dinitrobenzene and nitrochlorobenzenes[9]. (With nitroanisoles the amination in liquid NH₃ follows a pattern analogous to that of other amination reactions of class A.) There are numerous possible causes of the difference between the reactions of classes A and B. One may think of a different reaction mechanism, e.g. connected with complex formation between the nitrobenzenes and ammonia, or a reaction in a vibrationally highly excited level of the ground
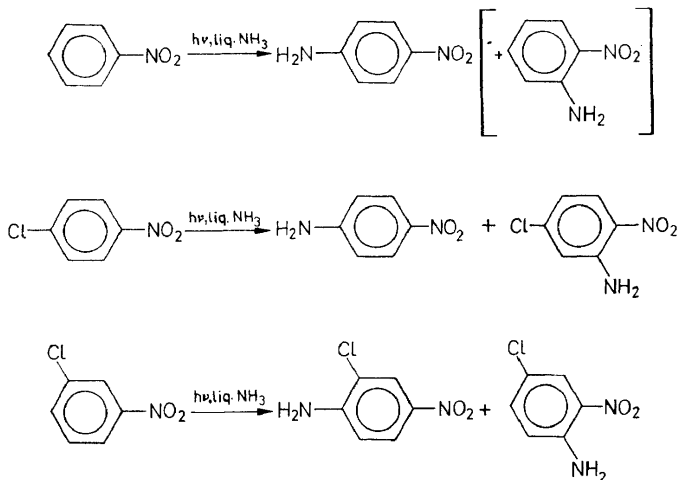
Figure 19. Photoamination in liquid ammonia of subsituted benzenes[9]

state reached as a result of internal conversion. Also triplet states or free radicals are not yet excluded in the reactions which until now have been studied only by isolation and characterization of the products formed†. One

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† Recent e.s.r. studies (with A. van Vliet) of the systems nitrobenzene/liq. NH₃ and *m*-nitroanisole/liq. NH₃ showed the rapid building up of an intense signal upon illumination; this signal seems to indicate the formation of the aromatic radical anion (for this possibility cf. ref. 11).

‡ In this context it is suggestive that in the reaction with excited nitroveratrole, the substitution by NH₂CH₃ and NH(CH₃)₂ seems to parallel the charge distribution less closely than the charged nucleophiles OH⁻ (and CN⁻).

feels curious, however, whether it is possible to bring the pattern described in this section in harmony with the picture developed for the reaction under section (A). It may prove essential that the reaction partner is electrically neutral as well as present in very high concentration. It might therefore be that the initial attack on the various positions in the excited aromatic molecule occurs without much discrimination and that the σ-complexes for the *ortho*, *meta* and *para* positions are formed at not too different rates‡. Then the percentage of product formation from the σ-complex, $k_p/(k_s + k_p)$, may exert a dominating influence. It is to be expected that this factor will be favourable for the formation of *p*-nitroaniline on account of merging resonance stabilization in the course of the process. *o*-Nitroaniline will be next and formation of *m*-nitroaniline will be least favourable.

In short one might say with respect to this class of photosubstitution that here the light may serve to bring the system to a high enough energy level in order that σ-complexes can be formed which practically cannot be reached in thermal reactions. The subsequent thermal reactions of the σ-complexes then, to a greater or lesser extent, determine the ratios of the quantum yields.

(C) PRESENT SITUATION

The problems indicated under A and B may look as if they are not too far from solution, e.g. by refining the tentative mechanistic picture given. We want to make it clear, however, that in the experimental data there are also problems, for which a solution or a semi-quantitative discussion at the moment still seems difficult and where only extensive experimental research may lead to further insight.

A first difficulty is offered by the photodeuteration of nitrobenzene, where the *para* position reacts fastest in accordance with charge distribution in the $\pi \rightarrow \pi^*$ as well as the $n \rightarrow \pi^*$ singlet. However, the reaction at *meta* (about half as fast as at *para*) proceeds much easier than one would predict on that same basis[5]. Possibly here—in the case of electrophilic substitution of an electron-poor excited aromatic system—the reaction is intermediate in following charge distribution and localization energy (the latter is calculated to be lowest at *meta* in S_1). Greater problems still arise when looking at the following compilation for the occurrence of photohydrolysis:
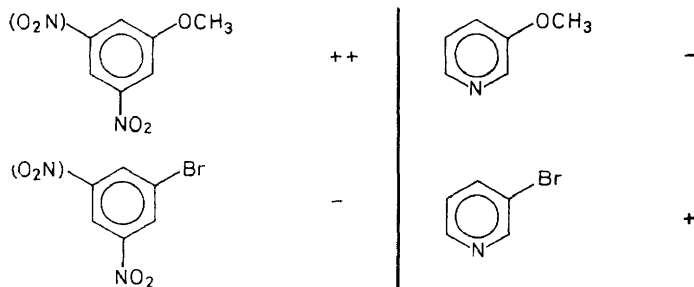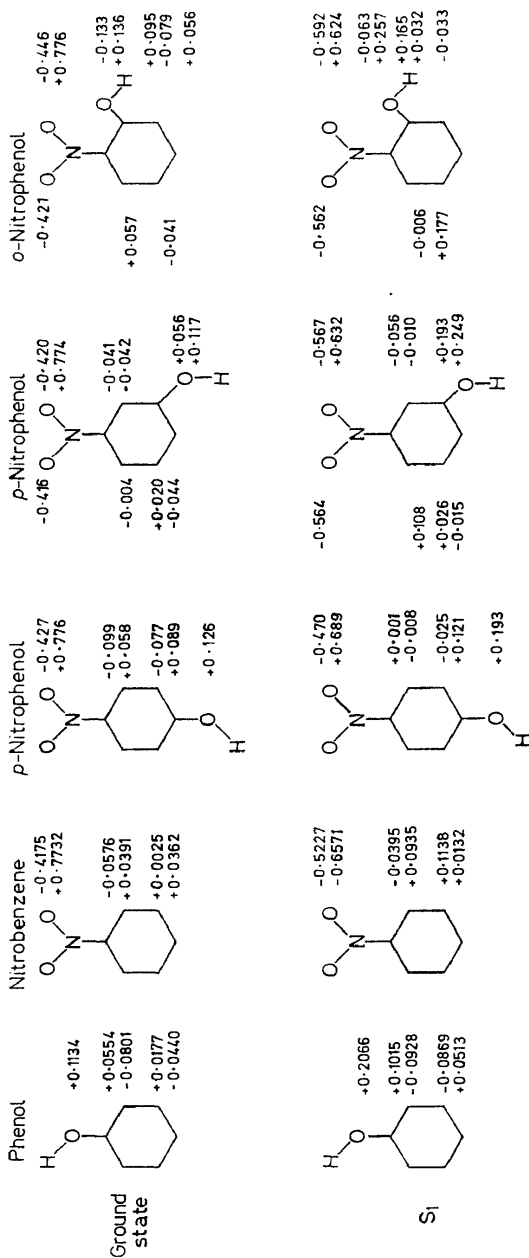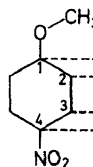
Figure 20. Calculated charge distribution in S_0 and the lowest excited singlet $\pi \rightarrow \pi^*$ for a few substituted benzenes

Other challenges to chemical research and thinking are offered by comparing the various ways of photoreaction of one and the same molecule (*p*-nitroanisole) with different substituting reagents.

	Charge distribution		Preferred orientation of substituent					
	$\pi \to \pi^*$	$n \to \pi^*$	D⁺	NH₂CH₃	Pyridine	OH⁻	NH₃	CN⁻
1	+0·12	−0·05		+		+		
2	−0·03	−0·08	+					+
3	−0·01	−0·05	+					
4	+0·00	−0·17			+	+	+	

The pattern of photodeuteration of *p*-nitroanisole is consistent with charge distribution in the $\pi \to \pi^*$ and the $n \to \pi^*$. The reaction with NH₂CH₃ [and NH(CH₃)₂] and with pyridine is also in harmony with charge-distribution in S₁, taking into account merging stabilization during product formation. The reaction with OH⁻ seems understandable although there is the fact that the substitution at 4 preponderates over that at 1. The substitution by NH₃ (liquid as well as conc. solution in water) at 4 and not at 1 seems difficult to explain; also the attack of CN⁻ at 2 offers serious problems as to its theoretical interpretation.

These examples clearly show that although some basic patterns in heterolytic photosubstitution begin to become experimentally and theoretically founded, there are, just like in ground state chemistry, many fundamental and stimulating problems in the variability and divergence of the phenomena observed; one could say that photosubstitution is reaching the stage of chemical maturity. In some cases we feel pretty sure that the reaction takes its start from the $(\pi - \pi^*)$ S₁ state. However, in many cases it remains to be established whether the photosubstitution starts from the $\pi \to \pi^*$ or the $n \to \pi^*$, from the singlet or from the triplet state. The calculation of charge hetero- and, in particular, of localization energies of substituted benzenes and densities cyclics in the excited states still may not have reached the exactness desired. The quantum yield of the reaction may be a function of the interaction of the electric charges of the ring carbon atoms and the substituting reagent, of the probability of falling down of the still excited "encounter pair" to σ-complex (or product), and of the yield of subsequent thermal product formation processes. The tentative picture given (*Figure 12*) should for the moment be considered as a working hypothesis. The investigation of the specificity connected with the detailed nature of the substituting species as well as of the role of the solvent has only just started.

In this paper the remaining provocative problems have been stressed perhaps more than the consistent aspects of the phenomena and the mechanistic interpretation arrived at. It seems appropriate therefore to conclude by mentioning the promising results obtained by application of flash photolysis to as yet only a few of the systems. Through the help of Professor Dr. G. J. Hoijtink at Amsterdam and Professor Dr. S. Claesson at Uppsala we were enabled to perform various flash experiments, using solutions of *m*-nitroanisole, of 3,5-dinitroanisole or of 2-bromo-4-nitroanisole in 0·05 N

NaOH. In all three cases intermediates were observed which had broad absorption bands (ranging from 400–600 mμ). The lifetime of the intermediates varied from ~0·1 sec to several seconds. After ~1 min the absorption spectra demonstrated that the final products were the same as observed in the photosubstitution reactions discussed above (nitrophenolate, dinitrophenolate, nitroguiacol and bromonitrophenol). No intermediates were observed in experiments with solution in water without alkali nor in alkaline solutions to which Br⁻, that suppresses the photoreactions[2g, 10], had been added.

It looks as if this way the possibility is open to study in a straightforward manner the intermediates, possibly the σ- and π-complexes presumed to occur in the photosubstitutions. This may offer a clue to unravel a few of the intriguing problems existing in the field of photochemical and also of thermal aromatic substitution reactions.

ACKNOWLEDGEMENT

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