Chemical Reviews

Photosubstitution Reactions of Aromatic Compounds

J. CORNELISSE and E. HAVINGA*

Department of Organic Chemistry, Gorlaeus Laboratories, University of Leiden, The Netherlands

Contents

I. Introduction

In this review a survey is given of experimental results and some pertaining rationalizations in the area of aromatic photosubstitution. The classification used is based on the type of aromatic nucleus and on the number of substituents. Thus, most of the numerous examples of aromatic photosubstitution discovered over the past two decades have been arranged according to the types of compounds undergoing these reactions, rather than according to similarities in their mechanistic aspects. That this choice has been made is not caused by a lack of information on the mechanisms of these reactions: a summary of the present state of our knowledge is given in the concluding discussion. Classifications of photochemical aromatic substitution reactions based on reaction type (e.g., homolytic or heterolytic; nucleophilic, electrophilic, or radical), character of the excited state (singlet or triplet; n,π^* or π,π^*), or kinetics (bimolecular or unimolecular) are certainly possible and meaningful.[128] At the same time it is considered useful to present a survey of aromatic photosubstitutions so arranged as to enable the reader to locate quickly which reactions have been described and investigated within certain classes of compounds.

The present review covers the literature up to the spring of 1974 and is more exhaustive in the field of heterolytic substitutions in carbocyclic aromatics than in radical substitutions and reactions of heterocyclic compounds.

II. Aromatic Hydrocarbons

A. Benzene

Photochemical reactions in which the unsubstituted benzene molecule undergoes substitution are known, but in many of these cases the reactive species is not a benzene molecule in an excited state. For example, in the photochemical reaction of benzene with BBr_3 or BI_3 which yields benzeneboron dihalides, the products are believed[1] to be formed by photolysis of the boron trihalides followed by reaction of the resulting dihalogenoboryl radicals with benzene. In the photochemical cyanation of benzene with cyanogen iodide, the cyano radical is the active species in the substitution reaction with ground state benzene.[2]

Photochemical ethoxycarbonylmethylation of benzene with ethyl haloacetate in the presence of metallic halides has been described.[3] Here photochemical excitation of benzene does occur, but the authors believe that the excited benzene molecule transfers its energy to a complex formed from metallic halide and ethyl haloacetate. The reactive species is considered to be a charge-transfer complex like $(MCl_{n+1}^- {}^+CH_2CO_2Et)^*$ which acts as an electrophilic reagent in its reaction with benzene in its electronic ground state.

Irradiation of benzene in the presence of potassium cyanide in an aqueous organic solvent does not lead to formation of detectable amounts of benzonitrile.[4] In this respect benzene differs from naphthalene, biphenyl, and azulene, which compounds do undergo substitution by

cyanide upon irradiation in the presence of KCN (vide infra).

The photochemical reactions described by Bryce-Smith et al.[5-7] in which benzene reacts with amines and with pyrrole lead to products which on oxidation (dehydrogenation) yield substituted benzenes. The reacting species appears to be benzene in its excited state, but the primary products are mainly 1,4-adducts rather than substitution products. However, the distinction with some of the photochemical reactions to be described further on in this article is not quite sharp, since in some of these cases formation of an adduct (complex) may also be the first step of the reaction, the substitution product being formed in a secondary oxidative process.

B. Naphthalene

The photocyanation of naphthalene is one of the first examples of a nucleophilic photosubstitution on an unsubstituted aromatic hydrocarbon. Until now, cyanide ion is the only nucleophile with which this type of reaction has been accomplished. From this and many other reactions (e.g., p-nitroanisole with cyanide ion, section III.A.1) cyanide ion appears to be particularly effective in displacing hydrogen from excited aromatic molecules, where other nucleophiles like hydroxide ion and methoxide ion are often unsuccessful in this respect.

Irradiation of 300 mg of naphthalene in 1500 ml of tert-butyl alcohol/water (1:2) with 0.1 M KCN for 12 hr in a Rayonet photochemical reactor (RPR 208, 2537 Å) afforded 20 mg of 1-cyanonaphthalene.[4,8] Other products
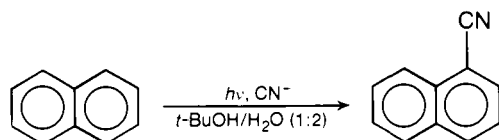

of the reaction are monocyanodihydronaphthalene and dicyanotetrahydronaphthalene 2-Cyanonaphthalene could not be traced. At present, no mechanistic details of this reaction are known. It is interesting to note that nucleophilic attack on the excited state of naphthalene leads to substitution at the same position where in the ground state electrophilic substitution (and probably also nucleophilic substitution) takes place preferentially.

Photochemical exchange of hydrogen in aromatic hydrocarbons is one of the very few examples of electrophilic photosubstitution.[9] The basicity of aromatic hydrocarbons in singlet and triplet excited states is much higher than in the ground state. Accordingly, the rate of hydrogen exchange in the excited state is higher than in the ground state.

Kuz'min et al.[10] studied the photochemical H–T exchange of naphthalene and anthracene in mixtures of acetic acid and sulfuric acid. Quantum yields varied between 10^{-4} and 10^{-2}, depending on the acidity of the medium. The authors did not compare the reactivities of the different positions in the aromatic molecules. Lodder and Havinga[11,12] irradiated naphthalene-1-d and naphthalene-2-d (and other compounds) together with CF$_3$COOH in n-hexane solution. They demonstrated the occurrence of photoprotodedeuteration. The ratio of the rates of the photodedeuteration at the α and β position is 7:2.[129] For the thermal exchange reaction the ratio was found to be 12:1. A similar increase in reactivity at the β position was found by Stevens and Strickler[13] who measured quantum yields of photoinduced hydrogen–deuterium exchange of α- and β-naphthalene-d_1 in moderately concentrated H$_2$SO$_4$.

C. Biphenyl

Photocyanation of biphenyl is a reasonably efficient reaction. Yields are higher than in the case of naphthalene. The products of the reaction are 2-cyanobiphenyl, 4-cyanobiphenyl, and at least two dicyano-substituted biphenyls which were not further identified.[4,14]
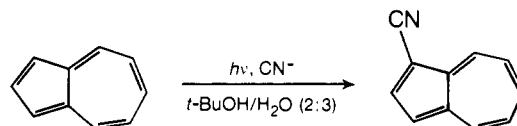

dicyanobiphenyls
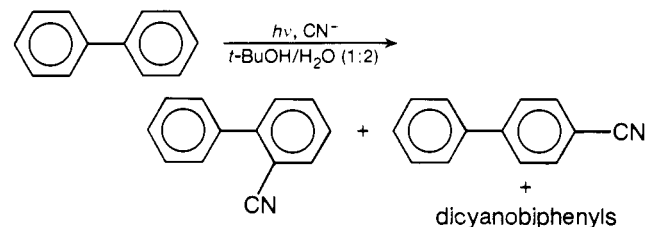
Biphenyl (200 mg) and 5 g of KCN in 1500 ml of tert-butyl alcohol/water (1:2) were irradiated in a Rayonet photochemical reactor (RPR 208, 2537 Å). After 10 hr 67.5% of the biphenyl had reacted. After 21 hr of irradiation the degree of conversion was 99%. The yield of 2-cyanobiphenyl proved to be independent of the time of irradiation (13.8% after 10 hr, 14.3% after 21 hr). The yield of 4-cyanobiphenyl decreases with increasing times of irradiation (28.6% after 10 hr, 17.5% after 21 hr). At the same time the yield of disubstituted compounds increases (10.6 and 22.6%, respectively). The sum of the yields of 4-cyanobiphenyl and the disubstituted biphenyls remains constant. Hence the dicyanobiphenyls are formed in a photochemical reaction from 4-cyanobiphenyl.

The photoreaction of biphenyl with cyanide ion can be sensitized with benzophenone. Product ratios are the same as in the direct irradiation.[14] It is concluded that the photocyanation of biphenyl most probably is a triplet reaction. Quantum yield measurements in the presence of triplet quenchers have not yet been attempted.

Allowing for the statistical factor, the ratio of the reaction rates at the ortho and para position in biphenyl is ca. 1:6. As in the case of naphthalene, the orientation of nucleophilic photosubstitution in biphenyl follows the same pattern as electrophilic (and nucleophilic) substitution in the ground state.

D. Azulene

The only nucleophile by which azulene has been found to undergo substitution in its excited state is again cyanide ion. The product of the photochemical reaction is 1-cyanoazulene.[4,8] From irradiation for 120 hr in a Rayonet photochemical reactor (RPR 208, 3000 Å) of a solu-

tion of 244 mg of azulene in 1500 ml of tert-butyl alcohol/water with 0.1 M KCN, 24 mg of 1-cyanoazulene was isolated; the amount of recovered starting material was 182 mg.

In the ground state of azulene, nucleophilic substitution occurs predominantly at the 4 position.[15,16] whereas electrophilic reagents attack at position 1. This is in accord with calculated charge densities:[8,17] in the ground state positions 1 and 3 bear the highest negative charge, while carbon atoms 4 and 8 are positively charged. In the excited state the situation is reversed. Nucleophilic substitution now occurs at position 1, i.e., again at the position that is to be expected on the basis of the calculated

charge densities: in the lowest excited singlet state as well as in the lowest triplet state positions 1 and 3 bear the highest positive charge.[8,17]

E. Other Aromatic Hydrocarbons

Phenanthrene yields 9-cyanophenanthrene in approximately 30% yield on irradiation in the presence of potassium cyanide.[8]

Fluorene behaves like biphenyl; the major product of photocyanation with KCN is 2-cyanofluorene.[14]
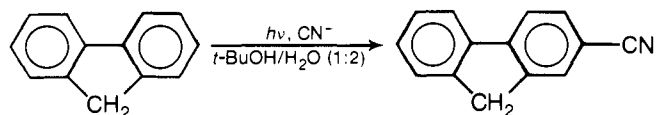
III. Monosubstituted Compounds

A. Monosubstituted Benzenes
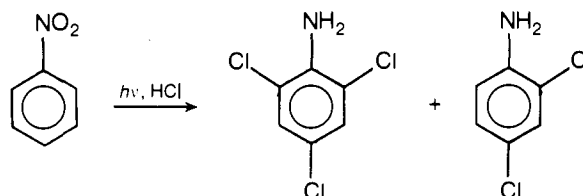
1. Nitrobenzene

Nitrobenzene is not a very reactive compound as far as photoinduced substitution is concerned. Whereas many derivatives of nitrobenzene on excitation react readily with pyridine, hydroxide ion, and methoxide ion to give substitution products, nitrobenzene itself is rather inert in the presence of these reagents. Four reactions have been reported in which nitrobenzene does undergo photosubstitution: photoreaction with concentrated nitric acid,[18] photoreaction with concentrated hydrochloric acid,[19] photoamination,[20-22] and photodeuteration.[23]

Irradiation of dilute solutions of nitrobenzene in 70% HNO$_3$ in nitrogen atmosphere with light of wavelengths above 366 nm affords m-dinitrobenzene, p-dinitrobenzene, and picric acid, each in roughly 20% yield.[18]
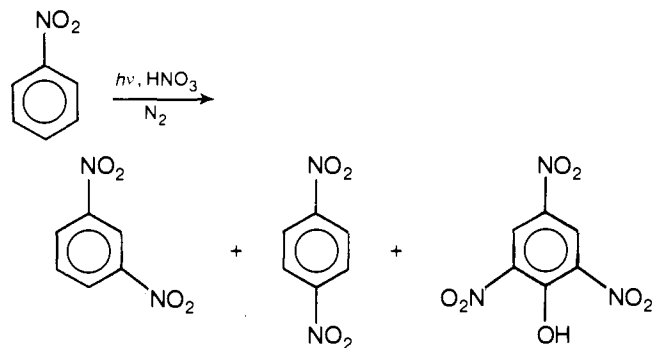

The course of the reaction is dependent on the amount of nitrogen oxides present. Addition of urea (which removes nitrogen oxides) increases the proportion of p-dinitrobenzene. Interruption of the nitrogen purge, which results in a build-up of the concentration of nitrogen oxides, leads to a higher relative yield of the meta isomer. The mechanism of this aromatic photonitration is still unknown; the authors[18] believe, however, that the reaction is not an electrophilic substitution on an excited state of nitrobenzene.

Letsinger and Wubbels[19] report that nitrobenzene (308 mg) in concentrated hydrochloric acid (500 ml) on irradiation (1200-W G.E. photochemical lamp; Pyrex filter; 10 hr) affords 2,4,6-trichloroaniline (44–62% yield) and 2,4-dichloroaniline (ca. 10%). The reaction rate depends upon both the hydrogen ion and the chloride ion concentration. A high concentration of the latter (>6 M) is required to achieve an appreciable rate. It has been suggested[19] that the protonated nitrobenzene in the excited state is attacked by chloride ion. Interestingly, in this reaction ortho/para substitution occurs. If the reaction

sequence is initiated by nucleophilic attack of chloride ion on the excited state of protonated nitrobenzene, this would mean that the protonated nitro group, being a strong electron acceptor, would effect the same type of substitution pattern in the excited state as in the ground state. These results have been confirmed by Hurley and Testa.[24] From their kinetic experiments they conclude that protonation takes place in the triplet state of nitrobenzene.

Photoamination[20-22] of nitrobenzene is also characterized by the need of a high concentration of nucleophile and by the occurrence of ortho/para substitution. The ortho/para substitution pattern is suggested to be, at least partly, due to the (thermal) product-forming steps, which favor more the ortho/para than the meta product. p-Nitroaniline (25%, based on the amount of converted starting material) and o-nitroaniline (1–2%) were obtained on irradiation of nitrobenzene in liquid ammonia at −60° with a high-pressure Hg arc.[22] A small amount of p-aminoazobenzene was also isolated from the reaction mixture.
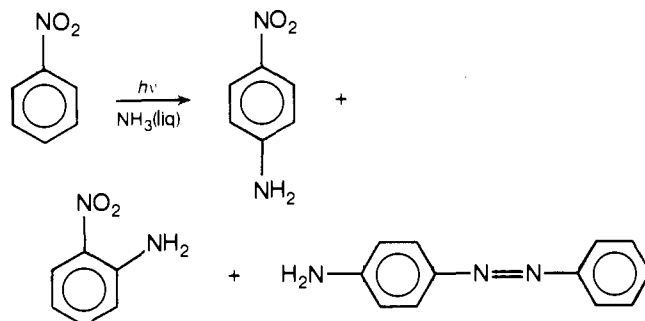
None of these products could be found in an irradiated solution of nitrobenzene in 15% ammonia/methanol. In this medium photoreduction of nitrobenzene probably takes place.[25] In 25% ammonia/water, formation of p-nitroaniline, if any at all, was extremely slow.

The photosubstitution of nitrobenzene in liquid ammonia can be sensitized by benzophenone. Irradiation in the presence of a 40-fold excess of benzophenone yields the same products as were found in the direct irradiation. Oxygen completely suppresses the photoreaction of nitrobenzene in liquid ammonia when light of wavelengths above 300 nm is used for excitation. This fact may be considered indicative of a triplet state reaction.[20] However, with unfiltered light from a high-pressure mercury source, there is no quenching effect by oxygen. It is argued[20] that on irradiation with the lower wavelengths, π,π^* excited singlet states of nitrobenzene are reached, which may react directly with ammonia. With light of λ >300 nm nitrobenzene is excited into its n,π^* singlet. It is conceivable that the relatively high electron density in the ring in this state prevents nucleophilic substitution from occurring. However, intersystem crossing may take place into the triplet manifold in which, as is known from the sensitization experiments, substitution by NH$_3$ occurs.

Apart from the stable products mentioned, two unstable photoproducts have been observed upon irradiation of nitrobenzene in liquid ammonia.[20] One is the nitroben-

zene radical anion, detected by electron spin resonance. Though from electrolysis experiments with nitrobenzene in liquid ammonia it could be concluded that generation of the radical anion may give rise to the formation of p-nitroaniline, the small yields of this reaction make it unlikely that this radical anion is an intermediate in the main pathway of the photosubstitution reaction.

The other unstable photoproduct has an absorption maximum in the near-ultraviolet at 335 nm. It is not an intermediate in the photosubstitution, since the reaction in which it is formed competes with the formation of p-nitroaniline. It is postulated[20] that the "335-nm species" may arise from attack on the nitrogen atom of the nitrobenzene radical anion by the ammonia molecule (or a radical derived from it). This would probably explain the experimental observation that on raising the temperature from $-60°$ to $-35°$ the "335-nm species" decomposes yielding nitrobenzene.

The assumption that photosubstitution of nitrobenzene by ammonia may occur in the excited singlet as well as in the triplet state implies that in both types of excited states nucleophilic substitution results in the formation of ortho/para isomers.

Photochemical hydrogen–deuterium exchange has been studied by de Bie and Havinga[23,26] and by Lodder and Havinga.[11,12] Nitrobenzene could be photodeuterated with difficulty and in strongly acidic media only.[23,26]

Cyanide ion and methoxide ion do not show photosubstitution in nitrobenzene. Instead, cyanide ion attacks the nitro group in photoexcited nitrobenzene, thereby converting it into nitrosobenzene.[14,27,28] The oxygen atom is transferred to the cyanide ion: cyanate ion has been detected[14,27] in the irradiated solution. 1-Nitronaphthalene (section II.B.1), on the other hand, yields a substitution product (1-cyanonaphthalene) on irradiation with cyanide ion. The same is true for other polycyclic aromatic nitro compounds and also for derivatives of nitrobenzene possessing electron-donating substituents[28] like methoxyl (cf. section III.A.1). This difference in behavior toward cyanide ion is ascribed[14,28] to the character of the reactive excited state. It appears that a low-lying n,π^* state (e.g., in nitrobenzene) undergoes reduction, whereas a low-lying π,π^* excited state (as in nitronaphthalene and the nitroanisoles) undergoes substitution by cyanide ion. Another reagent which may function both as reducing agent and as nucleophile is BH_4^-. Indeed, nitrobenzene yields aniline upon illumination in the presence of sodium borohydride, while 1-nitronaphthalene is photosubstituted to give naphthalene.[28]

2. Anisole

Nucleophilic photosubstitution reactions of anisole have been found by Barltrop, Bunce, and Thomson[29] and by Nilsson.[30,31] Barltrop and coworkers describe the irradiation, with the unfiltered light from a medium-pressure mercury arc, of equimolar proportions of anisole and piperidine leading to N-phenylpiperidine in 9% yield. It has been shown that the reaction is initiated by excitation of the anisole, not of the piperidine. Photoreaction of anisole with diethylamine gave diethylaniline in yields varying from 8 to 31%, depending on the anisole concentration. With ethoxide ion in ethanol phenetole was formed in 4% yield, while the reaction with cyanide ion in methanol produced benzonitrile (3%). The nucleophiles ethanol, acetic acid, acetate ion, and water were found to be unreactive toward photoexcited anisole.

The authors adopt the view that the mechanism of the light-induced replacement involves the attack of the nucleophile at the electron-deficient atom C-1 of the excited state of the aromatic substrate:[29]
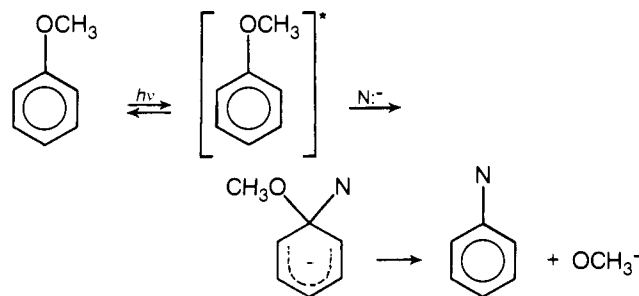
Nilsson[30,31] reports on the photolysis of anisole in the presence of cyanide ions in methanol. The products of the reaction are o- and p-cyanoanisole in the ratio 53:47, the amount of meta isomer being negligible. No mention is made of the formation of benzonitrile. These results clearly differ from those of Barltrop et al. The discrepancy may be explained by the fact that Barltrop's results are obtained in solutions purged with nitrogen, while in Nilsson's work oxygen is not excluded. If the formation of the o- and p-cyanoanisole proceeds via an intermediate σ complex, it is conceivable that in the product-forming step oxygen removes a hydride ion from the complex. In the absence of oxygen, cyanide will still attack at the ortho and para positions, but no substitution product will be formed. Instead, benzonitrile formed by attack of cyanide ion at the, probably less reactive, carbon atom bearing the methoxy substituent will be observed.

Benzene does not undergo photocyanation. Chlorobenzene is rather unreactive toward cyanide ion, whereas p-chloroanisole reacts readily upon photoexcitation.[32] These results, together with the observed substitution pattern in anisole, seem to indicate that the methoxy substituent has an activating, ortho/para directing influence. For a nucleophilic aromatic substitution this is rather surprising. In ground state aromatic substitution the methoxy group is found to have a deactivating effect on nucleophilic attack, the effect being strongest at the ortho and para positions. Consequently, the methoxy group is described as a deactivating meta director for nucleophilic aromatic substitution. For the excited state the reverse seems to be true.

A change in the orientation rule on going from the ground state to the excited state has also been observed for the nitro group (see sections III.A.1 and IV.A.2), which acts as a meta-directing substituent in nucleophilic aromatic photosubstitution. However, the nitro group activates both in the ground state and in the excited state, whereas the methoxy group exerts its activating effect only in the excited state. Calculated charge densities for singlet and triplet excited states of anisole[12] do not indicate that the methoxy group turns into an electron-withdrawing substituent upon excitation of the molecule. In the excited states its electron-donating effect seems to be even stronger than in the ground state. The question then arises whether the photocyanation of anisole is a real bimolecular aromatic substitution, Nilsson[31] proposes a mechanism in which the excited aromatic molecule undergoes photoionization; the resultant cation radical reacts with cyanide ion to form a radical σ complex. This radical may undergo oxidation to a Wheland-type intermediate which will yield the cyano-substituted product by losing a proton. Alternatively, the radical intermediate may disproportionate to an aromatic nitrile and a dihydro compound. So far, no experiments have been reported which support this postulated mechanism.

Photodeuteration of anisole, an example of electrophilic aromatic photosubstitution, has been found by de Bie and Havinga.[23,26] Lodder and Havinga[11,12] measured the

quantum yield of the photochemical tritiodeprotonation of anisole ($\phi = 6 \times 10^{-3}$ at 254 nm in n-hexane; tritiated trifluoroacetic acid: 0.146 mol/l.). They also determined the substitution pattern in the photoprotodedeuteration of anisole. The rates of photosubstitution for the ortho, meta, and para position are as 6:1:2. This is different from the pattern obtained in thermal deuterodeprotonation where the relative rate for meta substitution is much smaller (ortho:meta:para = 1:0:1).[11] The results cannot be rationalized on the basis of excited state charge densities alone; also other factors seem to be important in determining the course of the reaction.
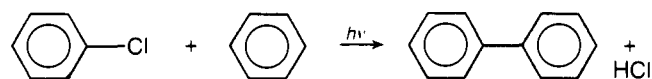
3. Halogenobenzenes

A large portion of the work published on photoreactions of halogen-substituted benzenes deals with the photochemical interchange of halogens at the aromatic ring. Examples are to be found in the work of Milligan and his coworkers[33] and in the review by Sharma and Kharash.[34] Since in many cases not the aromatic molecule but the reagent (for example, bromine or iodine chloride) is the excited species, such reactions are not included in this review.

Matsuura and Omura[35] irradiated 0.05 M solutions of bromobenzene in benzene with a low-pressure mercury lamp under nitrogen and obtained biphenyl in 40% yield. Hydrogen bromide has been observed as a reaction product. Various bromobenzene derivatives were photolyzed
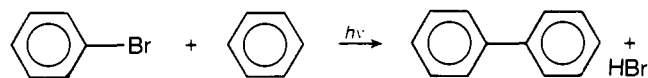
under the same conditions. The p-hydroxy-, p-methoxy-, p-methyl-, p-acetyl-, and p-carbomethoxybromobenzenes afforded the corresponding 4-substituted biphenyl derivatives, whereas the photolyses of p-amino-, p-nitro-, and m-nitrobromobenzene yielded no biphenyls. A reaction mechanism is proposed in which the first step upon excitation is dissociation of the bromo compound into a phenyl radical and a bromine atom. The phenyl radical then attacks the solvent to form a radical intermediate which may undergo hydrogen abstraction by either the bromine atom or a phenyl radical.

A similar reaction has been observed with chlorobenzenes by Robinson and Vernon.[36] Irradiation of a solution (6×10^{-3} M) of chlorobenzene in benzene (low-pressure mercury arc) afforded biphenyl in 43% yield (75.5% based on chlorobenzene decomposed). The ratio of HCl:biphenyl was found to be 1.04:1. A number of substi-

tuted chlorobenzenes show the same type of reaction. Among these are o-. m-, and p-methyl-, o-, m-, and p-hydroxy-, o- and p-cyano-, o- and p-methoxy-, o-chloro-, and p-aminochlorobenzene.

Photoreactions in which excited molecules undergo homolytic dissociation into a halogen atom and an aromatic radical have also been studied by Kuz'min and coworkers.[37] Photolysis of chlorobenzene and bromobenzene in methanol yields benzene; quantum yields are 0.02 and 0.3, respectively. Benzene is also the photoproduct of bromobenzene and of iodobenzene in hexane. For both compounds the quantum yield is 0.3.
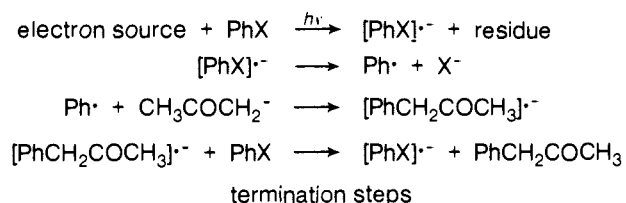
In mixtures of methanol and water, chlorobenzene and bromobenzene undergo photohydrolysis yielding phenol (quantum yields: 0.08 and 0.11, respectively). p-Bromotoluene is photohydrolyzed to p-cresol ($\phi = 0.05$). Fluo-

robenzene is unreactive in methanol/water, while iodobenzene in aqueous solvents disappears with a quantum yield of 0.3 but does not yield phenol.[37] The photohydrolysis reaction is thought to occur through the singlet excited state. The quantum yield decreases in the presence of chloride and bromide ions, and the relative hydrolysis yield depends linearly on the anion concentration. The effect is ascribed[37] to enhanced intersystem crossing of the excited singlet state to the triplet state. Addition of fluoride ions does not affect the quantum yield of the hydrolysis.

Barltrop, Bunce, and Thomson[29] investigated the photoreactions of fluorobenzene with a range of nucleophiles. Irradiation of fluorobenzene in piperidine afforded N-phenylpiperidine in 10% yield. From the photochemical reaction of fluorobenzene with methoxide ion in methanol anisole was obtained in 8% yield. With cyanide ion in the same solvent the product was benzonitrile (3%). Phenetole was formed in low yields (<1%) when fluorobenzene was irradiated in ethanol with or without hydroxide ion being present in the solution. From the illumination of fluorobenzene in alkaline aqueous solution only polymeric material (100%) was obtained.

Chlorobenzene behaves like fluorobenzene in its behavior toward piperidine, methoxide ion, and ethanolic hydroxide ion, but the percentage yields are lower, probably because chlorobenzene photopolymerizes more readily.

Recently, Rossi and Bunnett[38] described the reaction of halogenobenzenes with acetone enolate ion upon irradiation in liquid ammonia. From iodo-, bromo-, chloro-, and fluorobenzene and several other substituted benzenes, phenylacetone was obtained in 57–95% yield. The following mechanism, a photostimulated $S_{RN}1$, is proposed:

$$\text{electron source} + \text{PhX} \xrightarrow{h\nu} [\text{PhX}]^{\cdot-} + \text{residue}$$

$$[\text{PhX}]^{\cdot-} \longrightarrow \text{Ph}^{\cdot} + \text{X}^{-}$$

$$\text{Ph}^{\cdot} + \text{CH}_3\text{COCH}_2{}^{-} \longrightarrow [\text{PhCH}_2\text{COCH}_3]^{\cdot-}$$

$$[\text{PhCH}_2\text{COCH}_3]^{\cdot-} + \text{PhX} \longrightarrow [\text{PhX}]^{\cdot-} + \text{PhCH}_2\text{COCH}_3$$

termination steps

B. Monosubstituted Naphthalenes

1. 1-Nitronaphthalene

In the section on nitrobenzene (II.A.1) it was stated that this compound is not very reactive in photosubstitution reactions. However, nitrobenzene exhibits great photochemical activity under conditions where photoreduction can occur, as in 2-propanol.[39] For 1-nitronaphthalene, the situation is different. This compound does not undergo photoreduction in 2-propanol, but requires a more efficient hydrogen donor such as tri-n-butylstannane.[40] Photosubstitution, on the other hand, is more easily accomplished with 1-nitronaphthalene than with nitrobenzene. The difference in behavior between the two compounds in photoreduction and photosubstitution has been ascribed to a difference in triplet state character[14,28,40] (see also section II.A.1).

Like nitrobenzene,[19] 1-nitronaphthalene undergoes a photosubstitution reaction with hydrochloric acid. The reaction again is accompanied by reduction of the nitro group. Trotter and Testa[41] photolyzed 1-nitronaphthalene at 366 nm in 50% 2-propanol and water with varying concentrations of hydrochloric acid. The product of the reaction is 4-chloro-1-naphthylamine, its formation yield equalling the disappearance yield of 1-nitronaphthalene. Between 0 and 6 M HCl the quantum yield of the reaction

is proportional to the concentration of hydrochloric acid. With 6 M HCl the disappearance quantum yield is 1.28 ×
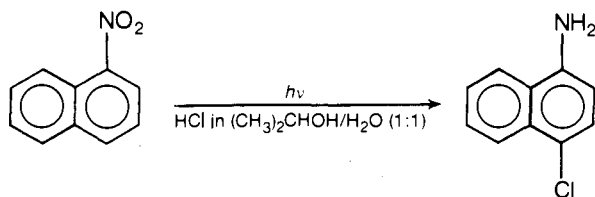
10^{-2}. The first step of the reaction sequence is thought to be protonation of 1-nitronaphthalene in its triplet state.

Although with 1-nitronaphthalene there is no substitution by chlorine at the position ortho with respect to the nitro group, one cannot say that there is a fundamental difference in substitution pattern between this compound and nitrobenzene. Such a difference does exist in the reaction with ammonia. Nitrobenzene in liquid ammonia is photosubstituted at the ortho and para positions,[22] yielding o- and p-nitroaniline. No information is available on a possible photoreaction of 1-nitronaphthalene in liquid ammonia. However, in a 15% solution of NH_3 in methanol, in which medium nitrobenzene fails to react, irradiation of 1-nitronaphthalene affords 1-aminonaphthalene in about 10% yield,[42] together with many by-products. Caution should be exercised in interpreting this result, because the possibility of photoreduction has not been excluded. However, the fact that nitrobenzene, known to be easier reduced than 1-nitronaphthalene, does not react in the same medium supports the assumption that the photoreaction of 1-nitronaphthalene to 1-aminonaphthalene is a real photosubstitution.

An interesting new type of photosubstitution has been found by Fráter and Havinga.[43,44] 1-Nitronaphthalene (and also 2-methyl- and 2-methoxy-1-nitronaphthalene) upon illumination in media such as alkyl chlorides, hexane/HCl, and acetic acid/HCl undergoes a substitution reaction in which the nitro group is replaced by chlorine.


R = H, CH₃, OCH₃
R' = H, alkyl
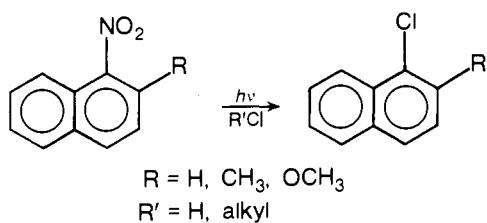
The reaction rate is solvent dependent; the relative rates in different solvents are: hexane/HCl = CH_2Cl_2/HCl = $CHCl_3$/HCl = CCl_4/HCl > acetic acid/HCl > tert-butyl chloride > allyl chloride = sec-butyl chloride > n-propyl chloride > CH_2Cl_2. No reaction could be detected in $CHCl_3$, in CCl_4, in methanol/HCl, or in butanol/CCl. The quantum yield of the reaction of 1-nitro- to 1-chloronaphthalene at 313 nm in tert-butyl chloride is 0.01. In hexane/HCl and comparable media the quantum yields are considerably higher. For the 2-methyl-substituted compound the quantum yield is 0.045.

These photoreactions proceed in a very clean fashion; the yields of products are very high. 1-Chloronaphthalene was isolated in 90% yield from an irradiated 10^{-3} M solution of 1-nitronaphthalene in $CHCl_3$/HCl. 2-Methyl-1-chloronaphthalene was obtained in 80% yield in tert-butyl chloride/HCl.

The mechanism of this type of photosubstitution is not known as yet. It has not been possible to detect nitrite ions in the reaction mixture. Fission of the C–N bond with formation of NO_2 and naphthyl radicals and subsequent

formation of chloronaphthalene does not seem likely in view of the fact that the reaction does not take place without HCl in either $CHCl_3$ or CCl_4. Tentatively, a kind of concerted mechanism is proposed[44] between the excited nitronaphthalene molecule and alkyl chloride (or HCl):
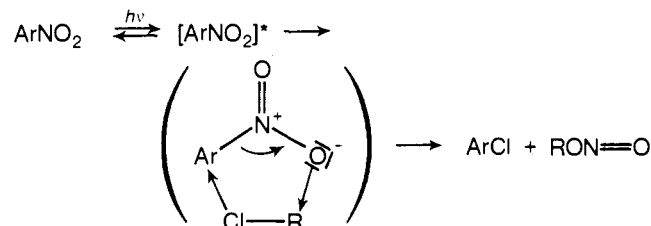

Other instances in which the nitro group of 1-nitronaphthalene is displaced have been found by Letsinger and his coworkers.[28,45] On irradiation in an aqueous solution (90% H_2O, 10% CH_3CN, v/v) containing cyanide ion (10^{-2} M) 1-nitronaphthalene (10^{-3} M) reacted rapidly. The product of the reaction is 1-cyanonaphthalene (23%).
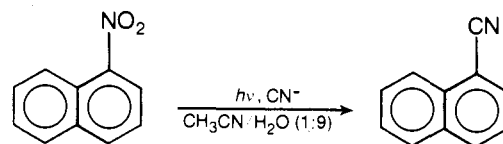

The chemical yield of 1-cyanonaphthalene was reported[45] to be higher (73%) after the solvent had been changed to a mixture of 95% CH_3CN and 5% H_2O. Quantum yield data indicate that the photoreactivity of 1-nitronaphthalene does not differ much in the two media. In water the quantum yield of disappearance of the nitro compound is 0.10, in the acetonitrile medium 0.082.

Illumination of 1-nitronaphthalene in the presence of sodium borohydride leads to direct replacement of the nitro group by hydrogen, a process which, like the photosubstitution of the nitro group by cyanide, appears to be a general reaction of polycyclic aromatic nitro compounds.[28] Irradiation of 100 mg of 1-nitronaphthalene and 100 mg of sodium borohydride in 200 ml of acetonitrile/water (95:5, v/v) for 35 min (G.E. 1200-W photochemical lamp through Pyrex) afforded 44 mg of naphthalene as the only product.
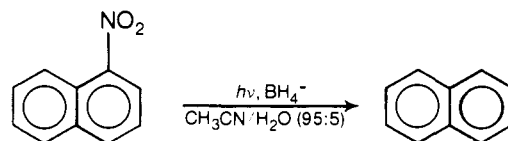
These photosubstitutions with cyanide and borohydride are characteristic of nitroaromatics with low-lying π,π^* excited states.[14,28] Compounds like nitrobenzene (section II.A.1) in which the lowest excited state has n,π^* character undergo photoreduction by these reagents.

The methoxide ion has proven its efficiency as a nucleophile in replacing the nitro substituent from 1-nitronaphthalene. Lok et al.[8,46] irradiated a nitrogen-flushed 6 × 10^{-4} M solution of 1-nitronaphthalene in methanol containing about 0.08 M $NaOCH_3$ with Pyrex-filtered light from a high-pressure mercury arc. 1-Methoxynaphthalene could be isolated from the reaction mixture in 50% yield.
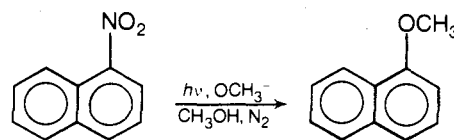
The reaction with ethoxide ion proceeds less smoothly. There are many side products and 1-ethoxynaphthalene could be isolated in only 2% yield.[8]

Photohydrolysis of 1-nitronaphthalene in alkaline medium leads to 1-naphthol. In the presence of oxygen the product is not photostable, but in nitrogen-purged solutions yields up to 15% can be obtained.[47]

2. 2-Nitronaphthalene

2-Nitronaphthalene has not been studied as extensively as its α isomer. According to Fräter and Havinga[44] it undergoes the same type of photosubstitution as 1-nitronaphthalene in CCl_4/HCl (cf. section II.B.1), although the reaction is much slower and many by-products are formed.

On irradiation in the presence of methoxide ion 2-nitronaphthalene undergoes a rapid reaction, but no 2-methoxynaphthalene is formed.[8] Instead, substitution occurs at other positions in the nitronaphthalene molecule.[47] No 2-cyanonaphthalene could be detected in an irradiated solution of 2-nitronaphthalene with cyanide ion in acetonitrile. In methanol with potassium cyanide, photosubstitution of the nitro group by cyanide takes place in low yield (<5%).

Most photoreactions of 2-nitronaphthalene in the presence of nucleophiles seem to yield mainly products in which not the nitro group, but one or more hydrogen atoms are displaced. The α positions appear to be the preferred sites of attack. In these reactions the presence of oxygen is crucial for substitution.[47]

Comparison of these results with those for 1-nitronaphthalene (section II.B.1) and naphthalene (section I.B) leads to the conclusion that the α position is much more reactive than the β position in photoreactions with nucleophiles.

3. 1-Methoxynaphthalene

In 1-methoxynaphthalene a cyano group is introduced at the 4 position upon irradiation in the presence of KCN.
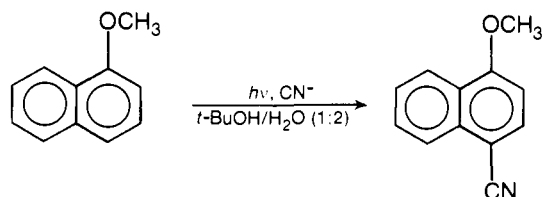
Irradiation of 350 mg of 1-methoxynaphthalene in 1500 ml of tert-butyl alcohol/water (1:2) with 0.05 M potassium cyanide for 30 hr in a Rayonet photochemical reactor (RPR 208, 3000 Å) afforded 161 mg of 1-cyano-4-methoxynaphthalene and 2 mg of 1-cyanonaphthalene.[48]

If the 1 and 4 positions in naphthalene derivatives may be regarded as "para" positions in analogy with benzene derivatives, the preference of the nucleophile for the 4 position in 1-methoxynaphthalene is in accordance with the observed para-directing effect of the methoxy group in anisole (section II.A.2). The fact that, in contrast to anisole, no ortho substitution is found in the naphthalene derivative may be explained in terms of the low reactivity at the β position in naphthalenes (section II.B.2).

4. 2-Methoxynaphthalene

2-Methoxynaphthalene undergoes a clean photoinduced reaction with cyanide ion.[49] The sole product of the reaction is 1-cyano-2-methoxynaphthalene in 82% yield, $\phi = 0.004$.

As with 1-methoxynaphthalene, the behavior of the β isomer can be rationalized in terms of the ortho/para directing effect of the methoxy substituent and the preference of nucleophiles for the α position of the naphthalene ring.

5. 1-Bromonaphthalene

Kuz'min, Mikheev, and Guseva[50] irradiated 1-bromonaphthalene in 20% methanol/water at different pH values
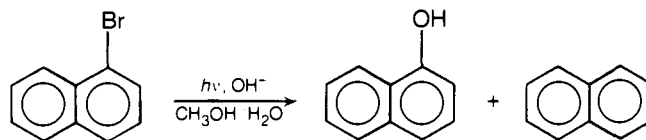
and studied the formation of α-naphthol and naphthalene. At pH values below 8 the quantum yields are independent of the pH. Between pH 8 and 14 the quantum yields of the formation of both α-naphthol and naphthalene increase with increasing hydroxide ion concentration. There exists a linear relationship between the logarithm of the quantum yield and the pH in this region. In view of the fact that the quantum yield of naphthalene formation depends on the hydroxide ion concentration, it is considered unlikely that this product is brought about by homolysis of the C–Br bond. It is suggested[50] that the first step upon excitation of the bromonaphthalene is transfer of an electron from hydroxide ion to the excited molecule. The radical anion then would dissociate into a bromide ion and a naphthalene radical, which would abstract a hydrogen atom from the organic solvent to give naphthalene.

C. Monosubstituted Biphenyls

1. 4-Nitrobiphenyl

The photoreactions of 4-nitrobiphenyl and 1-nitronaphthalene (section II.B.1) with cyanide ion are analogous; i.e., the nitro group is substituted.[14,51] The yield of
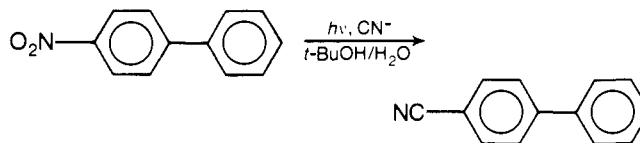
4-cyanobiphenyl, based on the amount of converted starting material is 45%. The quantum yield of the reaction at 313 nm has been measured as a function of the concentration of cyanide ion.[14] A linear relationship has been found between the reciprocals of the quantum yield and the cyanide ion concentration, indicating a bimolecular reaction between excited 4-nitrobiphenyl and cyanide. At high concentrations of nucleophile the quantum yield reaches a constant value of 0.18. The photoreaction can be quenched with 3,3,4,4-tetramethyldiazetine dioxide (singlet energy > 85 kcal/mol, triplet energy ~ 40 kcal/mol[52]). At a quencher concentration of 0.03 mol/l. the quantum efficiency has dropped to 0.02. The Stern–Volmer plot is not linear, however. At high quencher concentrations quenching becomes relatively more effective. It is postulated[14] that this effect may be due to "chemical quenching" of the excited singlet state (quenching by energy transfer is energetically impossible). It seems safe to assume that this photosubstitution reaction proceeds via the excited triplet state of 4-nitrobiphenyl.

2. 3-Nitrobiphenyl

3-Nitrobiphenyl is also substituted by cyanide ion on irradiation. Interestingly, in this case it is not the nitro

TABLE I. Quantum Yields of the Photohydrolysis of m-Nitroanisole at 313 nm at Different OH⁻ Concentrations

[OH⁻], mol/l. × 10³	φ	[OH⁻], mol/l. × 10³	φ
0.39	0.06	3.98	0.20⁵
0.61	0.08	5.25	0.21⁵
1.00	0.12	7.08	0.22⁵
1.58	0.13	7.76	0.23
2.24	0.16	7.94	0.23
2.46	0.18	9.77	0.22
3.02	0.19	10.47	0.22⁵

group that is displaced but the hydrogen atom at the 4' position leading to formation of 4-cyano-3'-nitrobiphenyl in high yield (77%).[14,51]
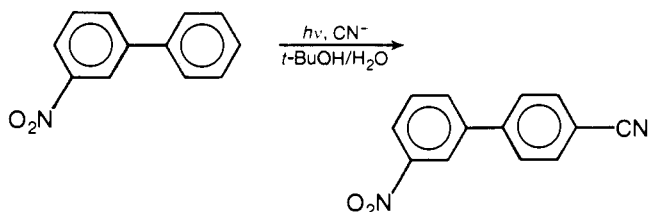
From the results of the photocyanation of biphenyl it can be seen that position 4 has a sixfold higher reactivity than position 2, whereas the 3 position is unreactive toward nucleophilic attack. This, together with the possibility of steric hindrance to substitution at positions next to the nitro group and the possible occurrence of "extended meta activation" by the nitro group (as observed in the nitrodimethoxynaphthalenes, see section IV.B.1), may explain the orientation of substitution in 3-nitrobiphenyl.
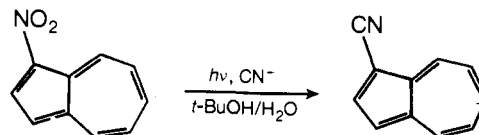
D. Monosubstituted Azulenes

1-Nitroazulene

Photochemical substitution reactions with 1-nitroazulene have been described by Lok et al.[8,46,53] On irradiation with methoxide ion in methanol 1-nitroazulene is converted into 1-methoxyazulene. The reaction is of synthetic utility, since 1-methoxyazulene is rather difficult to synthesize by classical methods. From 120 mg of 1-ni-

troazulene and 4.5 mg of sodium methoxide in methanol a yield of 24 mg of 1-methoxyazulene could be obtained after irradiation of the solution for 43 hr with Pyrex-filtered light from a high-pressure mercury lamp (Hanau TQ 150).
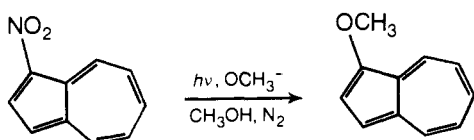
At 254 nm the quantum efficiency of this reaction is 0.004 at a sodium methoxide concentration of 1 M. The quantum yield decreases with increasing wavelength: at 313 nm φ = 0.0034, while at 366 and 405 nm the value has dropped to 0.0020. The quantum efficiency at 546 nm is estimated at <0.0010. The wavelength dependence of the quantum yield is seen as an indication of the possibility of intersystem crossing from higher excited singlet states. Quenching experiments with 3,3,4,4-tetramethyldiazetine dioxide point[53] to a triplet state as the reacting intermediate in the photomethoxylation reaction. The observation that the fluorescence of 1-nitroazulene[54] is wavelength dependent supports the assumption that the quantum yield of intersystem crossing varies with the wavelength of the exciting light.

Irradiation of 1-nitroazulene in the presence of cyanide ion affords 1-cyanoazulene.[8,46] From 40 mg of 1-nitroazulene and 1.56 g of potassium cyanide in 240 ml of tert-butyl alcohol/water (35:65) upon irradiation for 20 hr (Hanau TQ 150; Pyrex filter) 10 mg of 1-cyanoazulene was obtained.


Photoexcited 1-nitroazulene does not react with NH₃ or with pyridine.[8] It is also stable with respect to HCl in hexane or tert-butyl chloride.

IV. Disubstituted Compounds

A. Disubstituted Benzenes

1. Nitroanisoles

The nitroanisoles, especially m- and p-nitroanisole, are probably the most thoroughly investigated compounds in nucleophilic photosubstitution reactions. The photohydrolysis of m-nitroanisole is one of the very first examples of heterolytic aromatic photosubstitution that have been reported.[55,56] This reaction has intensively been studied by de Jongh and Havinga[57,58] and by den Heijer et al.[59] The photoamination of m-nitroanisole has been described by van Vliet et al.[22,25] Extensive investigations into the photochemistry of p-nitroanisole have been performed by Letsinger and his coworkers[45,60-63] and by Havinga and his coworkers.[64-67] m-Nitroanisole undergoes an efficient photoreaction with hydroxide ions in aqueous solution;[55,56] the methoxy group is displaced and the product of the clean reaction is m-nitrophenol, or rather m-nitrophenolate ion in the alkaline medium. The formation of methanol could be demonstrated by the oxidation to formaldehyde.
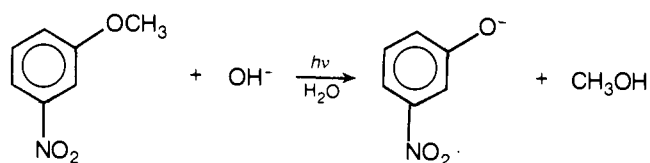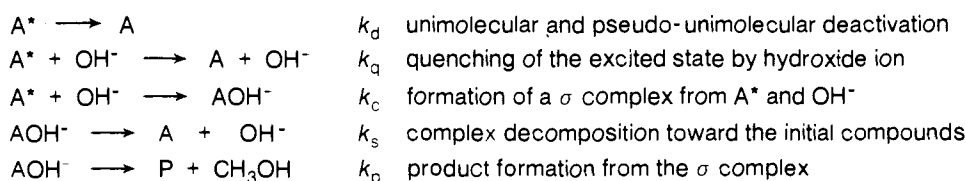

p-Nitroanisole is also photohydrolyzed in alkaline aqueous solution[60,64,66] but with a considerably lower quantum efficiency than the meta compound (see below). There are two products: p-nitrophenolate ion and p-methoxyphenolate ion.

From these facts the highly interesting conclusion may be drawn that the nitro group exerts a meta-directing influence toward nucleophilic substitution in the excited state. This is in striking contrast with the behavior of the nitro group in ground state reactions. One has, however, to reckon with the possibility that the higher quantum yield for the meta compound is caused by a longer lifetime in the excited state. An estimated lifetime for the reactive excited state of m-nitroanisole has been obtained from quenching experiments (vide infra), but for the para isomer no information about the lifetime is available. The fact, however, that in 4-nitroveratrole (section IV.A.3) the m-methoxy group is displaced almost exclusively in the photosubstitution seems good evidence of a real meta-directing influence of the nitro group in the excited state.

m-Nitroanisole is stable on irradiation in neutral solution. The quantum yields of the reaction were measured at 313 nm at different OH⁻ concentrations (Table I).[57,58]

SCHEME I

$A^* \longrightarrow A$ k_d unimolecular and pseudo-unimolecular deactivation

$A^* + OH^- \longrightarrow A + OH^-$ k_q quenching of the excited state by hydroxide ion

$A^* + OH^- \longrightarrow AOH^-$ k_c formation of a σ complex from A^* and OH^-

$AOH^- \longrightarrow A + OH^-$ k_s complex decomposition toward the initial compounds

$AOH^- \longrightarrow P + CH_3OH$ k_p product formation from the σ complex

The plot of $1/\phi$ vs. $1/[OH^-]$ appears to be linear up to a hydroxide ion concentration of about 7×10^{-3} mol/l.

Addition of alkali to a solution of m-nitroanisole in water does not substantially alter the ultraviolet absorption spectrum. This means that no ground-state complex between m-nitroanisole and OH^- is formed. The primary step of the photohydrolysis must therefore be excitation of the m-nitroanisole molecule whereupon attack by hydroxide ion takes place. The results are consistent with a reaction scheme as presented by de Jongh and Havinga[57,58] in which a molecule in an excited state, A^*, formed from a ground state molecule A by light absorption (and by intersystem crossing in the case the reaction proceeds via a triplet state), undergoes the processes shown in Scheme I. The relation between $1/\phi$ and $1/[OH^-]$ should then read

$$\frac{1}{\phi} = \frac{k_d}{k_c} \frac{k_s + k_p}{k_p} \frac{1}{[OH^-]} + \frac{k_q + k_c}{k_c} \frac{k_s + k_p}{k_p}$$

This equation describes the experimental figures at hydroxide ion concentrations up to approximately 7×10^{-3} mol/l. At higher values of $[OH^-]$ the quantum yield reaches a constant value. This limiting value of ϕ is significantly lower than the value predicted by the equation (i.e., the intercept of the straight line with the $1/\phi$ axis). At high nucleophile concentration the simple picture is no longer adequate. There may be several reasons, one of them being that encounters of OH^- with both triplet and singlet have to be accounted for.

At this moment there is no definitive proof for the occurrence of a σ complex. In nanosecond laser-flash photolysis experiments de Gunst[68] has found an extremely short-lived species ($\tau \simeq 10^{-9}$ sec) which is formed from the excited aromatic compound in the presence of nucleophile. This species may be an intermediate in the photosubstitution reaction. It is of interest to note that radical anions, which could also be traced in the flash experiments, do not function as intermediate in the photosubstitution reaction. In all cases studied thus far, the formation of substitution product precedes decay of the radical anion.

The photohydrolysis of m-nitroanisole is found to proceed via a triplet excited state[59] (in earlier reports a singlet excited state had been suggested as the reactive intermediate[57,69]). The reaction can be sensitized with benzophenone yielding m-nitrophenol as the only product. Addition of piperylene in concentrations $\geq 4 \times 10^{-2}$ M completely quenches the photoreaction of m-nitroanisole (2×10^{-4} M) with NaOH (10^{-2} M). 3,3,4,4-Tetramethyldiazetine dioxide[52] quenches the photoreaction in acetonitrile/water (1:1) as well as in water containing 2% methanol or 5% tert-butyl alcohol. Quantum yields were measured at various quencher concentrations. A linear relationship was obtained in a plot of $1/\phi$ vs. the concentration of the quencher. Assuming the quenching to be diffusion controlled, the lifetime of the reactive triplet state can be calculated from the analytical expression for the straight Stern–Volmer line. The value thus obtained is 24 nsec which is in fair agreement with the lifetime of 40 nsec deduced from the laser photolysis measurement.[68]

Finally, it deserves mentioning that de Jongh[57,58] proved that the photohydrolysis of m-nitroanisole is a real aromatic substitution; i.e., it is the bond between the aromatic carbon and the oxygen atom that is being broken. The photosolvolysis has been carried out in ^{18}O-enriched water (1.66% [18]O). The isolated m-nitrophenol was found to have taken up the [18]O quantitatively (1.51% [18]O); the nitro group contained less than 3% (0.04% [18]O over the natural concentration). On irradiation of m-nitrophenolate in the same solvent, no appreciable incorporation of [18]O occurred.
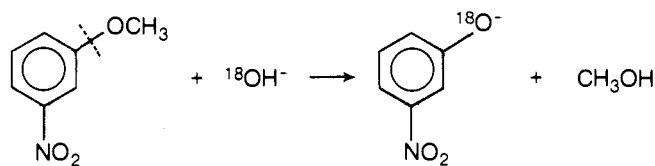

The photoreaction of m-nitroanisole with ammonia has been studied by van Vliet et al.[22,25] Irradiation with a high-pressure mercury lamp for 3 hr of a solution of 300 mg in 400 ml of liquid ammonia at $-60°$ yields the following products: m-nitroaniline (90%), 4-methoxy-2-nitroaniline (2%), and 6-methoxy-2-nitroaniline (<1%). Percentage yields are based on the amount of converted starting material (about 150 mg). m-Nitroanisole does not react with liquid ammonia in the dark.
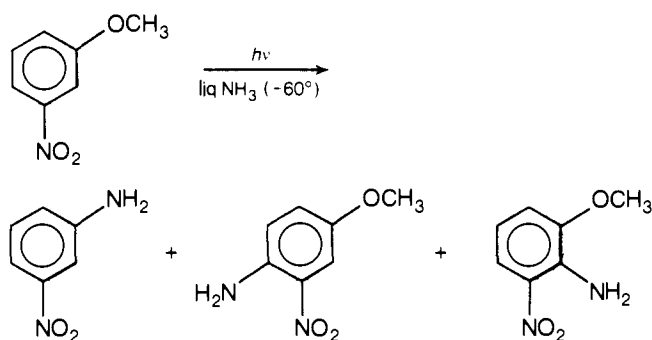
The photoamination of m-nitroanisole can also be performed in a solution of 15% NH_3 in methanol at room temperature. The products are m-nitroaniline (65%) and 4-methoxy-2-nitroaniline (6%). There is a shift in the product ratio as compared with the reaction in liquid ammonia in favor of substitution at the ortho position.

The behavior of m-nitroanisole in the photoamination reaction is in striking contrast to that of nitrobenzene (section II.A.1). With nitrobenzene mainly para and some ortho substitution is found and the reaction cannot be performed in 15% NH_3 in methanol. The photoamination of nitrobenzene may proceed via a triplet state (oxygen effect, possibility of sensitization). Irradiation of m-nitroanisole in liquid ammonia in the presence of a 40-fold excess of benzophenone afforded 2-methoxy-4-nitroaniline instead of m-nitroaniline. This means that a sensitized reaction can occur, but that now substitution at the para position takes place, whereas in the direct irradiation mainly meta and a little ortho substitution is observed. These facts constitute an argument for the hy-

pothesis that the unsensitized photoamination of *m*-nitroanisole proceeds via a singlet state.
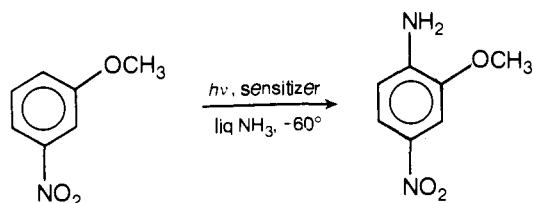
van Vliet[25] determined quantum yields of the photoamination of *m*-nitroanisole in methanol at different NH_3 concentrations. As in the case of the photohydrolysis, the quantum yield increases with increasing nucleophile concentration up to a certain value (12%), above which ϕ remains constant ($\phi = 0.42$). In the region where the quantum yield depends on the ammonia concentration there is the expected linear relationship between the reciprocal of the quantum yield and that of the ammonia concentration.

Letsinger and McCain[61] found that the methoxy group in *m*-nitroanisole can also be substituted by cyanide. Irradiation (1200-W low-pressure mercury arc; Pyrex filter) of 100 mg of *m*-nitroanisole and 400 mg of NaCN in 20 ml of *tert*-butyl alcohol + 450 ml of H_2O for 10 min afforded 32 mg of *m*-nitrobenzonitrile and 28 mg of unreacted *m*-nitroanisole.
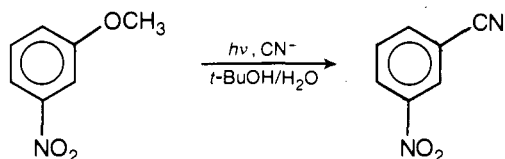
Methylamine is also reactive toward photoexcited *m*-nitroanisole (de Jongh and Havinga[56,57]). The reaction is slow, but a high degree of conversion (to N-methyl-3-nitroaniline) can be obtained. No quantum yields have been reported.

Letsinger, Ramsay, and McCain[60] irradiated *m*-nitroanisole (5.2×10^{-4} M) in water + pyridine at pH 6.2 (concentration of the free base 0.11 M), but no substitution products were isolated. Since photoexcited *m*-nitroanisole survives long enough to react with 0.02 M hydroxide, it also has ample opportunity to react with pyridine at a concentration of about 0.11 M. Letsinger and his coworkers conclude that the excited state of *m*-nitroanisole is not reactive toward pyridine. The possibility of a photosensitized reaction with pyridine has not been investigated.

From these data the behavior of photoexcited *m*-nitroanisole in substitution reactions seems to be comparatively simple. If substitution takes place, it occurs at the carbon atom bearing the methoxy group, with the notable exception of the photosensitized reaction with ammonia. With *p*-nitroanisole the situation is more complex. As will be seen from the following examples (see below), different nucleophilic reagents tend to attack at different positions on the aromatic ring. Letsinger and McCain[63] have pointed out that this may be caused by the fact that, while the position meta to nitro is still the most reactive one in the excited state, the leaving group at this position, a H-atom, is tightly bonded. As a consequence, leaving group tendencies of attacking species are here important in determining the course of the reaction and carbon atoms of secondary reactivity bearing substituents with good leaving group tendency may successfully compete with the meta position.

The photohydrolysis of *p*-nitroanisole has been investigated by Letsinger, Ramsay, and McCain[60] and by de

Vries and Havinga.[64,66] The main products isolated from the irradiation of a 3×10^{-3} M solution of *p*-nitroanisole in 0.1 N NaOH (Pyrex-filtered light from a high-pressure mercury lamp) are *p*-nitrophenol and *p*-methoxyphenol.
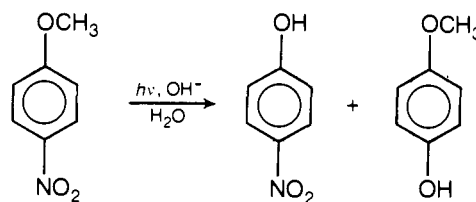
As in the case of *m*-nitroanisole, the quantum yield of disappearance of *p*-nitroanisole depends on the hydroxide ion concentration. The value, 6×10^{-1} mol/l., at which the quantum yield becomes constant ($\phi = 0.085$) is much higher than the corresponding value for *m*-nitroanisole, which is 7×10^{-3} mol/l. The maximum quantum yield is about three times as low as that of the meta compound. The quantum yield is independent of the wavelength of the exciting radiation. The ratio of *p*-nitrophenol and *p*-methoxyphenol formation is about 1:4 and does not depend on the hydroxide ion concentration or on the wavelength.

The photohydrolysis of *p*-nitroanisole can be sensitized by benzophenone[62,66] and quenched by fluorenone and sodium sorbate.[66] The product ratio in the photosensitized reaction is the same as in the direct irradiation. These results strongly suggest that also in the unsensitized reaction the substitution takes place in the triplet state.

van Vliet[25] found that *p*-nitroanisole reacts with ammonia when irradiated in liquid ammonia or in 15% ammonia/methanol. The product in both cases is, in low yield, *p*-anisidine.
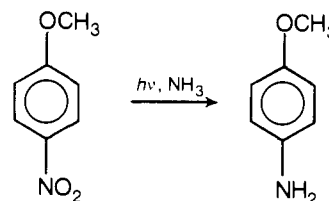
In view of the results obtained with nitrobenzene and *m*-nitroanisole in liquid ammonia, it is rather surprising that in *p*-nitroanisole the nitro group is converted into an amino group. It has not been established, however, whether this reaction is photosubstitution at the aromatic nucleus or photoreduction of the nitro group by ammonia.

p-Nitroanisole reacts readily with amines in aqueous solution. Kronenberg, van der Heyden, and Havinga[65] irradiated (Hanau Q 81, K_2CrO_4 filter) a solution of 1.7 g of *p*-nitroanisole in 3.7 l. of 6% dimethylamine and obtained a precipitate of 1.2 g (65%) of practically pure N,N-dimethyl-4-nitroaniline. From a solution of 1.7 g of *p*-nitroanisole in 3.6 l. of 7% methylamine, N-methyl-4-nitroaniline was obtained in 54% yield. McCain[70] reports the photochemical formation of N-ethyl-4-nitroaniline (46%) from *p*-nitroanisole and ethylamine (Scheme II).

SCHEME II
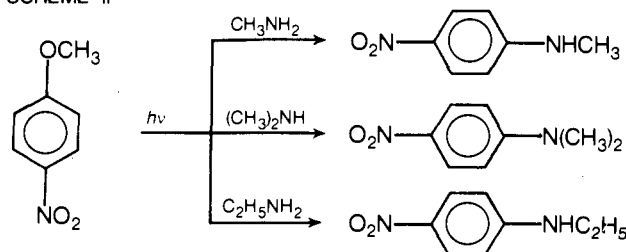
p-Nitroanisole seems to react more efficiently with aliphatic amines than m-nitroanisole. Unfortunately, no quantum yield data are available to justify this conclusion.

McCain[70] reports the formation of a substantial amount of nitrite ions (51%) in the photoreaction of p-nitroanisole with ethylamine. The corresponding aromatic compound without a nitro group has never been isolated.

Letsinger, Ramsay, and McCain[60] found that p-nitroanisole reacts readily with pyridine in aqueous solution on irradiation. The product of the reaction is 1-(p-methoxyphenyl)pyridinium nitrite (38% yield). The reaction proceeds in a clean fashion; 1 equiv of nitrite ion is liberated per mole of p-nitroanisole consumed.

4-Methylpyridine reacts with excited p-nitroanisole in an analogous way, forming 1-(p-methoxyphenyl)-4-methylpyridinium nitrite (54%).
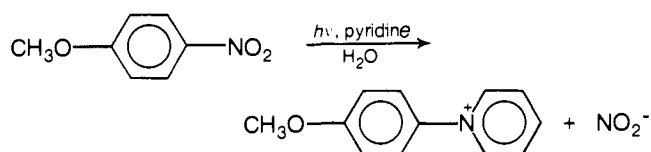
Rate data were obtained by Letsinger and his coworkers[60] for photoinduced reactions of p-nitroanisole with pyridine, 4-methylpyridine, and hydroxide ion. From plots of $1/k_{obsd}$ vs. $1/[N]$, where k_{obsd} is the pseudo-first-order rate constant for the reaction and $[N]$ is the nucleophile concentration, it was concluded that the overall process can be described by the following scheme:
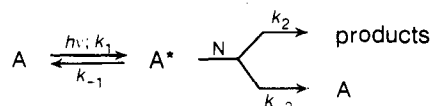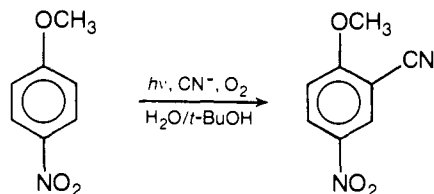

The observed rate constant may be expressed by the following equation:

$$\frac{1}{k_{obsd}} = \frac{1}{k_1}\left[1 + \frac{k_{-2}}{k_2}\right] + \frac{k_{-1}}{k_1 k_2[N]}$$

From experiments with different nucleophiles under identical experimental conditions (k_{-1}/k_1 constant) ratios of k_2 values were obtained. The relative reactivity of pyridine, 4-methylpyridine, and hydroxide in H_2O at 3° is 1:4.7:4.5. Further evaluation of the kinetic results shows that approximately three-fourths of the total number of excited p-nitroanisole molecules interact directly with the added nucleophile, giving either substitution or quenching at a nucleophile concentration of 0.1 M. For the reaction with pyridine in water at 3° it can be calculated that at least 3.6 molecules of excited p-nitroanisole are quenched by pyridine for each molecule that is substituted.

The photoreaction of p-nitroanisole with cyanide ion is particularly interesting, since with this nucleophile substitution takes place at the carbon atom meta to the nitro group. Letsinger and McCain[63] obtained 2-cyano-4-nitroanisole in 66% yield (based on 4-nitroanisole consumed) by irradiation (1200-W low-pressure Hg lamp) of 100 mg of p-nitroanisole and 400 mg of KCN in an aerated mixture of 480 ml of water and 20 ml of tert-butyl al-

cohol for 10 min at ice temperature. Yields are lower when longer irradiation times are used, demonstrating that the product is being consumed in a secondary, slower photochemical reaction.

When aqueous solutions of p-nitroanisole and potassium cyanide well purged with nitrogen are irradiated, the main product is no longer 2-cyano-4-nitroanisole but 3,3'-dicyano-4,4'-dimethoxyazoxybenzene.
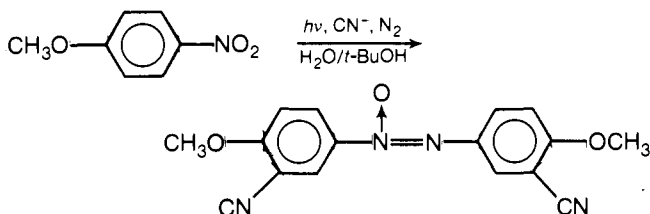
Letsinger and McCain[63] performed a detailed kinetic investigation of the photochemical substitution of p-nitroanisole with cyanide ion. They found the reciprocals of the quantum yield and the cyanide ion concentration to be linearly related. Furthermore, they investigated the effect of iodide ion on the substitution reaction. The iodide ion is a nucleophile which does not yield a substitution product. This ion was found to effectively inhibit the photoreaction of p-nitroanisole with cyanide ion. A similar retarding effect of halide ions on aromatic photosubstitution reactions has been found by de Jongh,[57] van Vliet,[25] de Vries,[66] and den Heijer et al.[59]

Pyridine may likewise act as an inhibitor of the cyanide reaction, but it also displaces nitrite to form a substitution product. Competition experiments between pyridine and cyanide were carried out by Letsinger and McCain.[63] The rate data calculated from the kinetic constants of the individual nucleophiles agreed quantitatively with the rates observed for mixtures of pyridine and cyanide. These findings lead to the conclusion that pyridine and cyanide ion compete directly for the same excited-state species of p-nitroanisole. It is suggested[63] that other nucleophiles, such as hydroxide ion, acting in the same concentration range, also interact with the same type of excited state of p-nitroanisole. From the various rate data it follows that the reactivity of nucleophiles toward photoexcited p-nitroanisole decreases in the order: iodide > cyanide > hydroxide > pyridine > 2,4,6-trimethylpyridine.

Letsinger and McCain[63] offer a possible explanation for the interesting observation that different nucleophiles substitute at different positions in p-nitroanisole. They argue that the position meta to nitro is the most reactive one in the excited state. When cyanide attacks at this position, a strong carbon–carbon bond is formed and the resulting intermediate complex survives long enough to react with oxygen and form 2-cyano-4-nitroanisole or to disproportionate and form the azoxybenzene derivative. When pyridine strikes at the meta carbon atom, an unstable intermediate is formed since pyridine is a good leaving group. Attack of pyridine at the meta position results in quenching of the excited state. Pyridine has a greater chance at the carbon atom bearing the nitro substituent since nitrite is a good departing group relative to pyridine.

The crucial point of this hypothesis is the assumption that the meta carbon atom in the reacting excited state, which most probably is a triplet state, is the most reactive one. Reliable data on charge distributions in the triplet state are still rather scarce. The calculations that have been made are in agreement with the assumption.

The relative importance of the ortho/para directing effect of the methoxy group and the meta-directing influence of the nitro group is not yet known. For substitution at the 2 position in 4-nitroanisole the two effects cooper-

ate. That in the photohydrolysis of p-nitroanisole substitution of the nitro group by hydroxide ion predominates, whereas in m-nitroanisole only the methoxy group is displaced in a clean reaction, is in complete agreement with the proposed ortho/para directing influence of the methoxy group (section II.A.2).

An effect termed "merging resonance stabilization" has been invoked[71] to rationalize the effect of the nucleophilic agent on the orientation of substitution. In terms of merging resonance stabilization it is easily explained that pyridine displaces the nitro group in p-nitroanisole, and amines substitute the methoxy group in the photoreaction.

It has been found[67] that cyanate ion behaves like cyanide ion in its photoreaction with p-nitroanisole. From oxygen-saturated, aqueous solutions of p-nitroanisole (3 × 10^{-3} M) and potassium cyanate (10^{-1} M) low yields (approximately 4%) of 2-amino-4-nitroanisole could be isolated after irradiation with a high-pressure mercury lamp. Most probably, the primary product is the isocyanate, which in a secondary, thermal reaction with water hydrolyzes to form the amino compound.
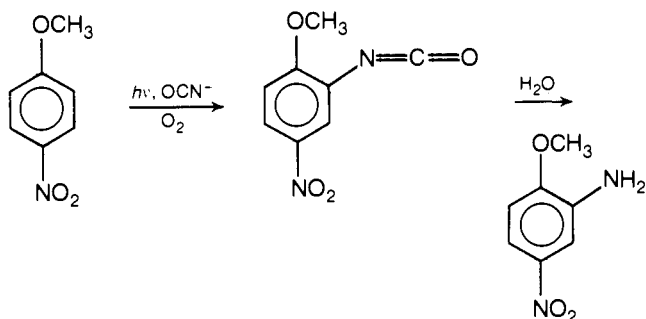

Support of this hypothetical reaction scheme is the observation that, when the reaction is performed in methanol as solvent, the product appears to be the methyl ester of 2-methoxy-5-nitrophenylcarbamic acid:
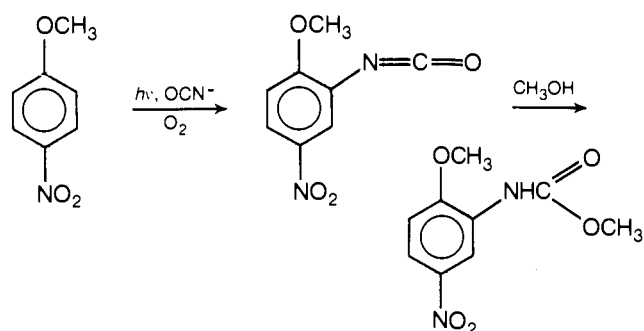

From a mechanistic point of view, an interesting aspect of this reaction is that substitution of hydrogen takes place (at the position meta to nitro) with the formation of a C–N bond.

Finally, an interesting solvent effect on the cyanide reaction discovered by Letsinger and Hautala[45] is worth mentioning. In aqueous medium (90% water–10% acetonitrile) high yields of 2-cyano-4-nitroanisole are obtained (ϕ = 0.32 at 317 nm). In a less protic solvent, the quantum yield is much lower (ϕ = 0.0064 at 310 nm) and several by-products are formed. It is suggested[45] that the effect of the solvent on the photosubstitution reaction may be attributed to changes in the relative height of the energy levels of n,π^* and π,π^* excited states. The photoinduced substitution reactions in p-nitroanisole are thought to proceed mainly (or only) via a π,π^* triplet state.
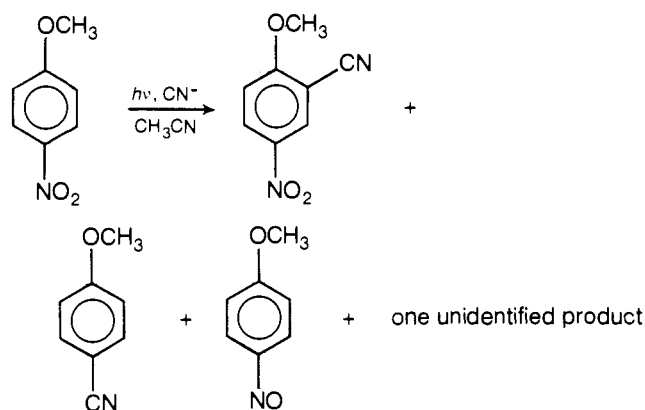
Not many photochemical reactions of o-nitroanisole are known. According to Letsinger and McCain[63] it resembles the para isomer in the photochemical reaction with cyanide ion. On irradiation in the presence of air, it is converted to 4-cyano-2-nitroanisole and 6-cyano-2-nitroanisole in yields of 29 and 26% (based on nitroanisole consumed), respectively.
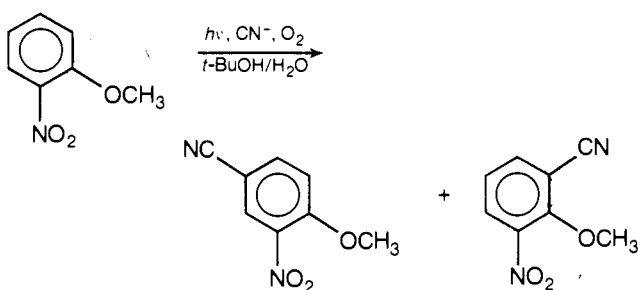
de Vries[66] investigated the photohydrolysis. From an irradiated aqueous (0.096 N NaOH) solution of o-nitroanisole it was possible to isolate o-nitrophenol and guaiacol in yields of 31 and 3%, respectively. This photoreaction
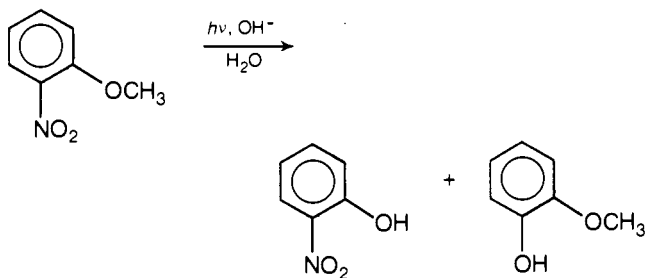
can be sensitized by benzophenone and quenched by sodium sorbate.

2. Nitrophenyl Phosphates and Nitrophenyl Sulfates

The three nitrophenyl phosphates and m-nitrophenyl sulfate were the compounds with which the phenomenon of photohydrolysis and of meta activation by the nitro group was first observed and studied (de Jongh and Havinga[57,72-74]).

The rate of the photohydrolysis of the monophosphate of m-nitrophenol does not depend on the hydroxide ion concentration in the pH range 4–12. At higher pH, the quantum yield increases with increasing hydroxide ion concentrations (Table II). It appears that part of the increasing effect can be ascribed to the higher ionic strength. In accord with the theory of the effect of ionic strength on the rates of thermal bimolecular reactions, it is concluded[73] from these data that at pH 10 the absence of a salt effect is consistent with the view of water being the reactive partner and that the increase of ϕ at

TABLE II. Quantum Yields at 313 nm of the Photohydrolysis of m-Nitrophenyl Phosphate at Various Hydroxide Ion Concentrations and Ionic Strengths

Medium	Quantum yield
Buffer pH 10	0.05
Buffer pH 10 + 0.85 M NaCl	0.05
0.010 M NaOH	0.05[5]
0.010 M NaOH + 0.99 M NaCl	0.08[5]
0.10 M NaOH	0.14
0.10 M NaOH + 0.90 M NaCl	0.18[5]
1.00 M NaOH	0.24

higher pH is caused by participation of hydroxide ion in the reaction. Further support of this hypothesis is obtained from experiments in which the photohydrolysis was effected in ^{18}O-enriched water.

On irradiation of a neutral solution of m-nitrophenyl phosphate no incorporation of ^{18}O into the m-nitrophenol formed could be found, meaning that in neutral medium the photohydrolysis occurs with O–P splitting; i.e., the reaction is no real aromatic photosubstitution. In alkaline medium (10^{-2} M KOH), however, ^{18}O-incorporation is found in m-nitrophenol as well as in the phosphate liberated. The enrichment corresponds roughly with 1/3 O–P splitting and 2/3 O–C splitting.
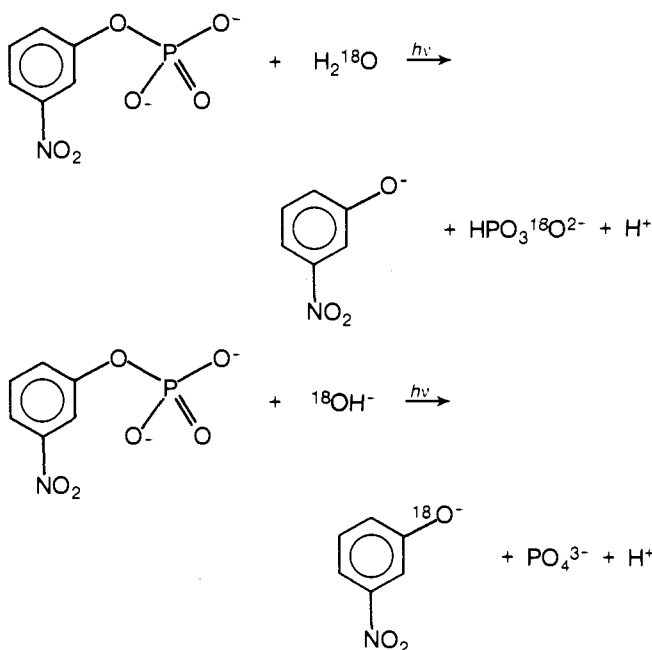
The methanolysis of m-nitrophenyl phosphate is also known.[55,56] The products of the irradiation of m-nitrophenyl phosphate in 100% methanol are methyl phosphate and m-nitrophenolate, indicating that as in the case of the reaction with water attack at the phosphorus atom has taken place.
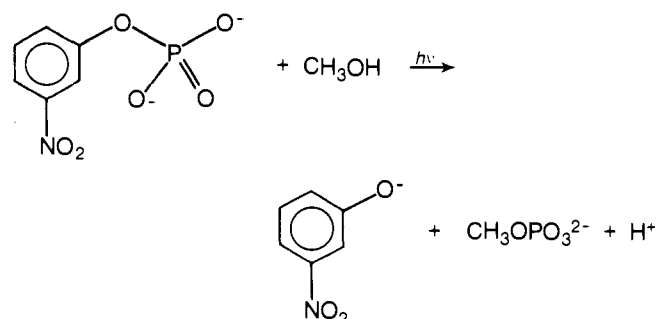
m-Nitrophenyl phosphate reacts with methylamine (1 M) in water albeit with a low rate. The product of the reaction is N-methyl-3-nitroaniline. It is interesting that with this reagent, like with OH$^-$, substitution occurs at the ring carbon atom.[55,57]
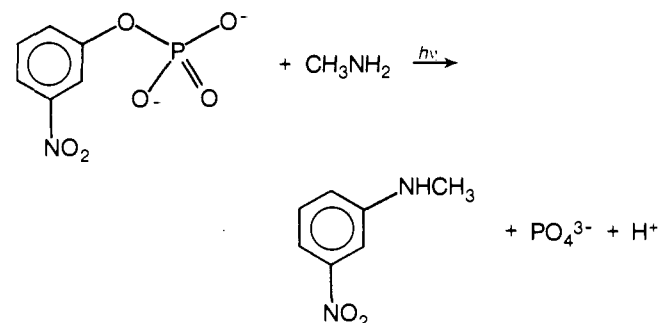

Letsinger and his coworkers[60,75] demonstrated that m-nitrophenyl phosphate does not react to any appreciable extent with pyridine. Its photochemical behavior toward hydroxide ion, pyridine, and amines is completely analogous to that of m-nitroanisole (section III.A.1).

The nitrophenyl phosphates exhibit an even stronger difference in reactivity between the meta and para isomer than the nitroanisoles. p-Nitrophenyl phosphate irradiated in alkaline aqueous solution undergoes a very slow reaction, in which p-nitrophenolate is one of the products. The quantum yield at 313 nm for the formation of free phosphate from a 2 × 10^{-4} M solution of p-nitrophenyl phosphate in 0.010 N NaOH is 0.002[73] (compared to 0.055 for the meta compound under the same experimental conditions).

p-Nitrophenyl phosphate (like p-nitroanisole) reacts readily with pyridine in the presence of light in aqueous solution.[60,75] The product, 1-phenylpyridinium 4'-phosphate salt, was obtained by Letsinger, Ramsay, and McCain[60] in 23% yield. As in the case of p-nitroanisole (section III.A.1), straight lines were obtained in plots of $1/k_{obsd}$ vs. $1/[N]$, where k_{obsd} is the observed pseudo-first-order rate constant and [N] is the nucleophile (i.e., pyridine) concentration.

Interestingly, Letsinger and his coworkers[60] observed that this photochemical reaction also occurs on irradiation of a frozen (solid carbon dioxide) dilute aqueous solution of p-nitrophenyl phosphate and pyridine.
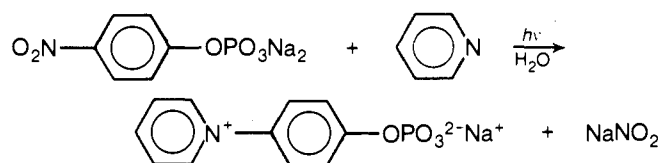

m-Nitrophenyl sulfate is photohydrolyzed very efficiently in aqueous solution, the quantum yield at 313 nm being about 0.5. The quantum efficiency of this reaction is independent of the pH of the medium: in 0.010 N HCl the value is 0.52 and in 0.010 N NaOH 0.50.[57,73] Evidently, in this case the reaction partner is water. Since the values of the quantum yields in acidic and alkaline media are almost equal, it is considered very unlikely that protonation (e.g., of the nitro group of the excited aromatic molecule) could play an important role in the photoreaction. With the sulfate it has not been established whether the attack of the water molecule occurs at the sulfur atom or at the ring carbon atom.

3. Dinitrobenzenes

van Vliet, Kronenberg, Cornelisse, and Havinga[22,25] investigated the photoreactions of the three isomeric dini-

trobenzenes in liquid ammonia. As with nitrobenzene or-
tho/para substitution is observed, but the reactions are
slow and yields are low.

p-Dinitrobenzene when illuminated (high-pressure Hg
lamp) in liquid ammonia at −60° afforded a small
amount of p-nitroaniline, m-Dinitrobenzene yielded 2,4-di-
nitroaniline as the major product. On irradiation of o-dini-
trobenzene under similar conditions o-nitroaniline and
probably a trace of 3,4-dinitroaniline were formed.
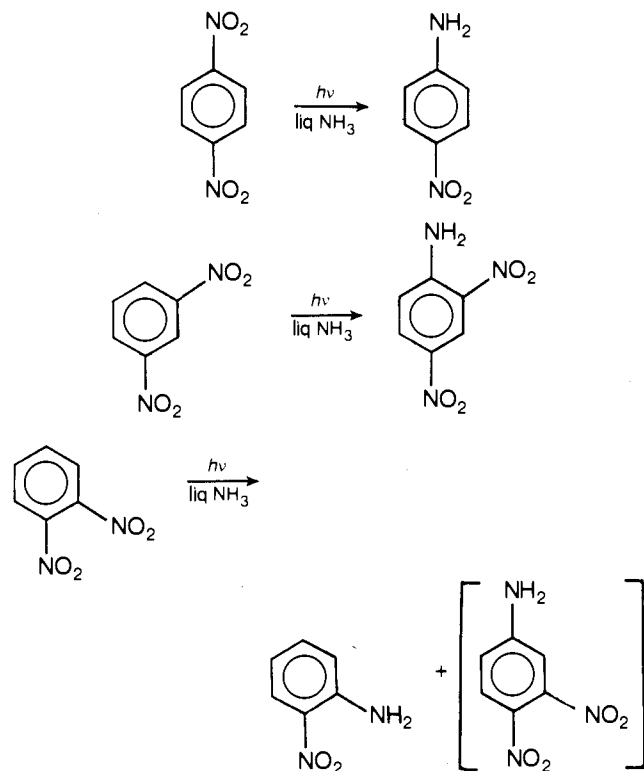
With p- and o-dinitrobenzene the same reactions are
observed in solutions of 15% ammonia in methanol
though the reaction rates are greatly reduced. The possi-
bility of reduction by methanol has not been excluded.

p-Dinitrobenzene reacts with hydroxide ion on irradia-
tion in aqueous tert-butyl alcohol, but the reaction rate is
very low.[60] Letsinger, Ramsay, and McCain[60] estimate
that the rate of formation of p-nitrophenol is about 1/100th
the rate at which p-nitroanisole reacts under the same
conditions.

4. Nitrophenols

Letsinger and Wubbels[19] describe the photoreaction of
p-nitrophenol with hydrochloric acid; they irradiated a ni-
trogen-flushed solution of 348 mg in 250 ml of concen-
trated hydrochloric acid for 93 hr. Isolation of the prod-
ucts yielded 315 mg (71%) of 4-amino-2,3,6-trichloro-
phenol and 84 mg (16%) of tetrachlorohydroquinone.
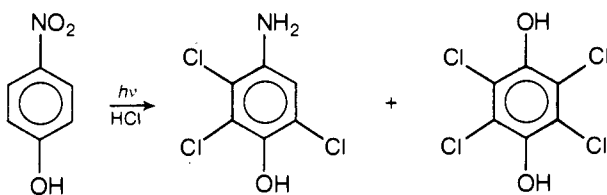
m-Nitrophenol in concentrated hydrochloric acid gave
3-amino-2,4,6-trichlorophenol (37%) and 3-amino-4,6-di-
chlorophenol (24%). These results are similar to those
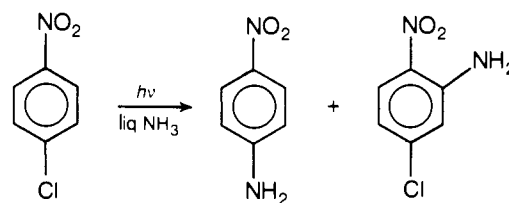obtained with nitrobenzene (section II.A.1).
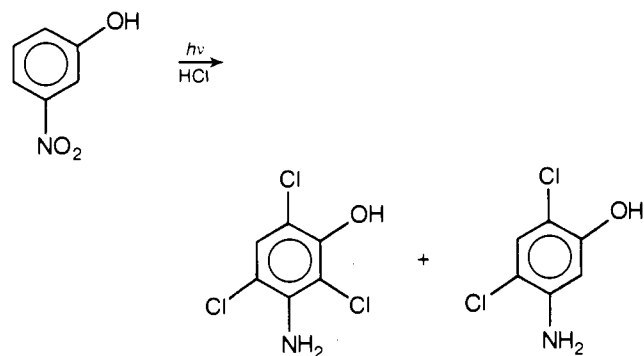
p-Nitrophenol fails to react with pyridine under condi-
tions which are known to be favorable to photoinduced
substitution (e.g., in p-nitroanisole, section III.A.1).[60]
This may be related to enhanced acidity and dissociation
of p-nitrophenol in the excited state.
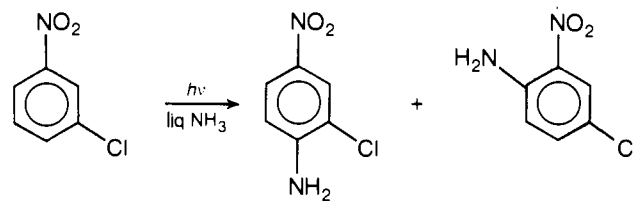
5. Chloronitrobenzenes

The chloronitrobenzenes undergo the same type of
photoinduced substitution in liquid ammonia as nitroben-
zene[22,25] (see also section II.A.1), only at the positions
ortho and para to the nitro group.

Irradiation, with light from a high-pressure mercury
lamp, of p-chloronitrobenzene in liquid ammonia at −60°
affords p-nitroaniline (45%) and 5-chloro-2-nitroaniline
(11%) (yields are based on the amount of chloronitro-
benzene consumed). This reaction cannot be accom-

plished in solution in 15% ammonia/methanol. A photo-
reaction does take place in this medium, but the prod-
ucts, which have not been identified, differ from those in
the liquid ammonia solution.[25]

m-Chloronitrobenzene, irradiated in liquid ammonia, af-
fords two substitution products, viz. 2-chloro-4-nitroani-
line and 4-chloro-2-nitroaniline. No m-nitroaniline has
been detected in the irradiated solution.

As its para and meta isomers, o-chloronitrobenzene
undergoes substitution at the ortho and the para position
relative to the nitro group. 3-Chloro-4-nitroaniline is the
major product, whereas very little o-nitroaniline is
formed.
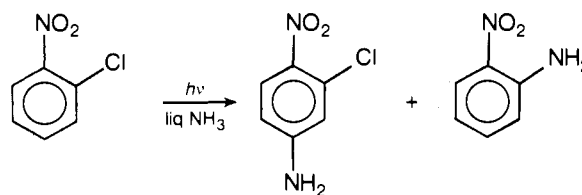
6. Bromonitrobenzenes

Photoamination of p-bromonitrobenzene has been found by van Vliet[25] to proceed in an analogous way as the corresponding chloro compound. Irradiation of p-bromonitrobenzene in liquid ammonia at −60° afforded p-nitroaniline (54%) and 5-bromo-2-nitroaniline (16%).

Nijhoff and Havinga[76,77] examined the photolytic behavior of m-bromonitrobenzene in alkaline aqueous solution (0.1 N NaOH, 10% methanol) to check whether the meta-directing influence of the nitro group can also lead to photonucleophilic substitution (by hydroxide ion) of bromine on the aromatic ring. This appears not to be the case. No significant formation of m-nitrophenol has been detected.

7. Fluoronitrobenzenes

m-Fluoronitrobenzene shows photosubstitution in aqueous alkaline solution yielding m-nitrophenolate.[78] Upon irradiation of 500 mg of m-fluoronitrobenzene in 1.5 l. of 1 N NaOH (containing 2% dimethyl sulfoxide) for 24 hr (high-pressure Hg lamp, Pyrex filter), a yield of 60 mg of m-nitrophenol can be obtained. The quantum yield of the photohydrolysis at 313 nm in 0.1 N NaOH solution is estimated to be 4×10^{-3}.
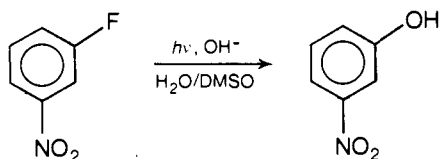
The quantum yield is much lower for the photosubstitution of m-fluoronitrobenzene than for m-nitroanisole (section III.A.1), but presumably higher than for m-bromonitrobenzene. The photohydrolysis of m-fluoronitrobenzene can be photosensitized with disodium naphthalene-2,6-disulfonate.[78] Whether the reaction proceeds via a triplet state in the case of direct excitation has not been ascertained.

p- and o-fluoronitrobenzene behave like the meta isomer on photolysis in aqueous alkaline solution. Although the corresponding phenols are the major products, azo and azoxy compounds are also found. Photoreduction by the solvent may be responsible for the formation of these products. Moreover, both p- and o-fluoronitrobenzene undergo a slow thermal reaction in alkaline solution, whereas m-fluoronitrobenzene is completely stable in the dark at room temperature.

In dimethyl sulfoxide m-fluoronitrobenzene can be photosubstituted with dimethylamine yielding inter alia m-nitro-N,N-dimethylaniline in low yield. Sensitization of the photoreaction with disodium naphthalene-2,6-disulfonate could not be effected.[47] In the solvents acetonitrile, water, and tert-butyl alcohol irradiation of m-fluoronitrobenzene in the presence of dimethylamine does not lead to photosubstitution; only photoreduction products could be isolated. In this connection it is of interest that m-fluoronitrobenzene behaves like nitrobenzene on irradiation with cyanide ion in aqueous solution; i.e., the nitro group is photoreduced to a nitroso group. This points to a lowest lying triplet state of n,π^* character (cf. section II.A.1). It is therefore not surprising that amines tend to give photoreduction with m-fluoronitrobenzene rather than photosubstitution and that quantum yields for substitution by OH⁻ are low.

8. Halogenophenols and Halogenoanisoles

Nucleophilic photosubstitution in halogenophenols and halogenoanisoles has been reported by Pinhey and Rigby.[79] In the cases they describe the solvents (methanol, ethanol, 2-propanol, or dioxane) act as nucleophiles.

Irradiation of m-chlorophenol in 2-propanol and in ethanol yields mixtures of substitution product in which the chlorine atom is displaced and phenol. The occurrence of the latter indicates that homolysis of the C–Cl bond and subsequent hydrogen abstraction from the solvent is involved.
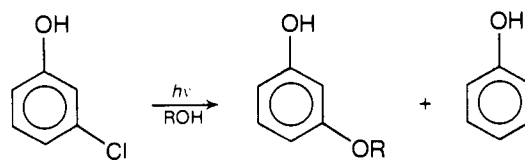

When R = isopropyl the yields of m-isopropoxyphenol and phenol are 62 and 19%, respectively. Irradiation in ethanol affords m-ethoxyphenol in 80% yield, while the yield of phenol is 13.5%.

On irradiation of m-chlorophenol in dioxane/water (95:5) phenol is formed in high yield (67%); considerable amounts of a substitution product, 2-(β-chloroethoxy)ethyl m-hydroxyphenyl ether, are also formed.
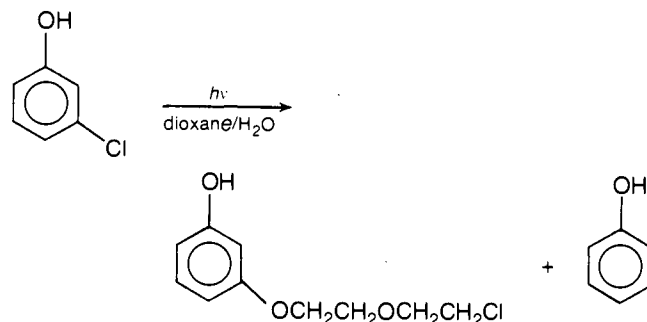
m-Bromophenol in 2-propanol yields only a small amount of photosubstitution product (8.6% m-isopropoxyphenol), phenol being the major product (73%). In the case of m-iodophenol the only product observed is phenol. An explanation is offered[79] on the basis of the decreasing strength of the carbon–halogen bond.

The chloroanisoles display the same type of reaction though in all cases studied the reduction product, anisole, predominates. 1-Isopropoxy-3-methoxybenzene is obtained from irradiation of m-chloroanisole in 2-propanol in 9% yield. In methanol the yield of substitution product is higher (28%). Photolysis of p-chloroanisole in methanol affords 1,4-dimethoxybenzene (14% yield), but 1,2-dimethoxybenzene could not be found as a product from o-chloroanisole.
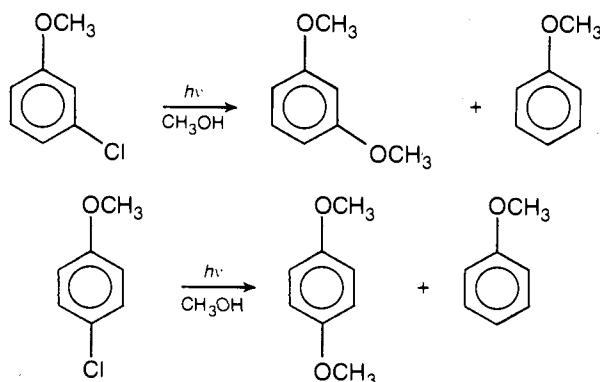
Omura and Matsuura[80,81] photolyzed halogenophenols in aqueous alkali and in aqueous cyanide solution. Irra-

diation of p-halogenophenols in aqueous alkali gives 2,4′-dihydroxybiphenyl as the major product in addition to phenol, hydroquinone, 2,4′-dihydroxy-5-halogenobiphenyl, and 4,4′-dihydroxybiphenyl (Scheme III).

SCHEME III

X = Cl, Br, I
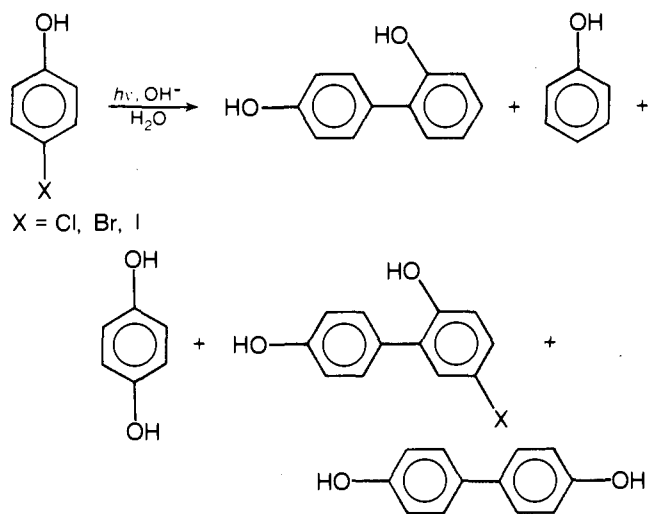
2,4′-Dihydroxy-5-halogenobiphenyl was isolated only in the case of p-chlorophenol. The yield of the major product, 2,4′-dihydroxybiphenyl, varies between 23 and 34%, depending on the nature of the substituent. The yield of phenol decreases in the order I > Br > Cl (13, 11.5, and 4.8%, respectively), while the yield of hydroquinone increases in the same order (0, 9.0, and 27%, respectively). The yield of 4,4′-dihydroxybiphenyl is always small, being highest (3.2%) in the case of p-iodophenol.

Homolytic fission of a carbon–halogen bond of the excited p-halogenophenols seems to be operative in this reaction. The p-hydroxyphenyl radical may abstract a hydrogen atom from the solvent to yield phenol. 4,4′-Dihydroxybiphenyl and 2,4′-dihydroxy-5-halogenobiphenyl are thought[81] to be formed, respectively, via addition of the p-hydroxyphenyl radical to the para or ortho position (with respect to OH) of a ground state p-halogenophenol molecule and subsequent loss of a halogen or hydrogen atom. The major product, 2,4′-dihydroxybiphenyl, may arise through thermal or photochemical reduction of 2,4′-dihydroxy-5-halogenobiphenyl. Support for this assumption comes from the observation that the ratio of the dehalogenated dihydroxybiphenyl to the compound containing halogen increases with increasing alkali concentration, higher reaction temperatures, and longer irradiation periods.

To account for the formation of hydroquinone a concerted reaction is assumed with a transition state of the following structure:
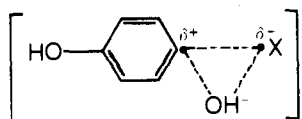

m-Chlorophenol on irradiation in aqueous alkali gives resorcinol in very high yield (74%).[80,81]

In aqueous cyanide solution the p-halogenophenols give p-cyanophenol in good yield (X = Cl 75%; X = Br 76%; X = I 65%). Small amounts of hydroquinone and 2,4′-dihydroxybiphenyl are found as by-products. A reaction scheme is proposed[81] with the same type of transition state as for the reaction in aqueous alkali:
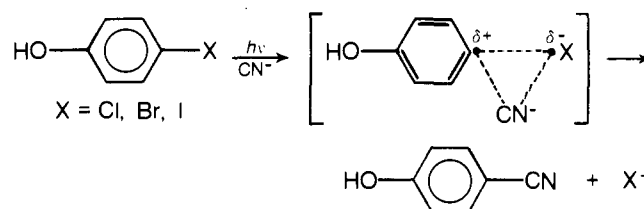

m-Chlorophenol yields only little m-cyanophenol (7.5%), resorcinol being the major product in this instance (72%). It is suggested[81] that the electrophilic character of the excited state molecule of m-chlorophenol is so strong that it can react with a water molecule, or that it reacts much faster with a hydroxide ion than with a cyanide ion.

p-Chloroanisole is very reactive toward cyanide ion on irradiation. p-Cyanoanisole could be isolated in 90% yield from an irradiated solution (high-pressure mercury lamp TQ 81, 20 min!) of 224 mg of p-chloroanisole in tert-butyl alcohol/water (1:3).[32]
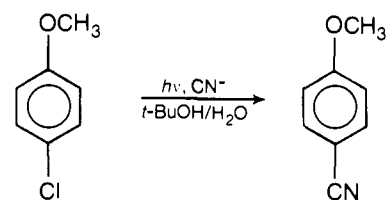
The chlorine atom in p-chloroanisole can also be displaced in a photochemical reaction with nitrite ion, as has been demonstrated by El'tsov and coworkers.[82] They obtained p-nitroanisole in 20% yield from an irradiated solution of p-chloroanisole in water containing 30% tert-butyl alcohol with 0.4 M NaNO₂.

El'tsov and coworkers[82] also found a striking difference between p- and m-chlorophenol in their photochemical behavior toward nitrite ion. p-Chlorophenol gives a good yield of p-nitrophenol on irradiation in an aqueous solution containing sodium nitrite, whereas from m-nitrophenol under similar conditions only traces of m-nitrophenol could be found. On the basis of ample experimental evidence, these reactions with nitrite ion are considered to be aromatic nucleophilic photochemical substitutions. The difference between the two isomeric chlorophenols may very well be ascribed to an ortho/para directing influence of the hydroxyl substituent, comparable to the ortho/para activating effect of the methoxy group (sections II.A.2 and III.A.9).
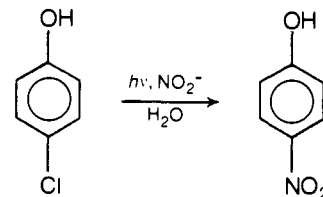
9. Dimethoxybenzenes

The photochemical reactions of the three isomeric dimethoxybenzenes with cyanide ion have been investigated by den Heijer et al.[32] The results are in complete agreement with the ortho/para directing effect of the methoxy group observed earlier (section II.A.2). In each of the three cases 200 mg of the starting material was irradiated for 3 hr (Hg lamp, TQ 81) in a solution of 0.08 M KCN in tert-butyl alcohol/water (1:3) (Scheme IV). Yields (based on the amount of consumed starting material) are as follows: ortho, 68%; meta, monocyano, 48%; dicyano, 10%; para, 21%.

SCHEME IV
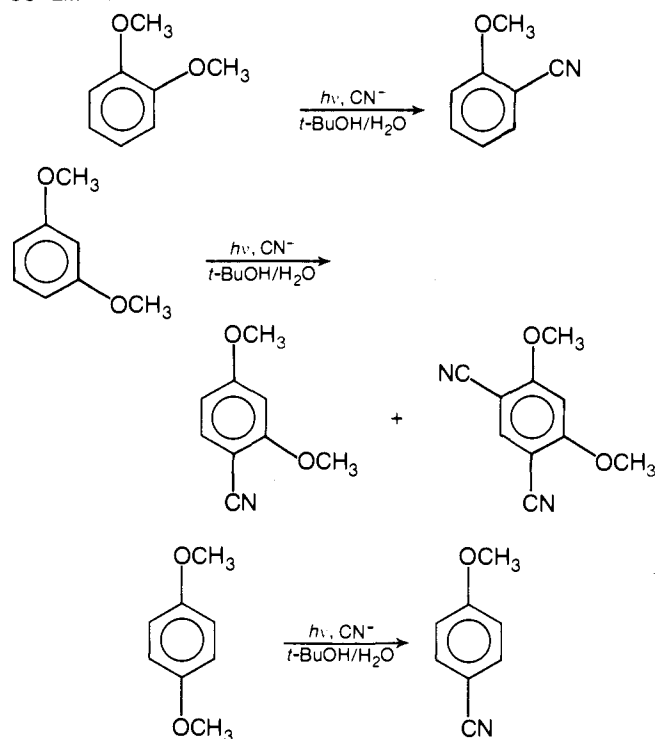
10. Halogenoanilines

Photochemical substitution of a halogen atom by a nitro group in p-fluoro-, p-chloro-, p-bromo-, and p-iodoaniline has been found by El'tsov, Frolov, and Kul'bitskaya.[82,83] The respective yields of p-nitroaniline are 18, 21, 20, and 10%. The irradiations were performed in aqueous methanolic solutions of sodium nitrite (0.4–0.6 M). The same reaction occurs with p-chloro-N,N-dimethylaniline; p-nitro-N,N-dimethylaniline was isolated in 36% yield.
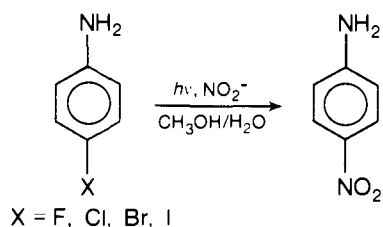

From o-chloroaniline the yield of o-nitroaniline is 8% and from the meta isomer no more than about 1% of m-nitroaniline is reported to be found. Thus, like other electron-donating substituents such as methoxy (section III.A.9) and hydroxy (section III.A.8), the amino group appears to exert a para/ortho directing influence on nucleophilic aromatic photosubstitution, the effect being strongest at the para position. El'tsov and coworkers[82] report that the presence of oxygen does not affect the yield of the replacement products. This result is considered to be in support of the view that the lowest excited singlet state of the halogenoanilines takes part in the photochemical reaction. For the ground state, two excited singlet states and the lowest triplet state charge densities on the various atoms and bond orders have been calculated by the SCF PPP method with configuration interaction.[82] For 4-chloro-N,N-dialkylaniline the results show that the amino substituent increases the electron densities in the ortho and meta positions of the aromatic ring following excitation to the lowest excited singlet state. The carbon attached to the halogen acquires a

positive charge. The charge distribution in the lowest excited singlet state agrees with the observed activation at the para position. Calculations of charge densities for the various excited states of m-nitroaniline are in accordance with the observed inactivity of this compound in nucleophilic photochemical substitution.

The photochemical reaction of p-chloroaniline with cyanide ion[82] is found to be effective, the yield of p-cyanoaniline being about 50%. Photoreaction of the same compound with thiocyanate ion affords p-thiocyanatoaniline in 10% yield.

11. Other Disubstituted Benzenes

Shapiro and Tomer[84] describe the photochemical reaction (2537 Å) of the toluene-p-sulfonylhydrazones of camphor and acetone with an excess of methyllithium. A fairly high amount (45%) of p-xylene is found, in addition to small amounts of other products (toluene and ethylbenzene).
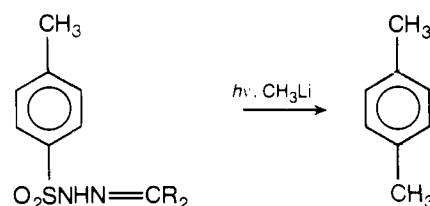

The same type of photochemical reaction occurs with sodium toluene-p-sulfinate and methyllithium. The major product of the reaction is again p-xylene.[84]

Frolov et al.[85] have found that p-aminobenzenesulfonamide, p-aminophenyl trifluoromethyl sulfone and p-aminophenyl methyl sulfone take part in a photochemical exchange reaction with various nucleophiles as cyanide ion, nitrite ion, and methoxide ion.

X = NH₂, CF₃, CH₃;   Nu⁻ = CN⁻, NO₂⁻, SCN⁻, CH₃O⁻
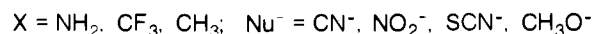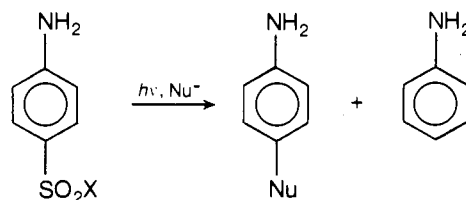
Letsinger and Colb[86] found replacement of methoxyl by cyanide on irradiation of 3-methoxyacetophenone in a solution of sodium cyanide (0.025 M) in acetonitrile/water
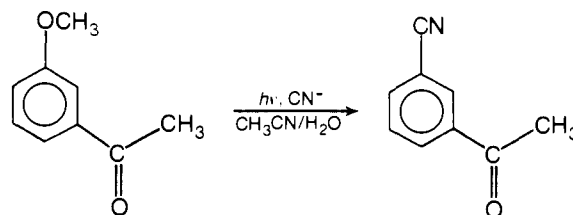
(5:1). Hydroxide is less reactive than cyanide, but it also attacks photoexcited 3-methoxyacetophenone in aqueous solution yielding 3-hydroxyacetophenone (isolated yield 66%).[86]

When the solvent is preponderantly water (less than 1% CH₃CN) irradiation with cyanide ion leads to 3-methyl-5-methoxyphthalide and probably 3-methyl-7-methoxyphthalide. The formation of the lactones is rationalized[86] on the basis of addition of cyanide ortho to the carbonyl group followed by protonation at oxygen, aromatization by tautomerization, hydrolysis of the nitrile group, and lactonization on acidification.
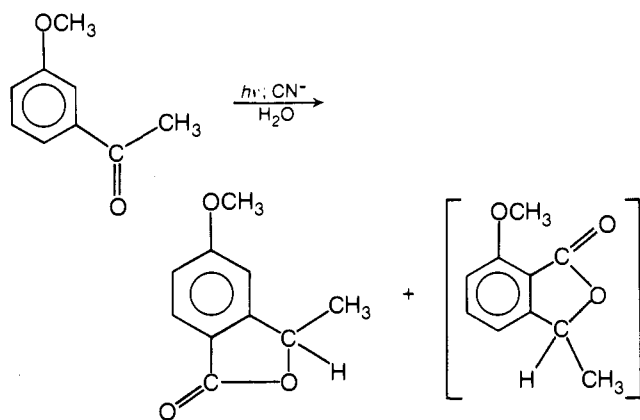
B. Disubstituted Naphthalenes

1. Dinitronaphthalenes

In section II.B.1 it has been mentioned that 1-nitronaphthalene in its excited state displays a greater reactivity toward nucleophiles than nitrobenzene. The dinitro derivatives show a similar difference. While the dinitrobenzenes are relatively unreactive on irradiation in the presence of nucleophiles, a very clean and efficient photohydrolysis has been found to take place in alkaline solutions of 1,6- and 2,7-dinitronaphthalene.[87,88] The products of these reactions are 6-nitro-1-naphthol and 7-nitro-2-naphthol, respectively. Beijersbergen van Henegouwen[87] found that the mononitronaphthalenes do not yield the corresponding naphthols on illumination in alkaline solutions containing atmospheric oxygen. In nitrogen-purged solutions small amounts of 1-naphthol can be obtained from 1-nitronaphthalene.[47] Evidently, the formation of nitronaphthols from the dinitronaphthalenes is facilitated by the mutual interaction of the two nitro groups. The greater photostability of the nitronaphthols as compared to the naphthols is probably also of importance. The difference between the dinitronaphthalenes and the dinitrobenzenes is presumably due to the same effect that causes nitrobenzene and the nitronaphthalenes to be different: n,π^* vs. π,π^* character of the reactive excited state.
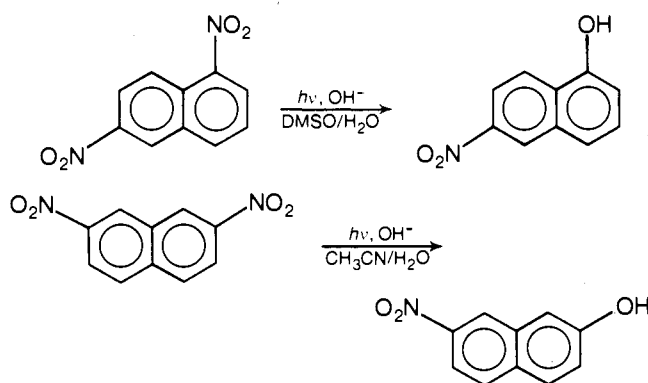
Quantum yields of these reactions were determined at 313 nm in dimethyl sulfoxide/water (7:18) with 0.8 N NaOH. The quantum yield of the formation of 6-nitro-1-naphthol from 1,6-dinitronaphthalene is 0.48; for the reaction in which 7-nitro-2-naphthol is formed from 2,7-dinitronaphthalene, $\phi = 0.34$.

Benzophenone can act as a sensitizer in the photohydrolysis of 1,6-dinitronaphthalene.[87,88] 6-Nitro-1-naphthol was the only product of the photosensitized reaction.

Quenching of the photoreaction of 1,6-dinitronaphthalene is reported to occur in the presence of fluorenone or

sodium sorbate. The triplet energy of 1,6-dinitronaphthalene is 56.2 kcal/mol; fluorenone has an E_T of 53 kcal/mol, while the triplet energy of sodium sorbate is estimated to be about 48 kcal/mol. It seems reasonable to assume that the suppression of the photochemical reaction is due to triplet quenching. A linear Stern–Volmer plot describes the dependence of quantum yield on quencher concentration.
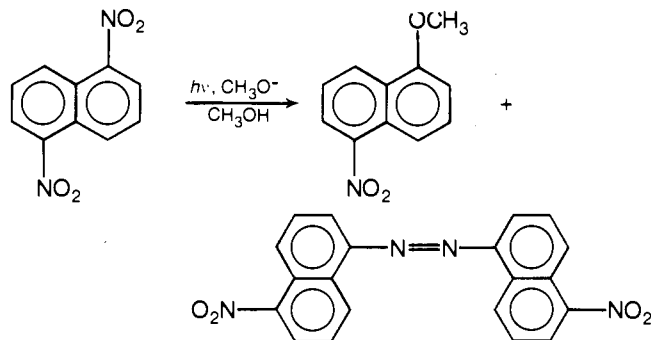
Irradiation of 1,6-dinitronaphthalene in aqueous acetonitrile solution containing 0.1 M KCN affords 1-cyano-6-nitronaphthalene by substitution of the α-nitro group.[89] In
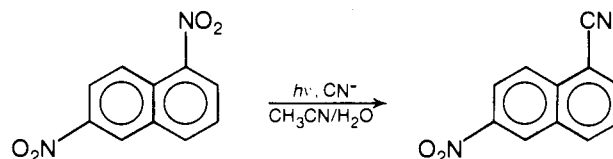
1,5- and 1,8-dinitronaphthalene both nitro groups can be substituted by cyanide. From 1,8-dinitronaphthalene, in addition to 1-cyano-8-nitro- and 1,8-dicyanonaphthalene, 1,4,5-tricyanonaphthalene was isolated in 14% yield.[8] 2,7-Dinitronaphthalene gives 2-cyano-7-nitronaphthalene in low yield.[48] Two substitution products were isolated in equal yield (8%) from the irradiation of 1,4-dinitronaphthalene with 0.01 M KCN in acetonitrile/water (1:1): 1-cyano-4-nitronaphthalene and 1-cyano-5,8-dinitronaphthalene.
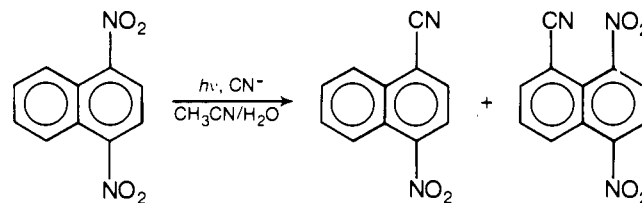
1,3-, 1,5-, and 1,8-dinitronaphthalene have been photolyzed in methanol containing 0.1 M sodium methoxide. Only from 1,5-dinitronaphthalene could an appreciable amount (11%) of substitution product be isolated:[8] 1-methoxy-5-nitronaphthalene. The major products (20–30%) from all three isomers are dinitroazoxynaphthalenes.

1,5- and 1,8-dinitronaphthalene on irradiation in CHCl₃/HCl show the same type of photochemical reaction as 1-nitronaphthalene, namely displacement of a nitro group by a chlorine atom.[43,44] 1,5-Dichloronaphthalene can be obtained from 1,5-dinitronaphthalene in 85% yield upon irradiation of the nitro compound in chloroform through which hydrogen chloride is passed. From 1,8-dinitronaphthalene a mixture of equal amounts of 1,8-dichloronaphthalene and trichloronaphthalene is obtained in an overall yield of 45%.[44]
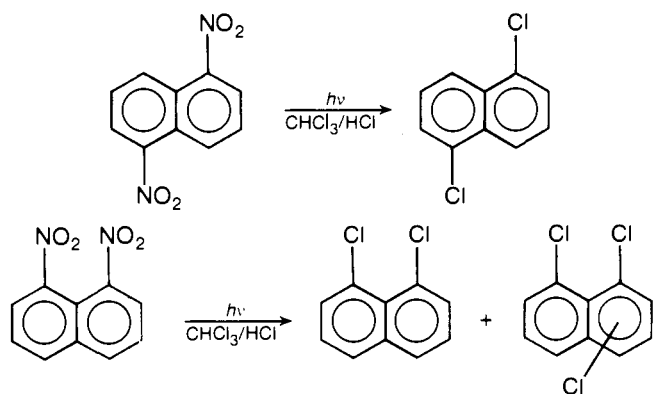
2. Dimethoxynaphthalenes

The photoreaction of 1,4-dimethoxynaphthalene with cyanide ion (0.05 M) in tert-butyl alcohol/water (1:2) has been investigated by Lok.[48] The product of the reaction is 1-cyano-4-methoxynaphthalene; this result would have been predicted on the basis of the para-activating effect of the methoxy group and the higher reactivity at the α position in naphthalenes. The yield of the reaction is poor, however; from 44 mg of starting material 1.4 mg of product was obtained after 6 hr of irradiation (3000 Å).

den Heijer et al.[32] irradiated 2,3-dimethoxynaphthalene in solution (tert-butyl alcohol/water, 1:3) with KCN (0.07 M). Again substitution takes place at an α position yielding 1-cyano-2,3-dimethoxynaphthalene by displacement of hydrogen, even though better leaving groups are available at the β positions. The yield (based on consumed starting material) is 12%.
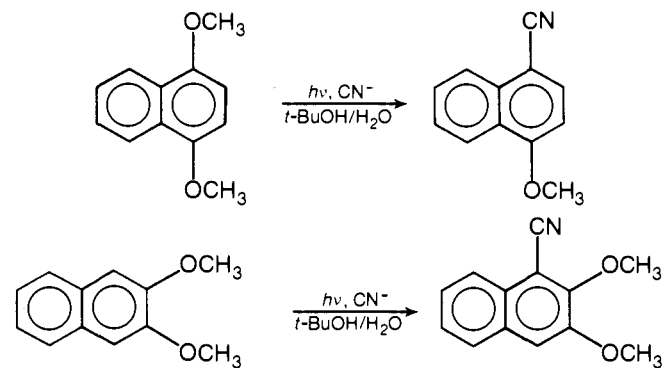
3. Methoxynitronaphthalenes

Of the fourteen isomeric methoxynitronaphthalenes nine have been investigated with respect to their photolytic behavior with one or more nucleophiles.

Havinga and de Jongh[56] report that 1-methoxy-3-nitronaphthalene shows a photochemical reaction with hydroxide ion comparable to that of m-nitroanisole (section III.A.1). The dependence of the quantum yield on the hydroxide ion concentration is similar to that of the benzene derivative; quantum yields are, however, 20 times lower.[90] The photohydrolysis can be quenched with 3,3,4,4-tetramethyldiazetine dioxide,[47] and the Stern–Volmer plot gives a straight line. At increasing quencher concentrations the quantum yield goes to zero. Surprisingly, sensitization of this reaction with benzophenone or triphenylene proved impossible. Photosensitization does
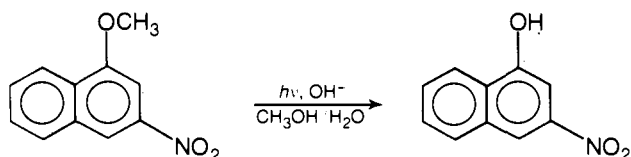

lead to reaction, presumably from the triplet, but no photohydrolysis could be detected.[47]

Lammers[47] found that 1-methoxy-3-nitronaphthalene reacts with methylamine on irradiation in aqueous acetonitrile solution. At 0.1 M CH_3NH_2 a 90% yield of N-methyl-1-amino-3-nitronaphthalene has been obtained. The quantum yield at 313 nm (1.35 M methylamine) is 0.09. With this nucleophile, sensitization could be easily accomplished with triphenylene. The reaction can be quenched by 3,3,4,4-tetramethyldiazetine dioxide.

Three other methoxynitronaphthalenes are comparable with m-nitroanisole. 1-Methoxy-6-nitro-, 2-methoxy-5-nitro-, and 2-methoxy-7-nitronaphthalene are photohydrolyzed to yield the corresponding nitronaphthols in mixtures of acetonitrile or dimethyl sulfoxide with aqueous sodium hydroxide.[87,88] In these three compounds the methoxy group is located at a position which is expected to be not reactive toward nucleophilic attack in the ground state of the molecule.

These findings lead to the conclusion that in the methoxynitronaphthalenes, as in benzene derivatives, the nitro group exerts a "meta" directing influence on nucleophilic attack in the excited state.
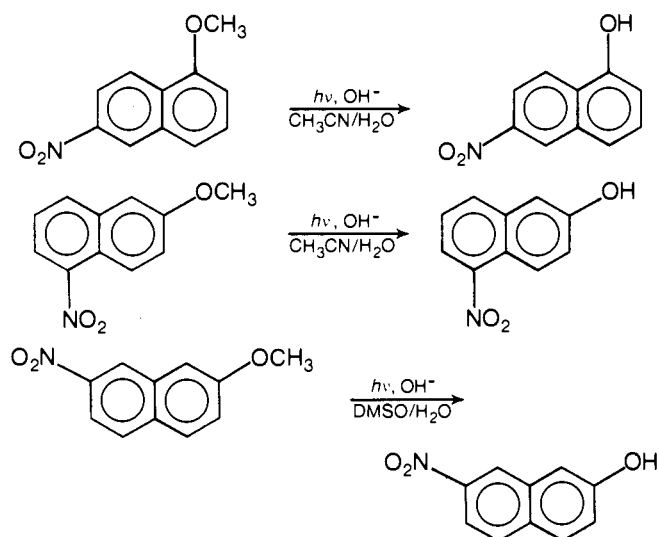
The quantum yields at 313 nm of these reactions have been measured in 5 × 10^{-5} M solutions in DMSO/2 N NaOH (7:18): 1-methoxy-6-nitronaphthalene, ϕ = 0.158; 2-methoxy-5-nitronaphthalene, ϕ = 0.054; 2-methoxy-7-nitronaphthalene, ϕ = 0.026.

The dependence of the quantum yield of the photohydrolysis on the hydroxide ion concentration has been studied for 1-methoxy-6-nitronaphthalene.[47,87] It has been found that a linear relationship exists between $1/\phi$ and $1/[OH^-]$ below concentrations of about 0.72 M. At higher concentrations the quantum yield remains constant with increasing pH. The reaction can be photosensitized with benzophenone, but quenching with 3,3,4,4-tetramethyldiazetine dioxide could not be accomplished. The same is true for the reaction of 1-methoxy-6-nitronaphthalene with methylamine in acetonitrile/water (1:1). In the direct irradiation (0.4 M CH_3NH_2) N-methyl-1-amino-6-nitronaphthalene was formed in 90% yield. Sensitization afforded the same product, but attempts to quench the reaction were unsuccessful.[47] Apparently, the triplet state of 1-methoxy-6-nitronaphthalene is reactive toward nucleophiles, but there is room for some doubt as to whether in the direct irradiation the reaction proceeds via this state. Positive evidence for a singlet state reaction is still lacking, however.

The third nucleophile with which excited 1-methoxy-

6-nitronaphthalene has been found to react is cyanide ion: 28 mg of 1-cyano-6-nitronaphthalene and 43 mg of unreacted starting material were isolated from an irradiated solution (2 hr; high-pressure Hg lamp TQ 81) of 100 mg of methoxynitro compound in 500 ml of acetonitrile/water (9:1).[89]
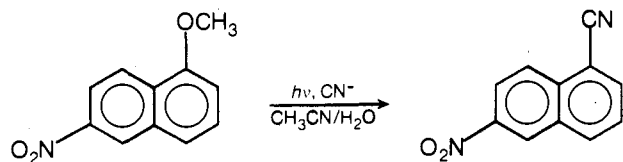
The reaction of 2-methoxy-1-nitronaphthalene on irradiation in alkyl chlorides or in hexane/HCl involving substitution of the nitro group by a chlorine atom has already been mentioned in the section on 1-nitronaphthalene (II.B.1).

Beijersbergen van Henegouwen and Havinga[87,88] found that irradiation of 2-methoxy-6- and 1-methoxy-5-nitronaphthalene in $CH_3CN/0.1\ N$ NaOH (1:4) does not lead to the formation of the corresponding nitronaphthols. By drawing resonance structures for the ground state it can be seen that in these molecules the two substituents are in a "para" position. Recently, Lammers[47] showed that the methoxy group in these compounds can be photosubstituted by hydroxide provided the reactions are performed in an oxygen-free atmosphere. That the nitronaphthols cannot be detected as photoproducts in the presence of oxygen is probably not caused by their photochemical instability. It seems worthwhile to investigate whether the reaction under nitrogen is an aromatic substitution, i.e., whether it proceeds with splitting of the band between the aromatic carbon and the oxygen atom.

1-Methoxy-5-nitronaphthalene has also been irradiated with sodium methoxide (0.1 M) in methanol. The possibility of photochemical exchange of methoxy groups by substitution at position 1 has not been investigated. Two products have been found: 1,2-dimethoxy-5-nitronaphthalene and 1,4-dimethoxy-5-nitronaphthalene, both in 10% yield.[47] Oxygen was not excluded. The positions at which substitution occurs are "meta" to the nitro group and "ortho" or "para" to the methoxy substituent. No displacement of the nitro group (at an α position and "para" to the methoxy at position 1) has been found, which is rather surprising in view of the easy reaction of 1-nitronaphthalene with methoxide ion (section II.B.1).
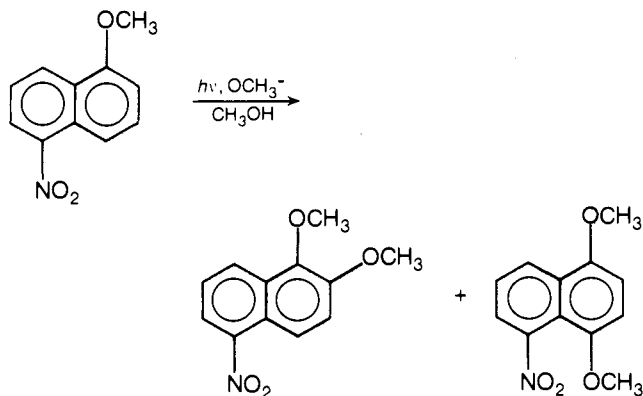

1-Methoxy-7-nitronaphthalene gives similar results; irradiation in methanol containing 0.1 M sodium methoxide affords 1,4-dimethoxy-7-nitronaphthalene in 20% yield.

1-Methoxy-4-nitronaphthalene has been the object of investigations by Letsinger and coworkers[28,45] and by Lok.[8] Three nucleophiles have been examined (CN^-,

BH_4^-, OCH_3^-) and, as 1-nitronaphthalene, they all give photosubstitution of the nitro group. Letsinger and Hautala[45] report that on irradiation in acetonitrile containing 5% water and 0.01 M KCN 1-cyano-4-methoxynaphthalene is formed with a quantum yield of 0.047. In a preparatory reaction the product was isolated in 70% yield. The same reaction is observed in water with 10% acetonitrile, but in this polar medium the quantum yield is drastically lowered to 0.00015. In 1-nitronaphthalene the solvent effect is much smaller (section II.B.1). The effect is discussed by Letsinger and Hautala[45] in terms of the nature $(\pi,\pi^*$ vs. $n,\pi^*)$ of the lowest triplet state.

The photoreaction of 1-methoxy-4-nitronaphthalene with sodium borohydride in acetonitrile (9:1) yields 1-methoxynaphthalene in 50% yield.[28] A similar solvent sensitivity has been found as in the reaction with cyanide ion; the reaction is about 100 times more efficient in 80:20 acetonitrile/water than in 10:90 acetonitrile/water.
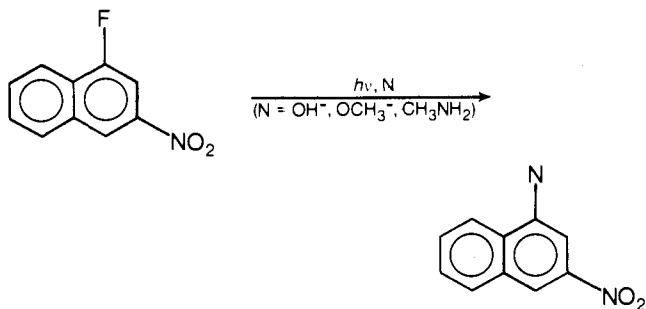
Lok[8] found that 1-methoxy-4-nitronaphthalene converts to 1,4-dimethoxynaphthalene (70% yield) via a photochemical reaction (high-pressure Hg lamp TQ 81, 30 min) in methanol (210 mg in 1.2 l.) containing sodium methoxide (0.1 M). With 1 M CH_3ONa the quantum yield at 366 nm is 0.19. The reaction can be sensitized with 2-acetonaphthone and quenched with 3,3,4,4-tetramethyldiazetine dioxide. At 366 nm (with 1 M CH_3ONa) a linear Stern–Volmer plot was obtained. With the assumption that the quenching is diffusion controlled, a triplet lifetime of 14 nsec can be calculated, a value which seems to be normal for nitroaromatics.[68]
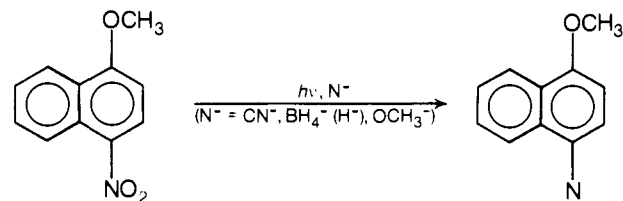
4. Halogenonitronaphthalenes

Lammers[47] investigated the photochemical substitution reactions of almost all fluoronitronaphthalenes. Of the twelve isomers studied only five will be mentioned here.

1-Fluoro-3- and 1-fluoro-6-nitronaphthalene (both "meta" isomers) undergo clean photosubstitution reactions in solutions containing nucleophiles (OH^-, OCH_3^-, CH_3NH_2, CN^-). In the photohydrolysis fluorine is substituted, and at 0.1 N hydroxide ion concentration both compounds have a quantum yield of about 0.3. The reactions can be sensitized with benzophenone and quenched with 3,3,4,4-tetramethyldiazetine dioxide or fluorenone. Stern–Volmer plots are found to be linear. Product yields are 70% for the 1,3 and 40% for the 1,6 isomer. Both compounds also react with methoxide ion (0.1 M in methanol) and give substitution of fluorine in 80 and 90% yield, respectively. With methylamine (0.1 M in acetonitrile/water, 1:1) 1-fluoro-3-nitronaphthalene is photosub-

stituted to yield N-methyl-1-amino-3-nitronaphthalene (70%).

Cyanide ion shows different behavior with photoexcited 1-fluoro-3-nitronaphthalene. Irradiation in acetonitrile/water (10:1) with 0.1 M KCN affords 3-cyano-1-fluoronaphthalene in low yield (8%). No replacement of fluorine by cyanide ion has been found.
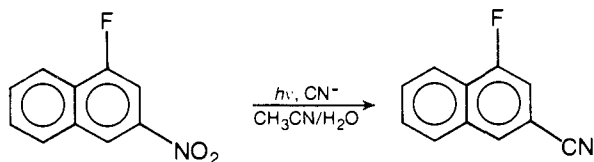
1-Fluoro-7-nitronaphthalene has its substituents in a "para" position. Photohydrolysis and photomethoxylation by replacement of fluorine can be accomplished (yields are approximately 50%), but, as in the case of the "para" methoxynitronaphthalenes, only in nitrogen atmosphere. The reaction with hydroxide ion can be sensitized with benzophenone.

The fluoronitronaphthalenes mentioned have the nitro group at a β position. Two isomers with an α-nitro group are 2-fluoro-5-nitro- and 1-fluoro-8-nitronaphthalene; with methoxide ion in methanol fluorine is photosubstituted, but there are also indications of replacement of the nitro group. With 2-fluoro-5-nitronaphthalene the photomethoxylation can be sensitized with triphenylene. Sensitization attempts were unsuccessful in the photohydrolysis of this compound, which in the direct irradiation yields 5-nitro-2-naphthol in 15% yield. In 1-fluoro-8-nitronaphthalene photosubstitution of fluorine by hydroxide proceeds in 25% yield (0.1 N NaOH in CH_3CN/H_2O, 1:1). As with the other "para"-substituted naphthalenes, the absence of oxygen is essential.

The photoreactions of 1-chloro-3-nitronaphthalene with hydroxide ion and methoxide ion are similar to those of the fluoro compound, but they proceed less cleanly and give lower yields.[47]

3-Chloro-1-nitro-, 1-chloro-, and 1-bromo-4-nitronaphthalene undergo substitution of the nitro group on irradiation in the presence of methoxide ion. From the 1,4 isomers, low yields of 1,4-dimethoxynaphthalene have been found.[48]

C. Disubstituted Biphenyls

1. Dinitrobiphenyls

The photoreactions of 4,4'-dinitrobiphenyl and 3,3'-dinitrobiphenyl were investigated by Vink et al.[14,51] Irradiation (Rayonet photochemical reactor, RPR 208, 3000 Å) of 200 mg of 4,4'-dinitrobiphenyl and 5.8 g of KCN in 1750 ml of tert-butyl alcohol/water (5:2) afforded 94.5% conversion after 1 hr. The two products found are 4-cyano-4'-nitrobiphenyl (10.4%) and 4,4'-dicyanobiphenyl (61.4%). Irradiation of 3,3'-dinitrobiphenyl under similar conditions for 6 hr afforded no cyano-substituted products. The starting material was largely recovered.
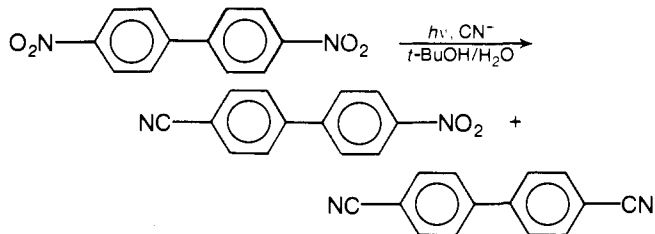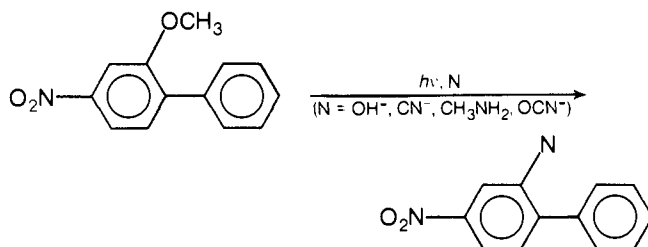

The results clearly illustrate the high reactivity at the 4 position in excited biphenyls. 3-Nitrobiphenyl yields 4-cy-

ano-3'-nitrobiphenyl on irradiation with cyanide ion. That a similar reaction does not take place in 3,3'-dinitrobiphenyl must be due to the presence of a nitro group near both 4 positions; whether this effect is electronic or steric has not yet been established.

2. Methoxynitrobiphenyls

The photoreactions of 2-methoxy-4-nitrobiphenyl with the nucleophiles CN^-, OH^-, CH_3NH_2, and OCN^- are completely analogous to those of m-nitroanisole (section III.A.1). The reactions proceed rapidly and with high yields of product. Invariably the methoxy group is substituted. Thus, 2-methoxy-4-nitrobiphenyl bears a closer re-

semblance to m-nitroanisole than to 4-nitrobiphenyl in its photochemical behavior, as is evident in particular from the results of the reaction with cyanide ion.[14,51]

The similarity in behavior of 2-methoxy-5-nitrobiphenyl and p-nitroanisole is less outspoken, although there is still a larger difference between 2-methoxy-5-nitrobiphenyl and 3-nitrobiphenyl. The photoreaction with cyanide ion yields two products: 3-cyano-2-methoxy-5-nitrobiphenyl (9%) and 5-cyano-2-methoxybiphenyl (9%). Products in which CN has been introduced in the unsubstituted ring (compare 3-nitrobiphenyl, section II.C.2) have not been found.
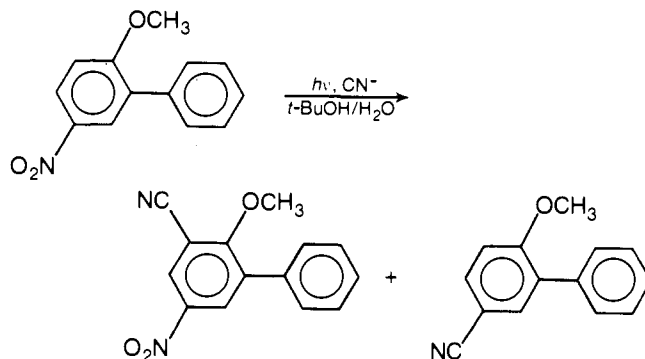
The formation of the trisubstituted compound is analogous to the reaction in which 2-cyano-4-nitroanisole is formed from p-nitroanisole (section III.A.1). Replacement of the nitro group by cyanide in p-nitroanisole is only observed in apolar media,[45] whereas in the biphenyl derivative it occurs in aqueous solution.

On irradiation of 2-methoxy-5-nitrobiphenyl (203 mg) in alkaline solution (0.1 N NaOH in tert-butyl alcohol/water, 1:2; Rayonet photochemical reactor, RPR 208, 2537 Å), a rapid reaction took place (53% conversion in 20 min). 2-Hydroxy-5-nitrobiphenyl was isolated in high yield (82.4%, based on amount of consumed starting material).[14]
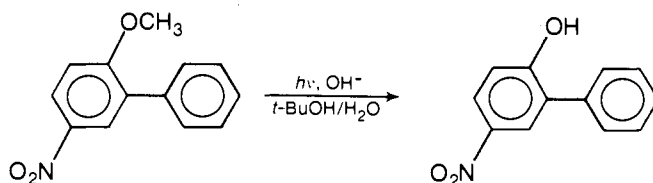
TABLE III. Quantum Yield at 313 nm for the Photohydrolysis of Various Dinitroanisoles in 0.01 N NaOH in Water with 2% Methanol

Compound	Product	Quantum yield
2,3-Dinitroanisole	2,3-Dinitrophenol	0.40
2,5-Dinitroanisole	2,5-Dinitrophenol	0.33
3,4-Dinitroanisole	3,4-Dinitrophenol	0.34
3,5-Dinitroanisole	3,5-Dinitrophenol	0.45
2,4-Dinitroanisole	2,4-Dinitrophenol	≤ 0.002

In p-nitroanisole both the nitro group and the methoxy group are substituted by OH^-, in a 4:1 ratio. The presence of a phenyl substituent thus acts in favor of substitution of methoxy. A similar effect has been found in 2,6-dimethyl-4-nitroanisole[66] where, despite the expected steric hindrance by the two methyl groups, only substitution of the methoxy group is found.

D. Disubstituted Azulenes

Certain 1-nitroazulenes substituted at the 3 position undergo substitution by methoxide ion on irradiation. The substituent may be S = NO_2, $COCF_3$, $COCH_3$, CHO, or CN. The main products of the reaction are 1-methoxy-3-S-azulene and 1,6-dimethoxy-3-S-azulene.[8,53] Product yields are 10–30% for the monomethoxy compound and

S = NO_2, $COCF_3$, $COCH_3$, CHO, CN
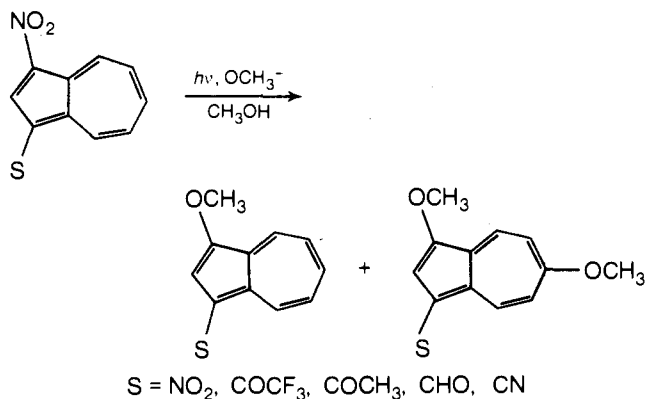
5–10% for the dimethoxy derivative. Irradiation of the products with one methoxy group did not give rise to formation of the disubstituted compounds. It is thought[53] that the 1,6-dimethoxy-3-S-azulenes are formed via 6-methoxy-1-nitro-3-S-azulenes by two consecutive photochemical reactions.

Irradiation of 1-nitro-3-S-azulenes in which S = Cl, Br, OCH_3, or CH_3 did not afford substitution products.

V. Trisubstituted Compounds

A. Trisubstituted Benzenes

1. Trinitrobenzene

An extensive kinetic investigation of the photochemical hydrolysis of 1,3,5-trinitrobenzene was made by Gold and Rochester.[91-93] The reaction products in aqueous alkali are nitrite and 3,5-dinitrophenoxide ions (more than 90%). The quantum efficiency of the reaction increases proportionally to the concentration of sodium hydroxide. The main absorbing species is a 1:1 complex between trinitrobenzene and hydroxide ion. After excitation of the complex a bimolecular substitution of nitrite by hydroxide ion may occur.
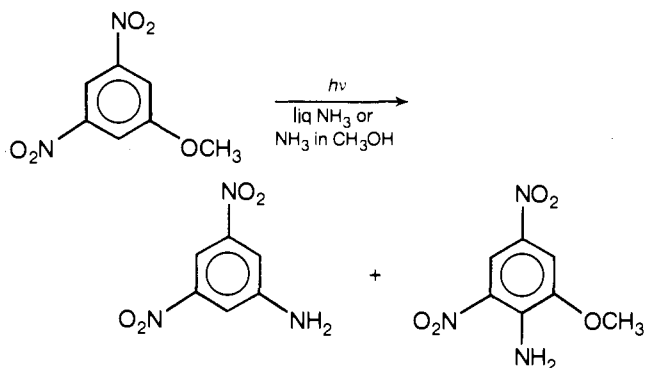
2. Dinitroanisoles

It has been attempted to accomplish photochemical substitution of the dinitroanisoles (all six isomers) using

hydroxide ion as a nucleophilic reagent.[66,77] The behavior of 3,5-dinitroanisole has also been investigated in liquid ammonia and in ammonia-containing methanol.[22,25]

Nijhoff[77] investigated the photohydrolysis of the five isomeric dinitroanisoles listed in Table III. In all cases the product is the expected dinitrophenolate. The quantum yields were measured at 313 nm in 0.01 N NaOH in water containing 2% methanol. The quantum yield for the photohydrolysis of m-nitroanisole is 0.22 (section III.A.1).

It is noteworthy that 2,4-dinitroanisole with its very low quantum efficiency is in this series the only isomer having no nitro group meta to methoxy. This reinforces the conclusion that a nitro group on the benzene ring exerts a meta-directing influence toward nucleophilic substitution in the excited state. The other isomer in which no m-nitro group is present has been studied by de Vries:[66] 2,6-dinitroanisole in 0.01 N NaOH (4% methanol in water) reacts only very slowly on irradiation with light of 313 nm, giving 2,6-dinitrophenol. Just as in the case of m-nitroanisole a linear relationship between the reciprocals of the quantum yield and the hydroxide ion concentration applies to the photohydrolysis of 2,3-, 2,5-, 3,4-, and 3,5-dinitroanisole.

Irradiation of 3,5-dinitroanisole in liquid ammonia or in methanol containing 15% ammonia affords two substitution products.[22,25] One of these, 3,5-dinitroaniline, is formed by displacement of the methoxy group, meta relative to both nitro groups, by an amino group. The other product, 2-amino-3,5-dinitroanisole, results from substitution at a position para to one of the nitro groups. Inter-

estingly, the product ratio depends on the solvent. In liquid ammonia the two products are formed in almost equal amounts, whereas in the methanol solution almost ten times as much 3,5-dinitroaniline is formed as 2-amino-3,5-dinitroanisole. It is instructive to compare these findings with the results from irradiation experiments with m-nitroanisole (section III.A.1) and m-dinitrobenzene (section III.A.3) in liquid NH_3 and in ammonia/methanol. The formation of 3,5-dinitroaniline from 3,5-dinitroanisole may be compared with the reaction of m-nitroanisole leading to m-nitroaniline. The latter reaction proceeds efficiently in liquid ammonia as well as in ammonia/methanol. The formation of 2,4-dinitroaniline from m-dinitrobenzene, however, which does take place in liquid ammonia, is not observed when the solvent is changed to 15% ammonia in methanol. Again, this is consistent with the fact that photoamination of nitrobenzene cannot be accomplished in methanol solution, but proceeds readily in liquid ammonia (section II.A.1). These results are in complete agreement with the observation that the yield of 2-amino-3,5-dinitroanisole is greatly lowered on going from liquid ammonia to ammonia in methanol.

Mechanistic studies of the photohydrolysis of 3,5-dinitroanisoles have been undertaken by Cornelisse and Hav-

inga[94] and by de Gunst.[68,95] The reaction can be sensitized with benzophenone and quenched with fluorenone. Quantum yields have been determined in dependence of the concentration of added 9-fluorenone. In the absence of quencher the quantum yield at 366 nm in acetonitrile/water (1:1) with 0.025 M NaOH is 0.51. With increasing quencher concentrations the quantum yield decreases until at 2.1 $\times$ 10^{-3} M 9-fluorenone a value of 0.30 is reached. Higher quencher concentrations could not be used because too large a fraction of the exciting radiation is absorbed by the quencher.

On plotting the reciprocal of the quantum yield vs. the quencher concentration a straight line was obtained with a slope of 670 l./mol and a value for the intercept of 1.9.[68,95] The quotient of slope and intercept gives the value for $k_q\tau$ = 350. Assuming the quenching to be diffusion controlled, the rate constant for the quenching process, k_q, can be calculated (with the modified Debije equation[96]) to be 1.3 $\times$ 10^{10} l. mol^{-1} sec^{-1}. For the lifetime of the excited state a value of 27 nsec is thus found.

Using conventional flash photolysis[68,94,95] and nanosecond laser photolysis,[68,95] three short-lived species have been observed in the system 3,5-dinitroanisole + hydroxide ion. One species with a relatively long lifetime (τ = 40 msec) and an absorption maximum at about 550 nm, which can also be generated electrochemically, has been identified by means of electron spin resonance as the radical anion of 3,5-dinitroanisole. The radical anion is not an intermediate in the photosubstitution reaction but it can lead, via proton abstraction from the solvent, to photoreduction products. The two other transients have absorption maxima at 412 nm (τ = 500 nsec) and 475 nm (τ = 12 nsec), respectively. During the decay of the 412-nm species the absorption of the radical anion at about 550 nm builds up. There is an isosbestic point at 535 nm. Unfortunately, the absorption maximum of the product, 3,5-dinitrophenolate anion, coincides with the 412-nm absorption. The 412-nm species, which is not found in solutions without nucleophile, is tentatively identified as a complex formed from the excited (triplet) 3,5-dinitroanisole and hydroxide ion. It may decay to ground state dinitroanisole (a process which amounts to quenching of the excited state by OH$^-$), to the radical anion, or to substitution product. The species with maximum absorption at 475 nm (lifetime 12 nsec at [OH$^-$] = 0.04 M) is also present in solutions without nucleophile, be it that in the absence of hydroxide ion its lifetime is longer, 55 nsec. This species, with a lifetime in the same order of magnitude as the quenched excited state (vide supra), is considered to be the triplet state of 3,5-dinitroanisole.

3. Dimethoxynitrobenzenes

van Vliet[25] studied the photoamination of 3,5-dimethoxynitrobenzene in liquid ammonia as well as in methanol containing 15% ammonia. The products are the
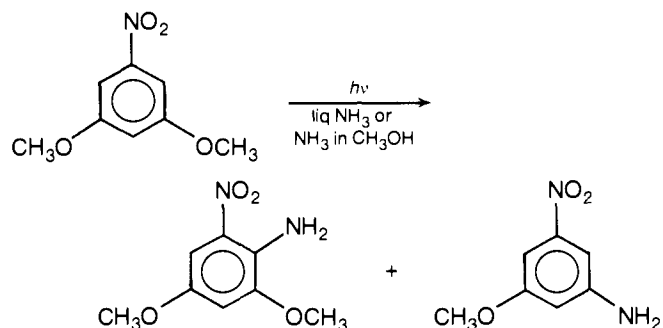
same in the two solvents, substitution taking place ortho and meta to the nitro group. 2,4-Dimethoxy-6-nitroaniline is the major product both in liquid ammonia and in ammonia/methanol. The product ratio in liquid ammonia is approximately 2:1, in ammonia/methanol changing to 10:1. The shift of the product ratio in favor of substitution at the ortho position in going from liquid ammonia to ammonia/methanol has also been observed with m-nitroanisole (section III.A.1).

4-Nitroveratrole undergoes a very efficient and clean photoreaction on irradiation in liquid ammonia or in 15% ammonia in methanol. In both cases the product is 2-methoxy-5-nitroaniline.[25] From the illuminated liquid ammonia solution the product can be obtained in 95% yield (based on the amount of 4-nitroveratrole consumed).
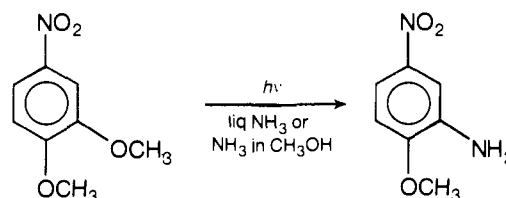
The quantum yield of the formation of 2-methoxy-5-nitroaniline from 4-nitroveratrole in methanol containing 15% ammonia is 0.47 at 313 nm,[25] slightly higher than the corresponding value for the formation of m-nitroanisole (0.42).

The orientation of the photoamination observed in these two dimethoxynitrobenzenes can be rationalized on the basis of meta activation by the nitro group and ortho/para activation by the methoxy substituents. In 4-nitroveratrole the combined effects promote substitution of the methoxy group meta to nitro. The fact that in the photoamination but also in the photoreaction of 4-nitroveratrole with hydroxide and cyanide exclusive substitution of the meta methoxy group occurs thus seems logical.

The photohydrolysis of 4-nitroveratrole has been studied by Stratenus.[97] Irradiation (high-pressure Hg lamp, Pyrex filter) of a solution of 250 mg of 4-nitroveratrole in 2.5 l. of 0.01 N NaOH in water containing 2% tetrahydrofuran affords 170 mg of 2-methoxy-5-nitrophenol, 30 mg of unconverted starting material, and 35 mg of unidentified by-products. No 2-methoxy-4-nitrophenol can be detected in the reaction mixture. The yield of 2-methoxy-5-nitrophenol based on the amount of consumed starting material is 77%. The quantum yield of the photoreaction at 313 nm in water/tetrahydrofuran (9:1) with 0.01 N NaOH was estimated to be 0.09.[97]
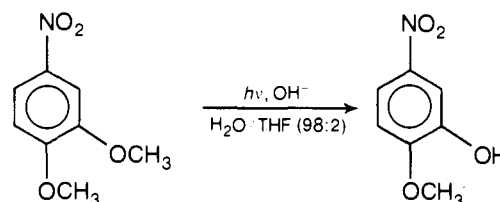
Thermal hydrolysis of 4-nitroveratrole in alkaline medium leads to the formation of 2-methoxy-4-nitrophenol, the para-substitution product.

In laser flash photolysis, de Gunst[68] has observed a short-lived species formed from m-nitroanisole which is probably the reactive triplet state with a lifetime of 40 nsec. The lifetime of the reactive excited state of p-nitroanisole is, as yet, unknown. Thus the fact that the quantum yield of the photohydrolysis is much higher for m- than for p-nitroanisole (section III.A.1) does not necessarily imply that the excited state of m-nitroanisole is

more reactive toward hydroxide ion than that of the para isomer. The phenomenon that the photohydrolysis of 4-nitroveratrole (and also the photoreaction with other nucleophiles) yields almost exclusively the meta-substitution product, whereas in the thermal reaction the attack takes place at the para position, points strongly to a real meta activation by the nitro group in the excited state. One has to bear in mind, however, that if these reactions proceed via an intermediate complex, the decay ratio of this complex is an important factor in determining the rate of product formation. The importance of the partitioning between the various reaction paths the complex can take is currently being investigated by Lodder[98] and will hopefully also become directly measurable by means of ultrafast laser spectroscopy.

The photoreaction of 4-nitroveratrole with methylamine is an example of the synthetic utility of aromatic photosubstitution.[99] Substitution occurs predominantly at the position meta to nitro. The product of the reaction, N-methyl-2-methoxy-5-nitroaniline (or N-methyl-4-nitro-o-anisidine) can only with difficulty be obtained by synthesis along classical lines.
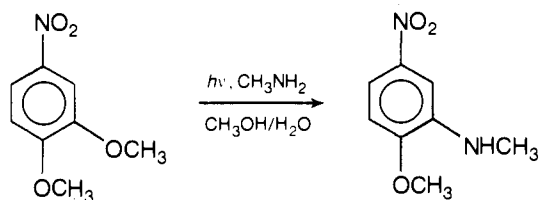
Kronenberg, van der Heyden, and Havinga[100] irradiated 1.473 g of 4-nitroveratrole in 3.8 l. of a 16% solution of methylamine in 30% methanol at room temperature (high-pressure Hg lamp, K_2CrO_4 filter). N-Methyl-2-methoxy-5-nitroaniline was isolated in 64% yield. The second main product was the para-substituted isomer, N-methyl-2-methoxy-4-nitroaniline, the ratio between the two isomers being 9:1.

In the presence of dimethylamine the reaction proceeds in a similar way, but the products are not photostable under the reaction conditions.[100] Probably, somewhat more of the para-substituted isomer is formed than in the case of the reaction with methylamine.

The preferential attack by amines at the meta position in the excited state of 4-nitroveratrole is in accordance with the reaction pattern found in the photohydrolysis. At first sight there seems to be a discrepancy, however, with the results that have been found with the nitroanisoles (section III.A.1). m-Nitroanisole reacts only slowly with methylamine, while photoreaction of the para isomer is quite efficient. As was argued before, the true reactivity of the meta isomer may still be greater than that of the para compound, the measured values being obscured by factors, the magnitude of which is hitherto unknown. Besides, the introduction of a strong electron-donating substituent may cause the stabilization during product formation in p-nitroanisole to be of greater importance than the directing effect of the nitro group.

2,5-Dimethoxynitrobenzene possesses one methoxy group meta with respect to the nitro substituent and the other one at an ortho position. Stratenus[97] found that on thermal reaction in alkaline solution hydrolysis takes place at the ortho position, whereas photochemical substitution occurs exclusively at the meta carbon atom.

Photocyanation has been studied with four of the isomeric dimethoxynitrobenzenes. As expected, the product from the reaction of 4-nitroveratrole with cyanide ion is 2-cyano-4-nitroanisole.[48] The quantum yield of the reaction at 313 nm (with 0.05 M KCN) is 0.08.
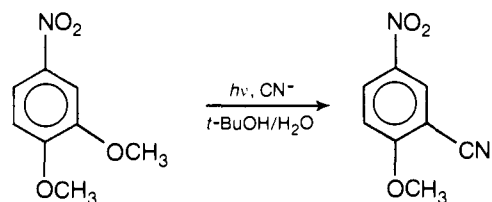
Wiegerink[101] studied the photochemical reactions with cyanide of 3,5-dimethoxy-, 2,5-dimethoxy-, and 2,4-dimethoxynitrobenzene (Scheme V). The results can be fully understood on the basis of meta activation by the nitro group and ortho/para activation by methoxy. As in the photoreaction with ammonia, the major product from 3,5-dimethoxynitrobenzene arises from substitution at the position ortho to the nitro group. The product ratio is approximately 4:1.

SCHEME V
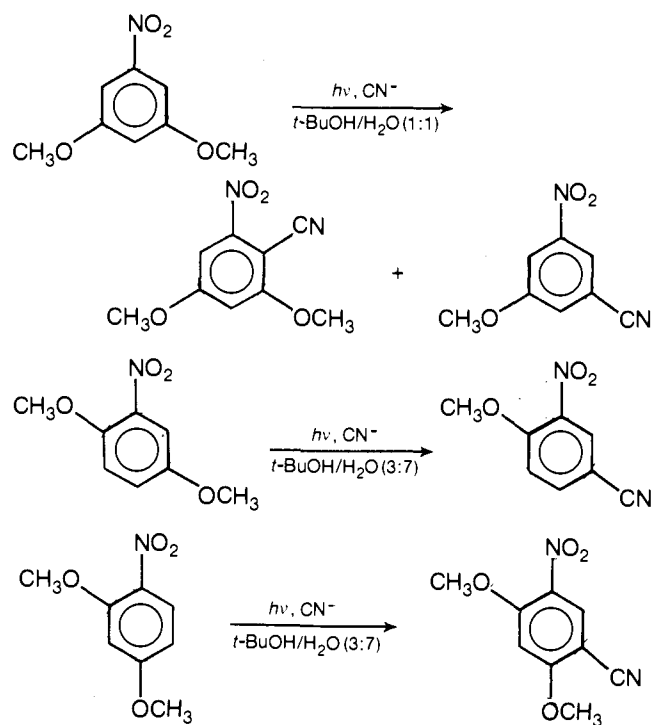
4. Trimethoxybenzenes

1,2,3- and 1,2,4-trimethoxybenzene were irradiated by den Heijer et al.[32] in tert-butyl alcohol/water (1:3) with cyanide ion. The major product from 1,2,3-trimethoxybenzene is 2-cyano-1,3-dimethoxybenzene (48%), while 1,3-dicyano-2,4-dimethoxybenzene is formed in smaller amounts (6%). The products from 1,2,4-trimethoxybenzene are 1-cyano-2,4-dimethoxybenzene (28%) and 1,5-dicyano-2,4-dimethoxybenzene (4%). Thus, substitution occurs consistently at the positions ortho and para to
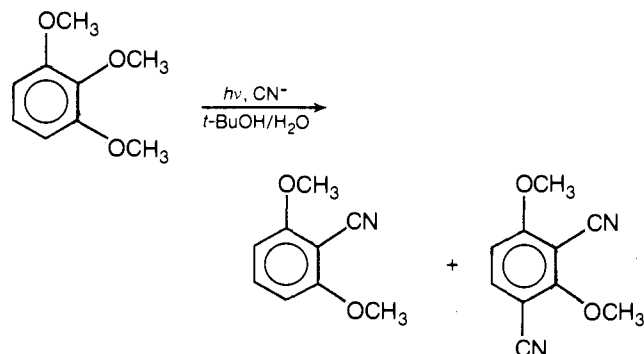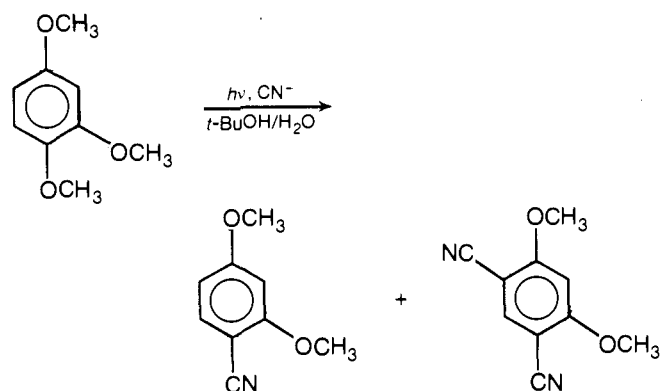
the methoxy groups, in accordance with the orientation found in anisole (section II.A.2) and the dimethoxybenzenes (section III.A.9). The dicyano-substituted compounds are probably formed in secondary reactions.

Lok and Havinga[102] irradiated 1,3,5-trimethoxybenzene (300 mg in 1.5 l. of *tert*-butyl alcohol/water, 1:2) with KCN (0.05 M). After 24 hr (Rayonet photochemical reactor, RPR 208; 2537 Å) 22 mg of 1-cyano-2,4,6-trimethoxybenzene and 160 mg of unreacted starting material were isolated.
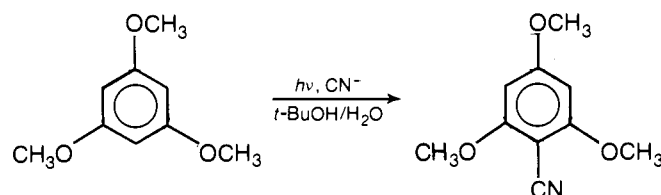
5. Alkyl- and Halogen-Substituted Nitroanisoles

Nijhoff[77] determined the effect of substituents on the quantum yield of the photohydrolysis of *m*-nitroanisole. Table IV lists the values of the quantum yield at 313 nm of several alkyl- and halogen-substituted *m*-nitroanisoles together with the value for *m*-nitroanisole itself. For the sake of comparison, the quantum yields of the dinitroanisoles are also included.

In the 3-substituted compounds (Table IV) there is no steric interaction between the substituent and the nitro group. 3-Chloro-5-nitroanisole and *m*-nitroanisole are photohydrolyzed with the same quantum yield. That of 4-chloro-3-nitroanisole is significantly lower. 3-Bromo- and 3-methyl-5-nitroanisole both have a lower quantum yield than *m*-nitroanisole; the values for 4-bromo- and 4-methyl-3-nitroanisole are considerably smaller. These differences point to steric hindrance of the nitro group by a substituent at an ortho position.

Nijhoff and Havinga[76,77] studied the photohydrolysis in alkaline media of 2-bromo- and 2-chloro-4-nitroanisole. The reactions were performed in mixtures of tetrahydrofuran and water (1:4) with 0.08 N NaOH. Irradiation of 2-bromo-4-nitroanisole (300 mg in 1 l. of the solvent; 2 hr; high-pressure Hg lamp, Pyrex, and K_2CrO_4 filter) yields two products. The major product is 2-methoxy-5-nitrophenol in 45% yield. The second compound has been identified as 2-bromo-4-nitrophenol, yield <10%.
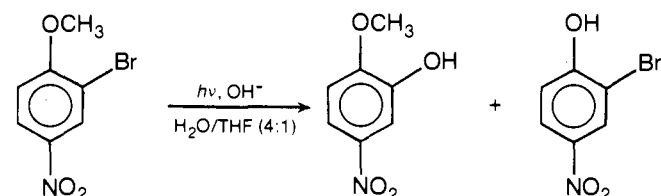

TABLE IV. Quantum Yields at 313 nm of the Photohydrolysis of Substituted *m*-Nitroanisoles in 0.01 M Sodium Phosphate–10% Tetrahydrofuran (pH 11.7)

| R	NO₂	NO₂	NO₂
H	0.31	0.31	0.31
NO₂	0.36	0.54	0.26
Cl	0.11	0.31	0.48
Br	0.01	0.19	0.41
CH₃	0.05	0.17	0.23
t-Bu	0		

The quantum yields at 313 nm for the formation of 2-methoxy-5-nitrophenol and 2-bromo-4-nitrophenol in 0.01 N NaOH (with 1% THF) are 0.09 and 0.03, respectively. In 0.1 N NaOH the corresponding values are 0.24 and 0.07. Straight lines describe the dependence of $1/\phi$ on $1/[OH^-]$.

The results with 2-chloro-4-nitroanisole are very similar to that of the bromo compound. The yield of 2-methoxy-5-nitrophenol is again 45%, but only a very small amount of 2-chloro-4-nitrophenol could be isolated.

The interesting point of this reaction is that the main photoreaction is substitution of a halogen atom meta with respect to the nitro group by hydroxide ion. Photosubstitution of the bromo substituent by OH^- could not be established with *m*-bromonitrobenzene (section III.A.6) and 1-bromo-3,5-dinitrobenzene.[77] o-Bromoanisole is likewise unreactive toward hydroxide ion on irradiation. Apparently, the reactivity of 2-bromo-4-nitroanisole results from combination of meta activation by the nitro group and ortho activation by the methoxy group.

Brasem et al.[78] found that 2-fluoro-4-nitroanisole undergoes an efficient photohydrolysis not only in alkaline medium, but also in neutral and even weakly acidic solutions (Scheme VI). The sole product of the reaction is 2-methoxy-5-nitrophenol by substitution of the fluorine atom. At pH 12 the quantum efficiency at 313 nm (in H_2O with 2% CH_3CN) amounts to 0.50. A value of 0.11 has been found for the quantum yield at pH 7 and pH 3. Apparently, the reactivity of photoexcited 2-fluoro-4-nitroanisole is so high that the water molecule is able to effect a smooth nucleophilic substitution at the ring carbon atom.

SCHEME VI
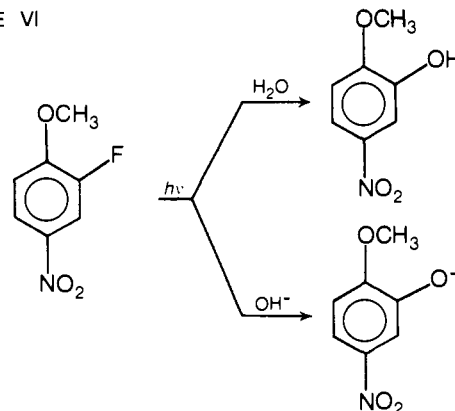
The reaction of 2-fluoro-4-nitroanisole with hydroxide ion can be sensitized with benzophenone and almost completely quenched with sodium sorbate. Other nucleophiles with which photosubstitution of the fluorine atom in this compound can be effected include methoxide ion,

TABLE V. Quantum Yields at 313 nm of the Photohydrolysis of 5-X-3-Nitrophenyl Phosphates at Various pH and Ionic Strengths

	X = H	X = Cl	X = Br	X = CH₃
Buffer, pH 10	0.05	0.15⁵	0.02⁵	0.01
0.010 N NaOH	0.05⁵	0.15⁵	0.02	0.01⁵
0.010 N NaOH + 0.99 M NaCl	0.08⁵	0.15	0.02⁵	0.01⁵
0.10 N NaOH	0.14	0.16	0.05	0.04
0.10 N NaOH + 0.90 M NaCl	0.18⁵	0.16	0.07	0.05⁵
1.00 N NaOH	0.24	0.16	0.16	0.10⁵

ethoxide ion, n-propoxide, and isopropoxide ion.[78] In the absence of light the solutions of 2-fluoro-4-nitroanisole containing the various nucleophiles are completely stable.

3-Chloro-4-nitroanisole on irradiation in 0.1 N NaOH yields almost exclusively 3-chloro-4-nitrophenol by substitution of the methoxy group.[66] No replacement of the halogen atom, which is situated ortho to nitro and meta to methoxy, has been found. The behavior of this compound differs from that of p-nitroanisole. Substitution takes place only at the carbon atom bearing the methoxy substituent, whereas in p-nitroanisole displacement of the nitro group is preponderant (section III.A.1) by a factor of 4. 3-Methyl-4-nitroanisole behaves like the chloro compound in its photoreaction; 3-methyl-4-nitrophenol is the major product.[66]

6. Alkyl- and Halogen-Substituted Nitrophenyl Phosphate

de Jongh and Havinga[57,74] studied the photosolvolysis of m-nitrophenyl phosphate, substituted at the 5 position with chlorine (bromine) as an electron-attracting group and with methyl as a (weakly) electron-donating substituent. Substitution at the 5 position has the advantage in that steric interaction is minimal. The compounds all show photochemical formation of the phenolate in alkaline solution. The quantum yields of the formation of the phenolate at 313 nm at dfferent pH and ionic strengths are presented in Table V.

The quantum yield of the photohydrolysis of 5-chloro-3-nitrophenyl phosphate is pH independent. This, together with the absence of an effect of added sodium chloride, points to a reaction with water only. With the 5-bromo- and 5-methyl-substituted compound the pH dependence of the quantum yield is similar to that of the unsubstituted compound; the participation of hydroxide ion in the solvolysis, however, occurs at higher pH values. The quantum yields of the two compounds are lower than that of m-nitrophenyl phosphate at all pH's used. It is suggested[74] that these results may be indicative of a shortened lifetime of the excited states of the bromo- and methyl-substituted compound.

7. Dichloroanilines

The photoreactions of 2,5- and 2,6-dichloroaniline with nitrite ion have been investigated by El'tsov, Kul'bitskaya,
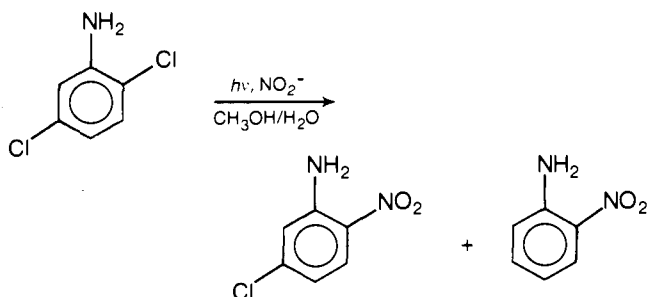

and Frolov.[82] In 2,5-dichloroaniline substitution of the ortho chlorine atom yields 5-chloro-2-nitroaniline (10%), which provides further evidence for the ortho-directing effect of the amino group in nucleophilic photosubstitution (cf. section III.A.10). In addition, dehalogenation occurs and o-nitroaniline is formed (10%).

Irradiation of 2,6-dichloroaniline with nitrite ion in solution affords 2-amino-3-chloronitrobenzene (10%) together with a small amount of o-nitroaniline.[82]

B. Trisubstituted Naphthalenes
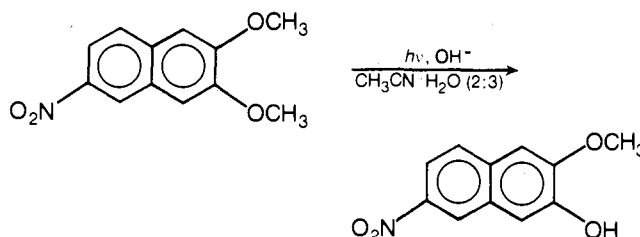
1. Dimethoxynitronaphthalenes

The photochemical hydrolyses of two dimethoxynitronaphthalenes in which the methoxy groups are in one ring and the nitro substituent is in the other were investigated by Beijersbergen van Henegouwen and Havinga.[87,88] Irradiation of 2,3-dimethoxy-5-nitronaphthalene in acetonitrile/water (2:3) with 0.06 N NaOH affords 3-methoxy-5-nitro-2-naphthol in high yield (77%). The
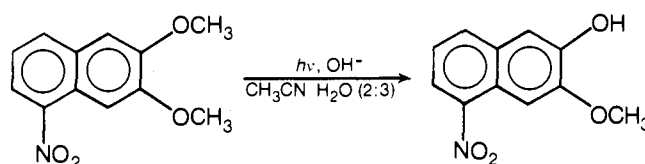
quantum yield of the reaction at 313 nm (measured in dimethyl sulfoxide/water, 7:18, with [OH⁻] = 0.14 N) is 0.10.[87]
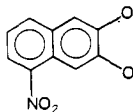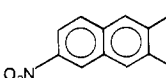
This result demonstrates that in the excited state the nitro group extends its directing influence into the other ring and photosubstitution occurs at the carbon atom which is not the most reactive one in the ground state. The effect is of the same nature as the meta-directing influence of the nitro group in benzene derivatives. Its existence had been expected from the results of the experiments with the methoxynitronaphthalenes (section III.B.3).

In 2,3-dimethoxy-6-nitronaphthalene it is the methoxy group at carbon atom 3 which, according to the meta activation principle, is expected to be the most reactive one in the photochemical reaction. Indeed, 3-methoxy-7-nitro-2-naphthol is the major product (66%) in the photohydrolysis. The quantum yield at 313 nm (0.11) almost equals that of the 5-nitro isomer.

The photohydrolysis of 2,3-dimethoxy-6-nitronaphthalene may be brought about by triplet sensitization with benzophenone. The product, 3-methoxy-7-nitro-2-naphthol, is the same as in the unsensitized reaction. However, quenching of the reaction could not be established;[87] in the presence of sodium sorbate in a concentration of 1.27 × 10⁻² M the quantum yield was not lower than in the experiment without quencher. The same concentration of sorbate lowers the quantum yield of the photohydrolysis of 1,6-dinitronaphthalene to 35%. Fluorenone was an equally inefficient quencher in the case of 2,3-dimethoxy-6-nitronaphthalene as sodium sorbate. It is therefore not unlikely that, although a triplet reaction is

TABLE VI. Calculated Charge Densities on Carbon Atoms 2 and 3 in 2,3-Dimethoxy-5-nitro- and -6-nitronaphthalene in the Ground and the First and Second Excited π,π^* Singlet State[103]

	S_0	S_1	S_2
	+0.001	+0.053	+0.021
	+0.011	+0.036	+0.048
	+0.011	+0.030	+0.121
	0.000	+0.127	−0.002

possible, the photohydrolysis of 2,3-dimethoxy-6-nitro-naphthalene is brought about largely by nucleophilic attack of hydroxide ion on the molecule in an excited, presumably π,π^*, singlet state.
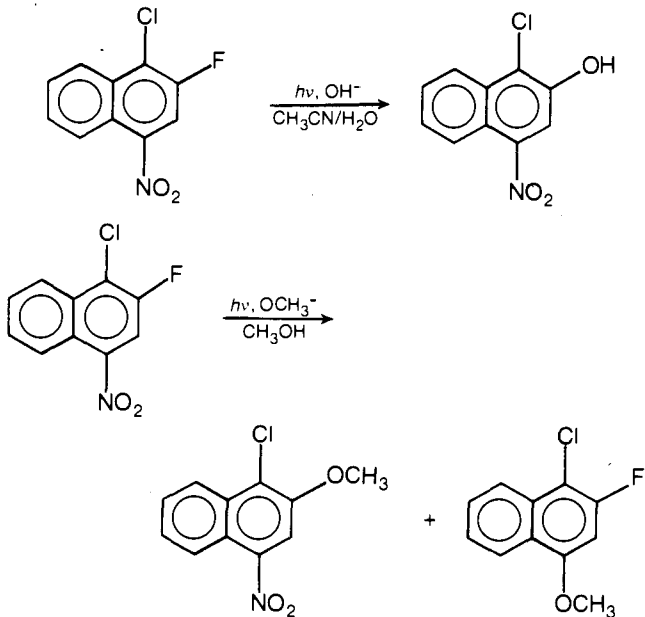
Charge densities on the various atoms of 2,3-di-methoxy-5-nitro- and -6-nitronaphthalene were calculated[103] for the ground state and the first and second excited π,π^* singlet states by means of the Pariser, Parr, Pople method,[104,105] taking into account configuration interaction of all singly excited states. In Table VI the results are shown for the carbon atoms bearing the methoxy substituents. It is easily seen from the table that the calculated charge densities in the first excited π,π^* singlet state are in complete agreement with the experimentally observed "meta"-directing effect of the nitro group in the photochemical reaction.

2. 1-Chloro-2-fluoro-4-nitro- and 2-Fluoro-1-methoxy-4-nitronaphthalene

Lammers[47] studied some photochemical reactions of 1-chloro-2-fluoro-4-nitronaphthalene and 2-fluoro-1-methoxy-4-nitronaphthalene. The results are meaningful because the reaction pattern strongly depends on the type of nucleophile used.

Photohydrolysis of 1-chloro-2-fluoro-4-nitronaphthalene in acetonitrile/water (1:1) containing 0.1 N NaOH affords 1-chloro-2-hydroxy-4-nitronaphthalene (8%, based on consumed starting material) as the only isolable substitution product. Photoreaction with methoxide ion (0.1 M) in methanol gives two products: 1-chloro-2-methoxy-4-nitro-

naphthalene (50%) and 1-chloro-2-fluoro-4-methoxy-naphthalene (12%). Rationalization of these results is based on the meta-activating effect by the nitro group and the high leaving group tendency of fluorine (relative to chlorine). In the thermal reaction, both with hydroxide and with methoxide, chlorine is substituted (Scheme VII).

2-Fluoro-1-methoxy-4-nitronaphthalene has been investigated with three nucleophiles[47,106] (Scheme VIII). The results are as follows: with OH^- (0.1 N in CH_3CN/H_2O, 1:1), substitution of methoxy yielding 2-fluoro-4-nitro-naphthol (25%); with OCH_3^- (0.04 N KOH in CH_3OH/H_2O, 2:1), substitution of fluorine yielding 1,2-dimethoxy-4-nitronaphthalene (90%); with CN^- (0.1 M in CH_3CN/H_2O, 4:1), substitution of nitro yielding 1-cyano-3-fluoro-4-methoxynaphthalene (30%).

SCHEME VIII
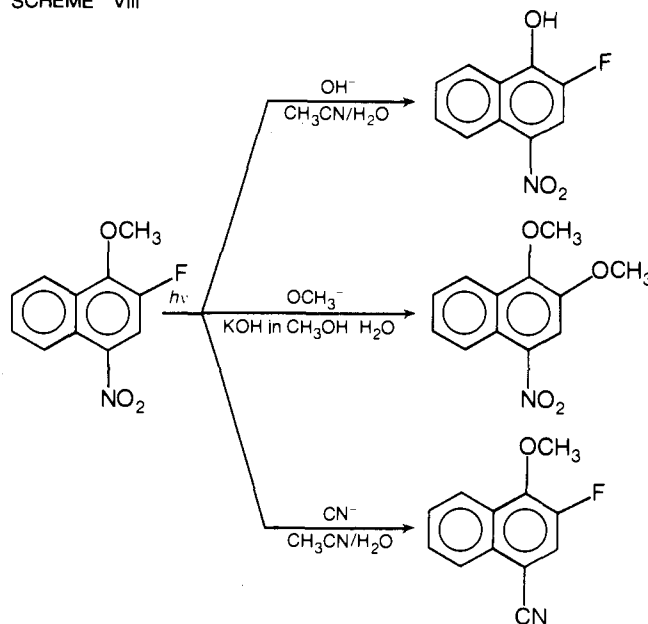
Photomethoxylation can also be performed in methanol with methoxide ion. In this medium, however, a very rapid secondary reaction (displacement of the nitro group) takes place. The primary product is obtained on irradiation in aqueous methanol containing KOH. Of course, photosubstitution of the methoxy group by methoxide cannot be detected without using isotopic labeling. With cyanide, there is also a secondary reaction which in this case leads to substitution of fluorine. It seems that all the orientation rules for nucleophilic aromatic photosubstitution mentioned in the previous sections are operative in the case of 2-fluoro-1-methoxy-4-nitronaphthalene.

The presently known rules can be briefly formulated as follows (cf. ref 71a): meta activation by the nitro group; ortho/para activation by the methoxy group (and other electron donors); high reactivity at the α position in naphthalene (and at comparable positions in other polycyclic aromatics); stabilization during product formation. Additional factors such as relative leaving group tendencies and solvent effects should not be disregarded.

In systems such as 2-fluoro-1-methoxy-4-nitronaphthalene with various nucleophiles some of the effects may counteract. The outcome of the reaction then depends upon their relative magnitudes. Further detailed investigations on complicated systems as the naphthalene derivatives mentioned in this section will enable us to gain more insight into this fascinating field.

SCHEME VII

VI. Heterocyclic Aromatic Compounds

Photosubstitution reactions and photoadditions of N-heterocyclic aromatic six-membered ring compounds have been thoroughly reviewed by Lablache-Combier.[107] Only some of the newer results in this field will be mentioned, with special emphasis on heterolytic photosubstitution reactions.

A. Pyridine

From a 1% solution of pyridine in cyclohexane after 24 hr of irradiation under nitrogen (Rayonet photochemical reactor, 2537 Å) bicyclohexyl, 2- and 4-cyclohexylpyridine, and 2,5-dicyclohexylpyridine were isolated by VPC in the ratio 20:10:10:1.[107,108] Only 2% of the pyridine had been converted.
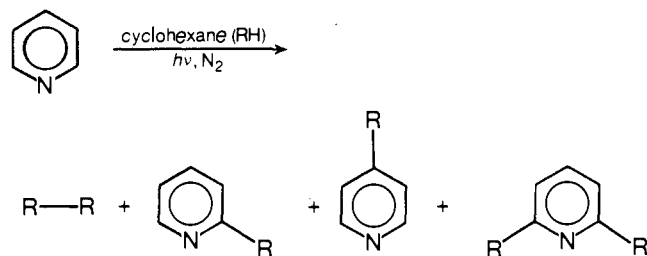

The reaction proceeds via the pyridinyl radical formed from the excited pyridine through abstraction of hydrogen from the solvent:
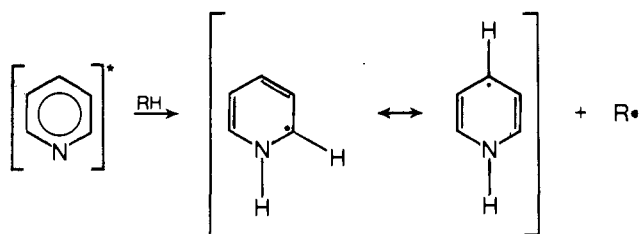
In the solvent cage the radicals combine to substituted dihydro compounds which on rearomatization yield the 2- and 4-substituted pyridine. A large fraction ($^2/_3$) of the substituted dihydro compounds is believed to rearomatize by loss of the substituent group as a radical, yielding pyridine and cyclohexyl radicals, from which radicals the dimer is thought to be formed in nitrogen atmosphere. In the presence of oxygen the yield of bicyclohexyl is reduced to one-tenth and cyclohexanone and cyclohexanol are formed, the yield of substituted compounds being reduced by only 20%.

Photoalkylation of pyridine with methanol has been described by Travecedo and Stenberg.[109] Irradiation of 0.1 M solutions of pyridine in HCl-methanol under nitrogen (Rayonet photochemical reactor, 2537 Å) produced 2- and 4-methylpyridine, 1-(2-pyridyl)-2-(4-pyridyl)ethane, and 1,2-di(4-pyridyl)ethane. The dipyridylethanes were obtained in yields of 1–3%, while the yields of 2- and 4-methylpyridine varied between 2 and 10%, the yield of the 4-methyl derivative being higher

The reactions are thought to proceed via the following intermediates:
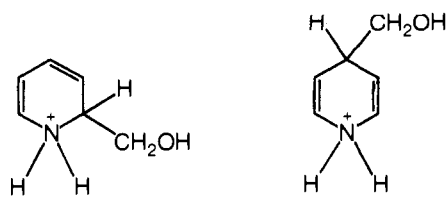
The dipyridylethanes arise in a photochemical reaction from the corresponding hydroxymethylpyridine compounds and not from the methylpyridines.

Photoreactions of nicotinic acid and other pyridinecarboxylic acids have been studied by Sugimori and his coworkers.[110-112] In acidic aqueous and alcohol solutions (pH 0–1) nicotinic acid is present in the pyridinium form
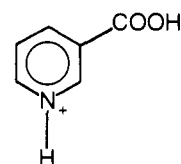
Irradiation in water gives 2-hydroxy-3-pyridinecarboxylic acid (40%); in acidic ethanol 4-ethyl-3-pyridinecarboxylic acid is produced (85%) (Scheme IX).

SCHEME IX
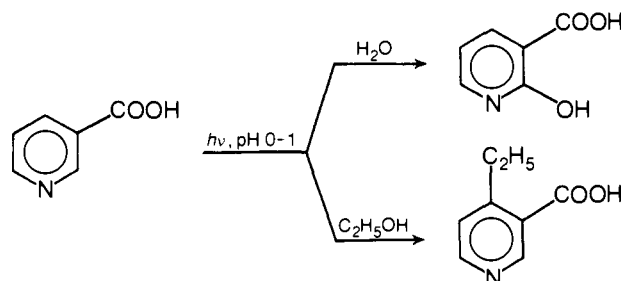
In alkaline aqueous solution (pH 13–14) the 3-pyridinecarboxylate ion appears to be photostable, whereas in alkaline ethanol rapid decarboxylation takes place yielding pyridine in 50% yield. These reactions cannot be quenched by piperylene.

In acidic aqueous solution 2-pyridinecarboxylic acid gives 6-hydroxy-2-pyridinecarboxylic acid (30%).[112] In acidic alcohol photoalkoxylation takes place; 6-ethoxy-2-pyridinecarboxylic acid is the main product, photoethylation being the minor reaction (Scheme X).

SCHEME X
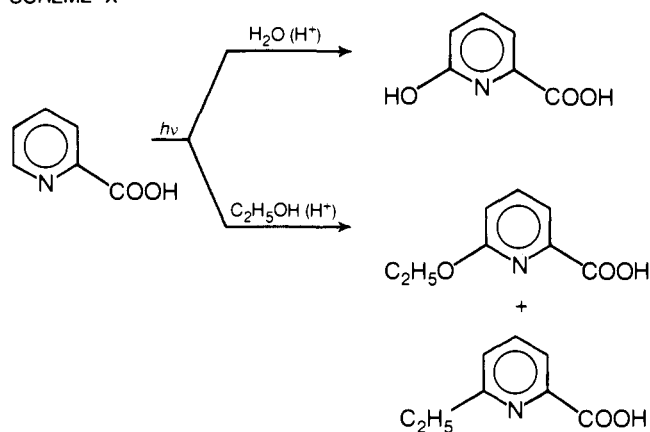
Photoalkoxylation was observed in acidic methanol as well as in acidic ethanol solution, but not in acidic 2-propanol solution. The reaction is thought to proceed via a complex, presumably an excimer.

Photoreactions of halopyridines have been investigated by van der Stegen.[113] 2-Chloro-, 2-bromo-, and 2-iodopy-

X = Cl, Br, I
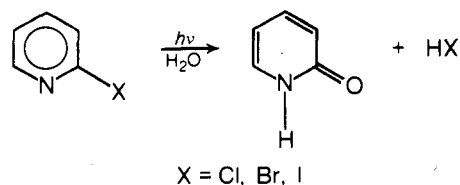
ridine undergo photohydrolysis in water to 2-pyridone, whereas 2-fluoropyridine does not show this reaction.

At pH 7 the quantum yields (265 nm) of the formation of 2-pyridone from the three 2-halopyridines are: Cl, 0.07; Br, 0.31; I, 0.15. At pH 13 the values are: Cl, 0.07; Br, 0.32; I, 0.14. With 2-bromopyridine the quantum yield was also measured at pH 4; ϕ = 0.29. The quantum yields of disappearance of the pyridine derivatives were found to be higher than those of 2-pyridone formation by a factor of about 1.5. They are independent of the pH of the medium except in acidic solutions where pyridine is largely present in the protonated form. Apparently, the excited pyridine derivative reacts with water, even at very high hydroxyl ion concentrations. If the reaction would stem from a triplet state, the pH independence of the quantum yield might be explained by assuming that the molecule in this state is so reactive that even in neutral solution every excited molecule reacts instantly with water. The intersystem crossing quantum efficiency then would be the limiting factor and use of the more powerful nucleophile OH$^-$ would not increase the quantum yield. However, for pyridine the quantum yield of triplet formation is 0.36,[114] and the values for the halo-substituted compounds, especially for bromo- and iodopyridine, will almost certainly be higher. Yet the quantum yields of 2-pyridone formation never exceed 0.32. Therefore such rationale for the constancy of the quantum yield is considered less attractive.

Homolytic cleavage of the carbon–halogen bond is not likely an essential step in the photohydrolysis reaction since 2-iodopyridine has a lower quantum yield than 2-bromopyridine and 3-iodopyridine (see below) does not even show the reaction.

To account for the observed facts a reaction sequence in which the primary step upon excitation consists of heterolytic cleavage of the carbon–halogen bond has been put forward.[113a] In such an AS_N1 type reaction formation of a positive ion in a dissociative step would be quantum yield determining.

Of several 3-substituted halogenopyridines investigated only 3-bromopyridine has been found to undergo photohydrolysis. The quantum yield of 3-hydroxypyridine formation at 265 nm has a constant value of 0.14 in the pH region 6–14. At pH 4 ϕ =0.12, while at lower pH values the quantum yield drops steadily until at pH 2.1 a value of zero is reached. The disappearance quantum yield of 3-bromopyridine almost equals that of product formation. 3-Chloro-, 3-cyano-, 3-iodo- and 3-methoxypyridine do not yield 3-hydroxypyridine upon irradiation in 0.1 N NaOH in water.

4-Bromopyridine on irradiation in water as well as in 0.1 N aqueous NaOH yields 4-pyridone. At pH 7 and at pH 13 the quantum yield is the same: ϕ = 0.2.

In methanol 2-bromopyridine yields 2-methoxypyridine
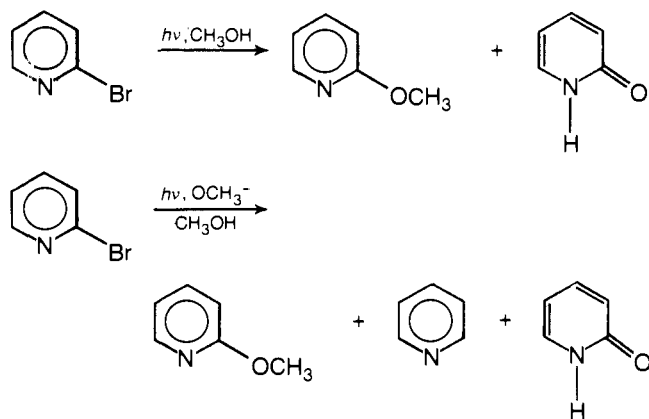
and 2-pyridone as photoproducts. In the presence of methoxide ion (0.1 M) 2-methoxypyridine, pyridine, and 2-pyridone were formed (ratio 10:4:3).

Irradiation of 2-bromopyridine in n-hexane and immediate extraction with water yields 2-pyridone, while similar treatment in deaerated n-hexane affords pyridine. Irradiation of 2-bromopyridine in n-hexane at higher concentrations yields a product which is thought to be a dimer. In n-hexane in the presence of furan 2-bromopyridine forms 2-(2′-furyl)pyridine as a photoproduct.

From irradiation of 3-bromopyridine in n-hexane and extraction with water pyridine is isolated as the main product.

Kuz'min and coworkers[37] irradiated 2- and 3-bromopyridine in various solvents and obtained results which are very similar to those reported by van der Stegen.[113a] They studied the effect of the presence of oxygen and heavy anions on the quantum yield of the photohydrolysis and concluded that the reaction occurs through the singlet excited state. In the presence of oxygen, the quantum yield of hydrolysis is unaffected, though side products are formed. The presence of chloride and bromide ions causes a decrease in the quantum yield; the relative hydrolysis yield depends linearly on the anion concentration. Addition of fluoride does not affect the quantum yield for hydrolysis which rules out the possibility of an increase in the ionic strength being responsible for the change in the quantum yield. The effect of chloride and bromide ions is ascribed to enhanced intersystem crossing.[37]

A nucleophilic photosubstitution reaction in a substituted pyridine N-oxide was found by Johnson and Rees.[115,116] Irradiation of 4-nitropyridine N-oxide with piperidine in ethanol at 334 nm causes a reaction, the product of which, 4-piperidinopyridine N-oxide, is the same as for the reaction in the absence of light. A bimolecular reaction between piperidine and excited 4-nitropyridine N-oxide is proposed.
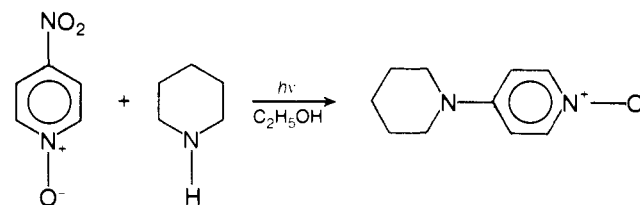
B. Quinoline and Isoquinoline

In acidic alcohol solution quinoline undergoes photoalkylation.[117] The products obtained from irradiation (high-pressure Hg lamp) of a N$_2$-flushed solution (0.001 M) of quinoline in 95% ethanol acidified with HCl are 2-ethylquinoline (7%) and 4-ethylquinoline (10%). The protonated quinoline in its excited state abstracts a hydrogen atom from the α position of ethanol, whereby hydrogen becomes attached to nitrogen. Radical combination may then take place at position 2 or 4 of the radical derived from quinoline. Loss of a water molecule and rearomatization yields the alkylated products. The quantum yield at 313 nm is 0.02.[118]

Yields of alkylated products are higher in the case of 8-methylquinoline: 2-ethyl-8-methylquinoline (10%) and 4-ethyl-8-methylquinoline (30%). Also, 6% of a dimer was isolated: 8-methyl-4-(3-quinolinyl)-8-methyl-1,4-dihydroquinoline.[118]

In acidified 2-propanol solutions quinoline does not yield photoalkylation products; instead, reduced quinoline dimers are formed in low yield.

From isoquinoline, irradiated in HCl-acidified ethanol, a 22% yield of 1-ethylquinoline was isolated. As with quino-

line, no photoalkylation could be found in acidified 2-propanol.[117,118]

Irradiation of quinoline in 95% ethanol without acid yields 2-(1-hydroxyethyl)quinoline (20%), together with a trace of 2-(1-hydroxyethyl)-1,2,3,4-tetrahydroquinoline (Scheme XI). From 8-methylquinoline a 15% yield of the 2-substituted quinoline derivative is found, whereas in this case the yield of the corresponding 1,2,3,4-tetrahydroquinoline is quite high (20%).[118] At the moment there does not seem to be a satisfactory explanation for the different reactivity at position 4 of quinoline in acidic and neutral alcohol solution.

SCHEME XI

R = H, CH₃
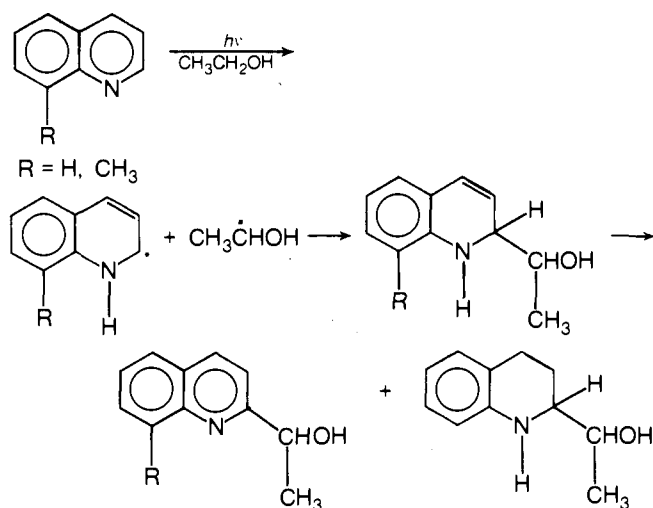
Quinoline and isoquinoline can be alkylated by irradiation of their solutions (10⁻² M) in benzene containing a carboxylic acid (10⁻² M) with a high-pressure Hg lamp in N₂ atmosphere.[119,120] As in the reactions with alcohol, photoalkylation of quinoline takes place at positions 2 and 4, whereas isoquinoline is alkylated at the 1-position only (Scheme XII).

SCHEME XII
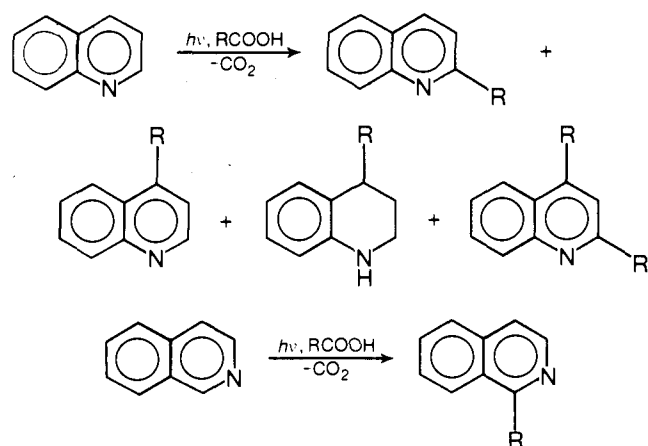
With quinoline the acids RCOOH, in which R = Me, Et, i-Pr, i-Bu, sec-Bu, and t-Bu, have been used. The yields of 2-alkylquinoline vary between 20 and 40% depending on the acid used; the highest yield is found with R = t-Bu. Only with acetic acid is an appreciable yield (10%) of 4-alkylquinoline found. 4-Alkyl-1,2,3,4-tetrahydroquinolines are formed in yields varying between 16 and 25%, except in the case of pivalic acid where no reduced quinoline has been found. The yields of 2,4-dialkylquinolines never exceed 6%.

Acetic acid, propionic acid, and isobutyric acid have been applied for the photoalkylation of isoquinoline. With acetic acid the yield of 1-methylisoquinoline is 10% while with the other two acids yields of 1-alkylquinoline are 20%.

The photoalkylations with carboxylic acid are thought to proceed via dihydro derivatives of quinoline and isoquinoline formed in an ionic process.[120] The excited quinoline captures a proton from the carboxylic acid, producing an excited complex. Decarboxylation yields an ion pair, whose combination yields a reductive alkylation product.

Castellano and Lablache-Combier[121] have investigated the photoreactions of quinoline and isoquinoline with cyclohexane and diethyl ether. Irradiation of a 1% solution of quinoline in cyclohexane (low-pressure Hg lamp) yields 2-cyclohexylquinoline (15%) and 4-cyclohexylquinoline (5%). In ether, 2-(1-ethoxyethyl)quinoline (20%) and 4-(1-ethoxyethyl)quinoline (10%) are formed. From isoquinoline in ether only 1-(1-ethoxyethyl)isoquinoline (5%) is obtained as a photoproduct. For these photoalkylations a radical mechanism is proposed[107,121,122] (see Scheme XIII). Probably, unstable dihydro derivatives are intermediates in the reaction, as in the photoalkylations in acid media. In contradistinction to the reaction of pyridine with cyclohexane, no bicyclohexyl has been found in the case of quinoline. This may be caused by rapid combination of the radicals, followed by rearomatization leading to cyclohexylquinolines. This hypothesis finds support in the observation that the yields of the reactions with quinoline are tenfold higher than those of pyridine.

SCHEME XIII
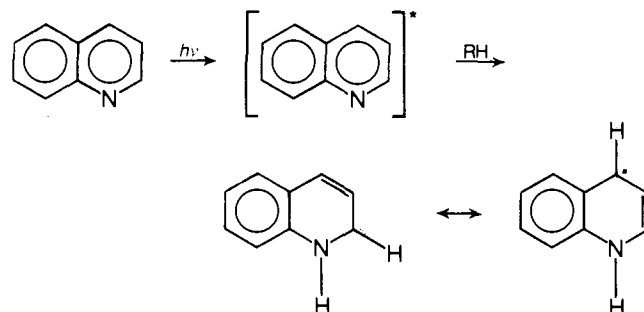
Hata et al.[123,124] have studied photoinduced substitution reactions of 2-cyanoquinoline. Irradiation of 2 × 10⁻² M solutions in 350 ml of an alcohol (ethanol, 1-propanol, 2-propanol, tert-butyl alcohol) with light of λ >300 nm in an oxygen atmosphere at room temperature results in replacement of the cyano group by a hydroxyalkyl group (Scheme XIV). With ethanol and 1- and 2-propanol the yield of hydroxyalkylated product is about 40%, with tert-butyl alcohol 14%. The same reaction, though with different yields, takes place in alcohol solutions acidified with HCl. These results differ from those with quinoline, in which photoalkylation is found in acidic alcohol solutions.[117,118]

Irradiation of 2-cyanoquinoline in the alcoholic solvent (not in tert-butyl alcohol) in an atmosphere of nitrogen gave an unidentified substance in addition to the photosubstitution product. There are indications[124] that the new compound is a derivative of a triazapentaphene. The yields of hydroxyalkylated products (around 30%) were lower than under O₂, the yields of the new compound varying between 17 and 25%. The nature of the unknown product does not depend on the alcohol used, but it is found neither in tert-butyl alcohol nor in acidified alcohol solution upon irradiation. The photosubstitution reaction cannot be quenched by piperylene, while the formation of

SCHEME XIV
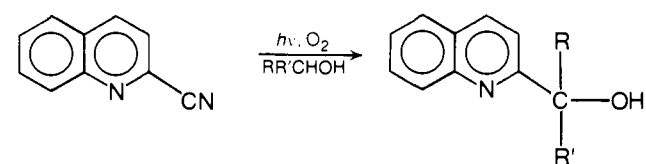
a, R=CH$_3$; R'=H
b, R=C$_2$H$_5$; R'=H
c, R=CH$_3$; R'=CH$_3$
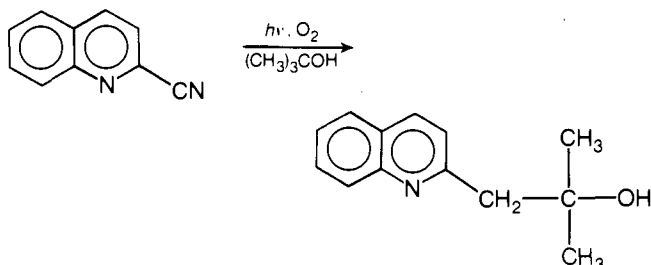
the unknown compound decreases with increasing piperylene concentration. Piperylene is able to quench the phosphorescence of 2-cyanoquinoline completely. These findings, together with the observed oxygen effect, point to a singlet excited state as the reactive intermediate in the photosubstitution.

Irradiation of 2-cyanoquinoline in diethyl ether also produces a photosubstitution product.[124] In an oxygen

atmosphere the yield is 32%, under nitrogen 21%, without any evidence of the formation of a triazapentaphene-like substance in nitrogen atmosphere. A satisfactory yield (59%) of the photosubstitution product is obtained upon irradiation in a HCl-saturated solution.
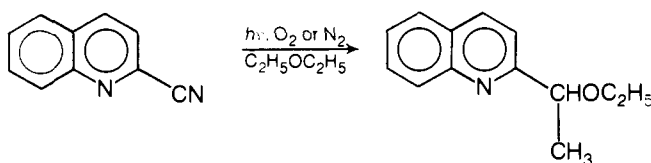
Irradiation of 2-cyanoquinoline dissolved in benzene containing a carboxylic acid (acetic acid, propionic acid, butyric acid, isobutyric acid, or trimethylacetic acid) under nitrogen or oxygen produces 2-alkyl- and 2-cyano-4-alkylquinolines. This photoalkylation is not quenched by the addition of piperylene.[124]

Letsinger[49] has irradiated 6-methoxyquinoline in aqueous solution containing cyanide or borohydride ion. With cyanide a rapid photosubstitution takes place (ϕ = 0.32) leading to 5-cyano-6-methoxyquinoline in high yield (92%). The photoreaction with borohydride gives reduction products.
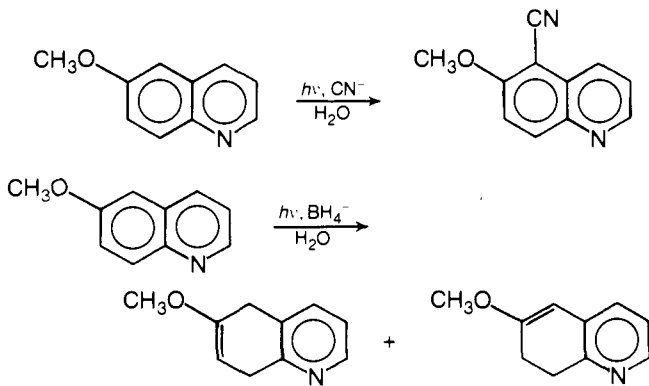

C. Quinoxaline

On irradiation in diethyl ether, quinoxaline undergoes substitution at position 2 yielding 2-ethylquinoxaline and 2-(1-ethoxyethyl)quinoxaline in the ratio 1:10.[125] The reaction proceeds via hydrogen abstraction from ether by the excited quinoxaline.
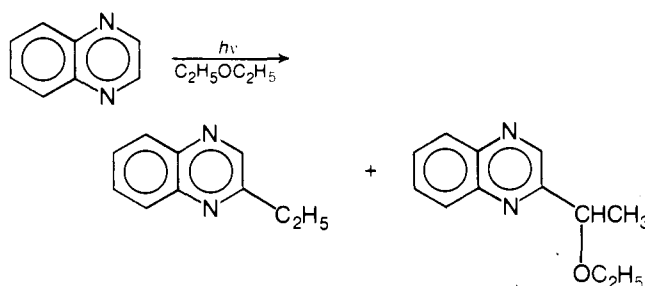
D. Thiophene

Groen and Havinga[126] investigated photosubstitution reactions of 2-nitro- and 2-bromo-5-nitrothiophene with various nucleophiles. Irradiation of 2-nitrothiophene in water (500 mg in 1200 ml) containing 0.1 M KCN with Pyrex-filtered light from a high-pressure Hg lamp (TQ 81) for 60 min yields 2-cyanothiophene in 56% yield.
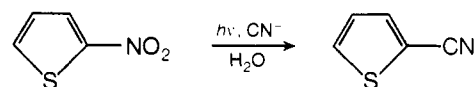
Other nucleophiles are also effective in photochemical substitution of the nitro group; reaction with sodium methoxide (0.1 M) in methanol affords 2-methoxythiophene (41%) and reaction with potassium cyanate (0.05 M) in methanol yields N-(2-thienyl)carbamic acid methyl ester (20%).

At sufficiently high cyanide concentration (0.01 M) the quantum yield (313 nm) of formation of 2-cyanothiophene reaches a maximum value of 0.39, which is equal to the disappearance quantum yield of 2-nitrothiophene. Linearity between the reciprocals of the quantum yield and the cyanide concentration indicates the occurrence of a bimolecular reaction between excited 2-nitrothiophene and cyanide ion. Sensitization of the reaction could be effected with acetone (2.5 × 10^{-2} M), while sodium sorbate was found to act as a quencher. These results show that the reaction proceeds mainly, if not entirely, via a triplet state. The authors[126] propose a reaction scheme in which the triplet state interacts with cyanide ion to form a complex which may dissociate into the cyano-substituted compound and nitrite ion or into the starting materials.

Assuming the quenching to be diffusion controlled, it is concluded from the dependence of the quantum yield on the cyanide concentration and from the Stern–Volmer plot obtained by the quenching experiments that the rate constant for reaction of the excited species with cyanide ion is 7.8 × 10^9 l. mol^{-1} sec^{-1} and for deactivation of the excited species by other pathways 2.2 × 10^6 sec^{-1}. Hence, the triplet lifetime of 2-nitrothiophene is 4.5 × 10^{-7} sec in water and 1.2 × 10^{-8} sec in a 10^{-2} M KCN solution.

Reaction of 2-nitrothiophene with methoxide ion has a considerably lower quantum yield (0.16 at 313 nm). This may be caused by an unfavorable decay ratio of the intermediate complex.

Introduction of a bromine atom into the 2-nitrothiophene molecule results in a considerable increase in the quantum yield of the reaction with cyanide ion: from 0.39 for 2-nitrothiophene to 0.59 for 2-bromo-5-nitrothiophene.

E. Furan

Nucleophilic photosubstitution in 2-nitrofuran was studied by Groen and Havinga.[126] Irradiation of 2-nitrofuran in water (500 mg in 1 l.) containing 0.05 M KCN with Pyrex-filtered light from a high-pressure Hg lamp (TQ 81) for 25 min produced 2-cyanofuran in 54% yield.
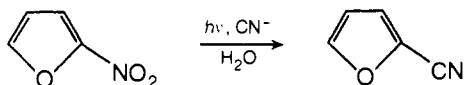
Interestingly, the quantum yield of disappearance of 2-nitrofuran (0.51 at 313 nm) was found to be independent of the cyanide concentration. On the other hand, the quantum yield of formation of the nitrile increases with increasing CN^- concentration, approaching the value of 0.51 at sufficiently high concentration (ca. 1 M). This suggests that at low cyanide concentrations water acts as a nucleophile according to:
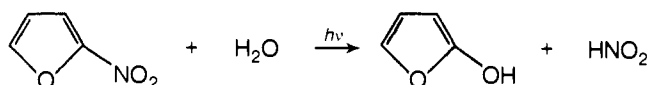
The formation of 2-hydroxyfuran (or rather its stable tautomer $\Delta^{\alpha,\beta}$-butenolide) and of nitrite ion upon irradiation of 2-nitrofuran in water could be demonstrated.

Sensitization of the reaction with cyanide ion could be accomplished with acetone (5 × 10⁻² M), while quenching was found to occur in the presence of sodium sorbate. From the quenching data the triplet lifetime of 2-nitrofuran in pure water is calculated to be 3.0 × 10⁻⁹ sec, more than 100 times shorter than that of 2-nitrothiophene. In 0.1 M KCN solution the yield of 2-cyanofuran is 77%, indicating that under these conditions reaction with CN^- is over three times faster than that with water. Yet, it was found that the presence of this amount of cyanide hardly affects the triplet lifetime.
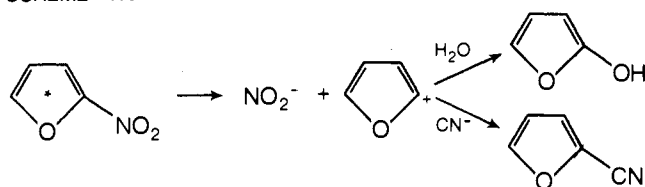
These results are interpreted to imply that the reactive species undergoing substitution is not the molecule in its triplet state but a species formed from that state in a dissociative process as in an S$_N$1 type reaction (Scheme XV).

SCHEME XV

A similar mechanism has been proposed by van der Stegen[113a] for the photohydrolysis of bromopyridines (section V.A). It may also be operative in the classical examples of photohydrolysis of m-nitrophenyl sulfate[57,73] (section III.A.2) and 5-chloro-3-nitrophenyl phosphate[57,74] (section IV.A.6) where photosubstitution by water occurs and no increase in the quantum yield is observed in the presence of even relatively high concentrations of hydroxide ion.

VII. Concluding Discussion

A. Nature of the Reactions Described in This Review

The authors have offered a review of reactions that in their overall stoichiometry can be classified as nucleophilic aromatic photosubstitutions. First of all one may wonder why the rapidly growing list of these nucleophilic

substitutions is so much larger than that of the electrophilic aromatic photosubstitutions. Of these only a few well-studied examples have been recorded to date (e.g., light-induced exchange of hydrogen isotopes in acidic media,[12] photodeboronation[127]). Although this may partly be accidental our experience teaches firstly that electrophilic reagents often are efficient quenchers of excited aromatic molecules and secondly that media containing a concentration of electrophile high enough to react efficiently with very short-lived species are not easily found. In these respects the situation with nucleophilic reaction partners is considerably easier.

Next, it should be pointed out that in this review we have brought together a variety of reactions, that—although in a formal sense classifiable as nucleophilic aromatic photosubstitutions—may follow different pathways and show different mechanisms when looked at in more detail. We feel safe to assume that the oldest representatives (photohydrolysis and photoamination of aromatic ethers and esters) as well as a large number of the more recent examples are essentially of a heterolytic nature indeed. Closely related to these "genuine" heterolytic photosubstitutions are those processes where in a first step a relatively stable addition product is formed that in a second stage may aromatize to substitution product. Then there is a class of photoreactions leading to substitution products that in the primary step are of a homolytic nature, proceeding through radical pairs or free radicals as intermediates.

The authors considered it appropriate to plan this review primarily as a descriptive one with emphasis on experimental results, particularly as it probably covers reactions of differing nature. On the other hand, we feel that we would not do justice to the subject and not render the expected service to the reader if we would not add a few summarizing remarks on mechanistic aspects. Understandably we prefer to do so with regard to those aromatic photosubstitutions that we believe to represent genuine nucleophilic displacements at the ring carbon atom (cf. Cornelisse, de Gunst, and Havinga[71b]).

B. Characteristics of Nucleophilic Aromatic Photosubstitutions

(a) Whereas some nucleophilic photosubstitutions seem to start from the lowest $\pi \rightarrow \pi^*$ singlet of the aromatic partners, most reactions of this type have been found (sensitization, quenching, laser photolysis) to be initiated by an encounter between the nucleophile and the aromate in its lowest $\pi \rightarrow \pi^*$ triplet. From a practical point of view this implies that, although generally the reactions can be performed in a variety of solvents (water, tert-butyl alcohol, acetonitrile, etc.), one should see to it that in the medium used the lowest triplet has $\pi \rightarrow \pi^*$ character.

(b) The primary chemical reaction step often seems to consist of complex formation between the excited aromate and the nucleophilic partner (exciplex, excited π or σ complex?; lifetime ~10⁻⁷ sec). This complex may dissociate into starting compounds back again, it may transform into the products of a substitution reaction, or it may form the aromatic radical anion. The formation of substitution product is completed within a period of 10⁻⁶ sec or less (photoflash). The radical anion (lifetime 10⁻³–1 sec, depending on its structure, the medium, and the conditions) cannot be intermediate in the route to substitution product; it may upon protonation transform into reduction products (azo compounds).

(c) The rate constants for the bimolecular reaction of the (triplet) excited aromatic compound and the nucleo-

phile are $\frac{1}{3}$–$\frac{1}{100}$th that of quenching by triplet quenchers. Assuming the latter to be approximately diffusion controlled, this leads to values of 10^{-10}–10^{-8} (l. mol^{-1} sec^{-1}) for the rate constants of the photosubstitution. The lifetimes of the excited triplets studied thus far vary from 10^{-7} to 10^{-9} sec (in the absence of nucleophile and quencher).

C. Orientation Rules

From the experimental data could be deduced some four "orientation rules" that play a major role in determining the position where the new substituent will become attached as a result of nucleophilic photosubstitution: (a) meta orientation with regard to a nitro group (and possibly other electron-attracting groups like –C≡N, –C(=O)R); (b) ortho/para orientation with regard to alkoxy groups (and probably other electron-donating groups: –N<, alkyl); (c) "α-reactivity" in bi- and tricyclic aromatics (i.e., position 1 in naphthalenes and azulenes, 9 in phenanthrene, 2 and 4 in biphenyls, etc.); (d) merging (resonance) stabilization during product formation. We present in Scheme XVI a few reactions to exemplify these four orientation rules.

D. Interpretation

The characteristics of the bimolecular nucleophilic aromatic photosubstitutions as summarized in sections VII.B and VII.C (Orientation Rules), in particular, can be tentatively rationalized on the basis of a few major effects.

1. The meta orientation by a nitro substituent, the para orientation by methoxy, as well as the orientation in azulenes (preference for position 1 and 3) may be correlated with the charge distribution in the $\pi \rightarrow \pi^*$ excited aromatic compound. The positions preferentially attacked are exactly those that according to Pariser, Parr, Pople calculations bear a relatively positive charge in the first $\pi \rightarrow \pi^*$ singlet (and, in the few cases where calculations were made, also in the lowest $\pi \rightarrow \pi^*$ triplet). At the
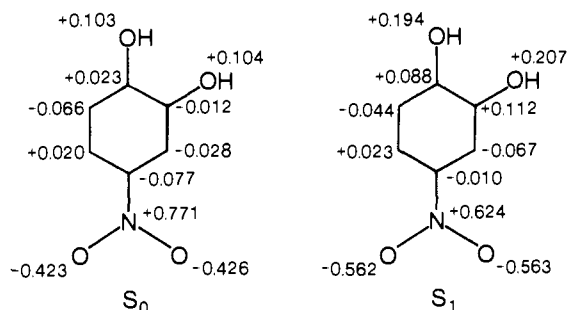
moment there is not much sense in speculation about the main effect of the charge distribution, whether it is an attraction during the diffusion-controlled approach of the reaction partners promoting encounters of the nucleophile and the positive sites of the excited aromatic molecule or whether it is mainly operative in the encounter complex, the nucleophile still having the possibility of choosing the most favorable position for reaction. Probably both effects cover part of the overall influence.

The α-reactivity in polycyclic aromatic compounds (naphthalenes, etc.) might be correlated in a similar way, e.g., with calculated low free valency numbers. It may also have its basis in the effect discussed in the next section.

2. The second major effect determining the position of nucleophilic aromatic photosubstitution has been described in rule d: merging (resonance) stabilization during product formation. It is not clear as yet whether this effect

SCHEME XVI
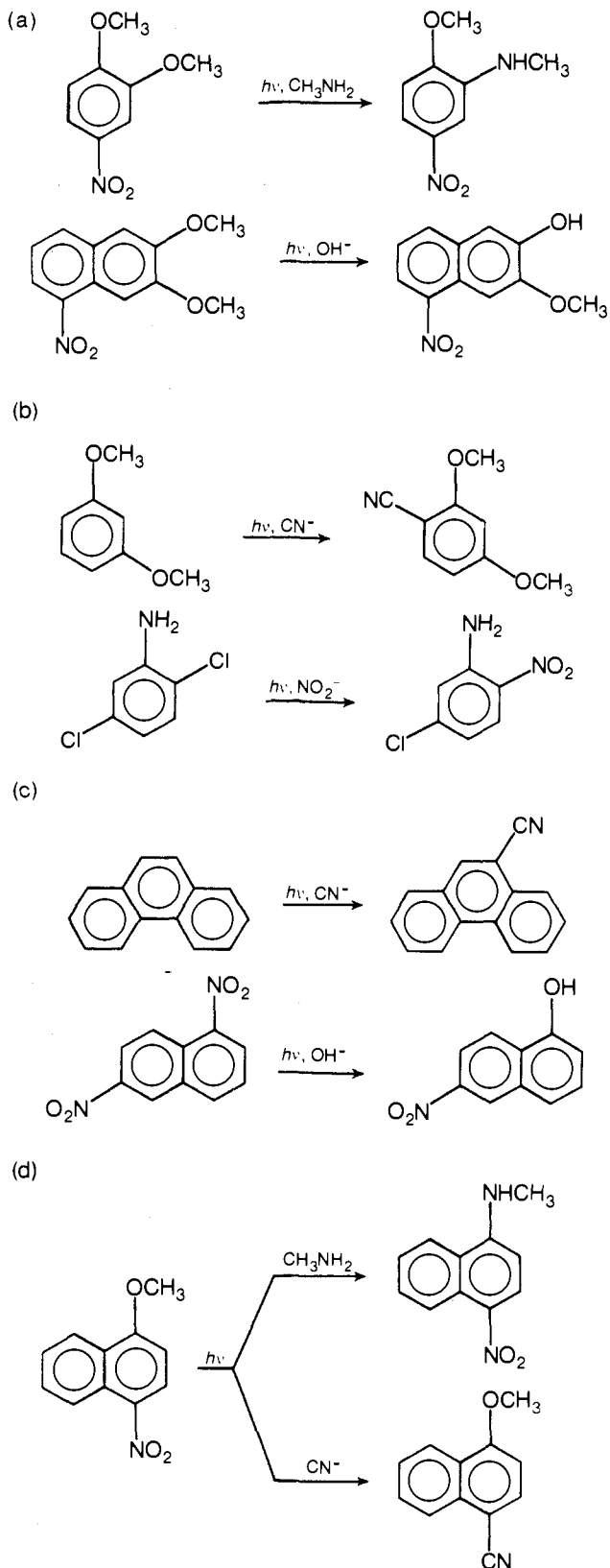
comes into play in a final "thermal" reaction step (e.g., the conversion into substitution product of a ground state σ complex) or in a process starting directly from an electronically or vibrationally excited state. The authors feel that in the latter case one should remain very reserved in attempting to mechanistically explain this effect, however strongly it may appeal to the chemist's intuitive thinking. We know very little about the factors determining the direction and pathway that an excited species chooses to

follow during its relaxation in a liquid medium. The effect of merging stabilization during product formation rationalizes a considerable number of characteristic orientations, e.g., the photoaminations in liquid ammonia at positions ortho and para relative to the nitro group. It probably accounts for many of the specific influences of the nature of the nucleophile on the orientation pattern, and it may also play a role in the ortho/para orientation by alkoxy substituents in photocyanation.

To complement the rationalizations suggested in sections VII.D.1 and 2 we wish to make a few additional remarks.

1. As stated above, orientation rule b—ortho/para orientation by alkoxy groups for CN^- as a nucleophile—can be described as (partly) due to stabilization during the formation of the cyano methoxy compounds. For other nucleophiles (OH^-, OCH_3^-) this overlap and cooperation of rules b and d does not hold. Charge density calculations for the lowest excited states of anisole supply some motivation for activation at the para positions only. One might find a lead to explain the relative preference for the ortho/para positions in accepting contributions from limiting structures of the type
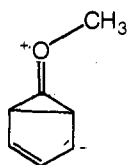
However, it is not easy to adopt this as a rationale for the *activating* influence of the methoxy group unless one resorts to rather ad hoc assumptions as favorable lifetime or intersystem crossing of the methoxy-substituted aromatic compounds.

2. Usually in nucleophilic aromatic photosubstitution the reaction is first order with respect to concentration of both excited aromate and nucleophile. In a few characteristic exceptions the rate of photoreaction is independent of the nucleophile concentration. The quantum yields of photohydrolysis of *m*-nitrophenyl sulfate, 3-nitro-5-chlorophenyl sulfate, a number of bromo- and chloropyridines, and 2-nitrofurans do not vary with change of pH. Recent investigations suggest that we may have to do with an $A_{SN}1$ reaction, the primary and quantum yield determining process being the generation of aromatic cations and subsequent reaction with the nucleophiles present to product molecules. Whereas in such cases the overall quantum yield of consumption of the aromatic compound remains constant, product composition can be easily varied by changing the nature and concentration of the nucleophiles in the medium.

3. Perhaps in future mechanistic rationalization steric relationships should receive more attention. The reacting "aromatic" excited species may quite well be nonplanar. Whereas even in the ground state aromatic molecules may considerably deviate from planarity without suffering too large an increase in energy, the properties of triplet benzene indicate that such species should be described as very flexible.

4. A very instructive result has been obtained recently by systematic study of the values of the quantum yield of nucleophilic aromatic photosubstitution as a function of the concentration of nucleophiles and quenchers.[47] Comparing, e.g., 1-fluoro-3-nitronaphthalene and 1-methoxy-3-nitronaphthalene, in their triplet state reacting with OH^- or CH_3NH_2, the methoxy group is photosubstituted with lower quantum yield than fluorine at the same nucleophile concentration. Curiously, the rate constant of reaction of the excited fluoronitronaphthalene ($k = 10^8$ l. mol^{-1} sec^{-1}) is smaller than that of the excited methoxynitronaphthalene ($k = 10^9$ l. mol^{-1} sec^{-1}). However, this is overcompensated by the considerably longer triplet lifetime of the fluoro- than that of the methoxynitronaphthalene (2×10^{-7} sec vs. 3×10^{-9} sec). This exemplifies the necessity of breaking down the quantum yield values by considering specifically such factors as rate of reactions, lifetime (intersystem crossing efficiency) in case one aims at an understanding of reactivities, and specific orientation rules in aromatic photosubstitution and related photochemical processes.

In this review the authors cover the greater part of the nucleophilic aromatic photosubstitution reactions known to date and—in this concluding section—a summary of the generalizations and orientation rules established. The great variety of the reactions and their specificity, often complementary to that of their thermal cousins, opens important possibilities to synthetic chemistry, the more so since the available orientation rules, when applied judiciously, have good predictive value.

Whereas the situation is encouraging also from the viewpoint of the theoretical chemist, it should be emphasized that a detailed and quantitative description of the course of events leading from light absorption to substitution product still is a goal for the (near) future. Probably in the next decade will be established a number of mechanistic aspects of aromatic photosubstitution that are unsettled at the moment. We may hope for a predictive quantitative treatment of reaction rates of excited molecules, of quantum yields, etc. On the other hand, the phenomena in the field are so rich in variation, each excited aromatic compound and nucleophilic reaction partner showing individuality, that these photoreactions will remain intriguing and provide excitement to the experimentalist as well as to the theoretical chemist for a long time to come.

VIII. Addendum

The manuscript for this review was completed about a year ago. Since that time many new aromatic photosubstitutions have been discovered, and more insight has been gained into the mechanisms of aromatic photochemical substitution reactions. Some of the most important new facts will be briefly described in this addendum.

Photocyanation of benzene (section II.A) has been accomplished.[130] The reaction can be performed in the presence of KCN and ammonium persulfate in *tert*-butyl alcohol/water. The persulfate probably assists in the photoionization of benzene and/or in the removal of hydrogen.

It is no longer true (section II.B) that cyanide ion is the only nucleophile with which aromatic hydrocarbons can be photosubstituted. In the presence of $(NH_4)_2S_2O_8$, naphthalene can be photohydroxylated in alkaline solution.[131] The yield of naphthols is low, owing to their photochemical instability.

Wubbels and Letsinger[132] have investigated in detail the photoreaction of nitrobenzene with hydrochloric acid that they had earlier discovered.[19] The major products of the photoreaction of nitrobenzene in 12 *M* aqueous HCl are 2,4,6-trichloroaniline (44–61%) and 2,4-dichloroaniline (10%). Twelve monosubstituted nitrobenzenes, with electron-donating as well as with electron-accepting groups, were also studied and found to follow a similar pattern, polychloroanilines being the major products. In the photoreaction of nitrobenzene, 4-chloronitrosobenzene is considered to be an intermediate; it is converted to the photoproducts when placed in the reaction medi-

um in the dark. In the primary step, photoexcited nitrobenzene accepts an electron from Cl^-. Protonation then gives rise to $[PhNO_2H, Cl \cdot]$. Coupling of the geminate radicals at the para position and subsequent acid-catalyzed tautomerization yields 4-chloronitrosobenzene hydrate. In methanolic HCl (12 M) the major product is N-(4-chlorophenyl)hydroxylamine. Its formation can be rationalized by a similar mechanism. An analogous reaction scheme is proposed by Cu and Testa[133] for the photoreduction of 5-nitroquinoline in aqueous 2-propanol solution containing HCl, yielding 5-amino-6,8-dichloroquinoline.

With 3-bromonitrobenzene (and also with the 2 and 4 isomers) an interesting photosubstitution was discovered in the aqueous HCl medium: bromine was replaced by chlorine.[132]

The meta compound undergoes a smooth direct substitution whereas the ortho (and possibly also the para) isomer seems to react via a radical intermediate.[134] These results are especially important in view of the fact that earlier attempts to bring about photosubstitution in 3-bromonitrobenzene (with OH^-) met with failure (see section IV.A.6.)[76,77]

Photoinduced hydrogen isotope exchange in anisole and toluene has been studied by Spillane.[135] On irradiation of the monodeuterated anisoles in acetic acid, extensive D–H exchange was observed, particularly in o-deuterio anisole. Because of the competing photoreaction of anisole with acetic acid,[12] reproducible results are not easily obtained. With toluene photolytic reactions are of lesser importance. Spillane irradiated deuterated toluenes and found that the ratio of excited-state reactivities is approximately 2:1:1.4 for the ortho, meta, and para positions, respectively. The picture is similar to that found by Lodder and Havinga[11,12] in anisole: 6:1:2 for the excited state, compared to 1:0:1 for the ground state. Toluene has also the ratio 1:0:1 in its ground state.[136]

Further examples have been described by Bunnett et al.[137,138] of the S$_{RN}$1 mechanism. This mechanism was first recognized for substitutions at aliphatic carbon by Kornblum et al.[139] Kim and Bunnett[140] first described it for aromatic substitution. The reactions can be performed in liquid ammonia stimulated by the solvated electrons of alkali metals; they also occur under stimulation by light (without need for an alkali metal). Electron transfer from a strong electron donor to an aryl halide and subsequent ejection of halide ion creates an aryl radical (see also section III.A.3). The radical may combine with a nucleophile, e.g., acetone enolate ion[38] or 2- or 4-picolyl anion (in liquid ammonia).[138] The S$_{RN}$1 reaction can be expected to find considerable synthetic application. El'tsov and coworkers[141,142] have described photoreactions in which aromatic compounds with electron-donating substituents (mostly amino and methoxy) undergo substitution by cyanide ion and sulfite ion. In aromatic sulfones, sulfonamides, and sulfoxides with electron-donating substituents in the ortho, meta, or para positions the sulfur-containing group is displaced by a cyano group on uv irradiation in the presence of potassium cyanide.[141] In compounds with the general formula RC_6H_4Y (where R is a donor substituent and Y = Cl, Br, I, or SO_2X) the group Y is displaced by a sulfonic acid group on uv irradiation in aqueous solutions of sodium sulfite.[142] Acceptor substituents retard the process and the yield of substitution product decreases in the sequence para = ortho > meta and on passing from chlorine to bromine and iodine derivatives (see also section IV.A.10).

Griffiths and Hawkins[143,144] report that 1-methoxyanthraquinone undergoes photochemical nucleophilic substitution with ammonia and with primary aliphatic amines to give 1-amino- or 1-alkylaminoanthraquinone in good

yields. The reaction does not occur with secondary amines and primary arylamines. Hydroxide ion and cyanate ion are also effective as nucleophiles in displacing the methoxy group in 1-methoxyanthraquinone. Párkányi et al.[145] reported on photohydrolysis of methoxynitronaphthalenes (see also section IV.B.3). Six isomers were studied: 1-OCH$_3$-2-NO$_2$-, 1-OCH$_3$-4-NO$_2$-, 1-OCH$_3$-5-NO$_2$-, 2-OCH$_3$-1-NO$_2$-, 2-OCH$_3$-5-NO$_2$-, and 2-OCH$_3$-6-NO$_2$- naphthalene. Reactions were carried out in 40% acetonitrile/60% 0.1 N aqueous NaOH solution at 245 nm. The 1-OCH$_3$-2-NO$_2$-, 1-OCH$_3$-4-NO$_2$-, 2-OCH$_3$-1-NO$_2$-, and 2-OCH$_3$-5-NO$_2$- naphthalenes gave the corresponding nitronaphthols as the main reaction products. In the case of 1-OCH$_3$-4-NO$_2$- and 2-OCH$_3$-1-NO$_2$-naphthalene also the formation of the corresponding methoxy naphthols was observed.

The photoisomerizations of diaryl-α-keto sulfides to thiaxanthone derivatives described by Praefcke and his coworkers may occur via a nucleophilic substitution mechanism and thus form an example of intramolecular nucleophilic photosubstitution.[146,147]

There are now strong indications that in molecules with electron-donating groups nucleophilic photosubstitution proceeds via cation radicals, photoionization being the primary reaction step. Such a mechanism would explain the observed activating effect of groups like methoxy and amino (see, for example, sections III.A.2, IV.A.8, IV.A.9, and IV.A. 10). It would also be consistent with the ortho/para directing effect of electron donors in nucleophilic aromatic photosubstitution. Finally, it would provide a rationale for the observation that electrophilic photosubstitution in aromatic molecules with donating groups is very inefficient.

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