

Photochemical cyanation of aromatic compounds

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Abstract

Photocyanation of aromatic compounds is reviewed, with emphasis on the differences between cyanation at a substituted vs. an unsubstituted position, and the various mechanisms of photocyanation that have been established. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: Aromatic; Photochemical; Cyanation; Mechanism; Review

1. Scope of photocyanation

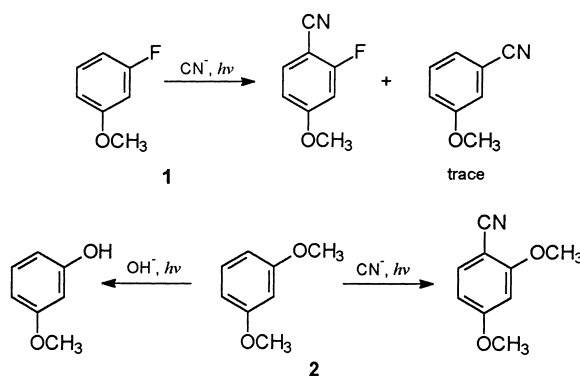
Aromatic nitriles are usually prepared by thermal reactions of inorganic cyanides with aryl halides, sulphonates and diazonium salts or by dehydrating oximes and amides [1]. Photochemical cyanation can also be used to prepare aromatic nitriles, often in good yield and with high regioselectivity, but to date, in common with other nucleophilic aromatic substitutions, it has found little synthetic application [2,3].

A large body of work in the 1960s and 1970s established orientation rules for photochemical nucleophilic substitutions [4]. Although almost all common nucleophiles have been reported to participate in these reactions, cyanide ion, and perhaps OCN^- [5], is exceptional in that it can promote substitution even at an unsubstituted position, i.e., replacement of H by CN.

Photosubstitutions of the nitroanisoles and nitroveratroles were among the earliest $\text{S}_{\text{N}}\text{Ar}^*$ (photochemical nucleophilic aromatic substitution) reactions studied. Irradiation of *m*-nitroanisole in *t*-butyl alcohol/water, for example, gave *m*-nitrophenolate in high yield upon photohydrolysis with hydroxide ion [6], and *m*-nitrobenzonitrile (~50%) with NaCN [7]. Among dimethoxynitrobenzenes, substitution by CN^- and OH^- occurs exclusively at a methoxy group that is *meta* to NO_2 if one is present [8]. Electron donating substituents on the arene, such as OCH_3 and NH_2 , facilitate nucleophilic photosubstitution at *ortho* and *para* positions [9]; the *meta* position is often reported as being activated by electron withdrawing groups, but in practice, the nitro group appears to be almost unique in this regard (see later).

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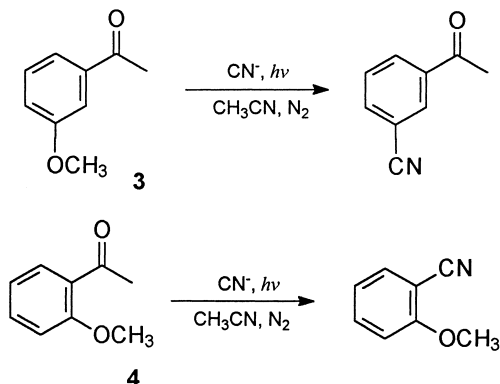
The parallel between CN^- and OH^- breaks down upon irradiations of *o*- and *p*-nitroanisoles. With OH^- , the products are mixtures of the nitrophenolates and methoxyphenolates, representing replacement of OCH_3 and NO_2 , respectively [8,10], but with NaCN substitution occurs exclusively *meta* to NO_2 . From *p*-nitroanisole, for example, the product was 2-methoxy-5-nitrobenzonitrile upon irradiation in air; under nitrogen, 3,3'-dicyano-4,4'-dimethoxyazoxybenzene became the major product [7]. The former reaction is a formal replacement of H^- by CN^- , and so an oxidizing agent is required. The conclusion is that in air, O_2 functioned as the oxidant, whereas under nitrogen this role was taken by the NO_2 group, which was reduced to the corresponding azoxy compound.



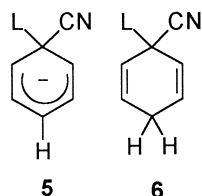
A parallel situation exists for 3-fluoroanisole (1) and 1,3-dimethoxybenzene (2), for both of which the orientation rules suggest nucleophilic substitution *para* to the methoxy group. When hydroxide was used as the nucleophile the only product was 3-methoxyphenol [11] corresponding to the replacement of fluoride, a good leaving group in photoreactive aromatic substitutions, because there is

no good *o*- or *p*- leaving group. Irradiation of **1** with KCN in *t*-butanol–water, however, gave 2-fluoro-5-methoxybenzonitrile as the major product, with only traces of 3-methoxybenzonitrile [11]. For **2** (and also for 1,3,5-trimethoxybenzene) photocyanation of a hydrogen atom *ortho/para* to methoxy was preferred over replacement of the *meta* methoxy. This suggests that a key difference between cyanide and other nucleophiles is its poor leaving group ability: when OH[−] attacks **2**, we infer that the reaction is unproductive (OH[−] leaves again) except when attack occurs at the *meta* position, where OCH₃[−] is an alternative leaving group. For CN[−], however, we must assume that once cyanide has attacked at the preferred *ortho/para* positions, the reaction is committed to that pathway.

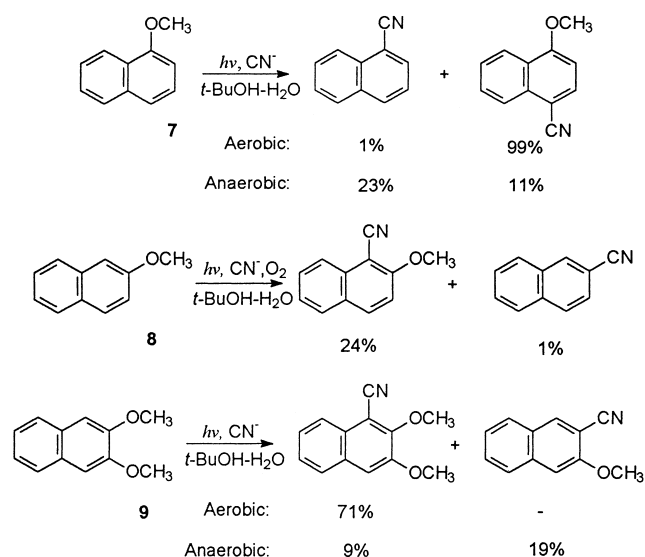
Kuzmic and Soucek [12] studied photohydrolysis and photocyanation of a series of 4-*X*-veratroles, which offer an intramolecular test of whether photosubstitution will proceed *m*- or *p*- to the *X* substituent. Although their data are not completely clear, the 4-NO₂ group exerted a much stronger *m*-directing effect than 4-CN or 4-COCH₃. Van Riel et al. [13] explain the directing effect of the NO₂ group in terms of its ability to stabilize the nascent σ -complex (see below).



An exceptional photocyanation reaction occurred with certain acetophenones [14]. 3-Methoxyacetophenone **3** underwent substitution at the methoxy group (*m*- to acetyl) in 70% yield when irradiated with NaCN or (CH₃)₄NCN, but 2-methoxyacetophenone **4** afforded 2-methoxybenzonitrile under similar conditions. The latter product involves formal displacement of COCH₃ by CN, a remarkable reaction that includes C–C cleavage. Unusually for a photocyanation, the acetyl displacement was inhibited by the presence of air or water. The mechanisms of these reactions are not established, however, and the reaction of the 3-methoxy compound may well be more complex than direct substitution *meta* to acetyl.



The ability of CN to replace H allows the direct preparation of nitriles from unsubstituted arenes, procedures that normally require multi-step syntheses. Photocyanation has been achieved for naphthalene [15–19], biphenyl [16,20], phenanthrene [15,19,21], and pyrene [15]. From naphthalene, the photocyanation products under N₂ are 1-cyanonaphthalene, a monocyano-dihydronaphthalene and a dicyanotetrahydronaphthalene. As with *p*-nitroanisole, these reactions occur better under aerated conditions, when atmospheric oxygen functions as an oxidant. As will be discussed in the context of mechanism, photocyanations involving the replacement of H by CN can be expedited with added oxidant, such as hydrogen peroxide or potassium persulfate, both of which serve to oxidize the intermediate anionic σ -complex **5** (or its protonated analog, the HCN adduct **6**). Alternatively, electron-accepting compounds such as dicyanoarenes can be used, but this changes the reaction mechanism.



Polycyclic aromatic compounds undergo preferential photocyanation at position 1 in naphthalene and azulene, positions 2 and 4 in biphenyl, and position 9 in phenanthrene. Under aerobic conditions 1-methoxynaphthalene (**7**) photocyanates at C-4, an α -position (“*para*” to methoxy) rather than at C-2 (β , “*ortho*”), and 2-methoxynaphthalene (**8**) photosubstitutes the α -hydrogen at C-1. In 2,3-dimethoxynaphthalene (**9**) the hydrogen atom at C-1 (α , *ortho/meta*) is replaced by cyanide instead of the better methoxy leaving group at the β position [11]. These observations parallel the relative reactivities of α and β positions of naphthalene in ground state substitutions. However, under N₂, methoxy substitution appears to be the main reaction path for these compounds and the hydrogen displacement becomes insignificant [11]. One rationalization of these observations is the reaction scheme shown in Fig. 1, with the preference for *para* substitution in the presence of oxygen implying $k_2 > k_1$. In the absence of oxidant, intermediate **7a** almost always reverses to the starting material and 1-cyanonaphthalene is formed via ipso substitution.

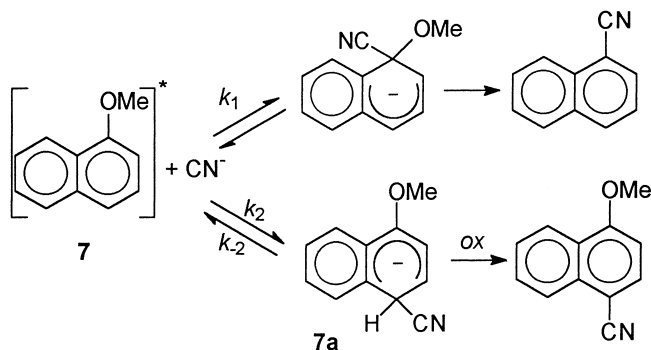
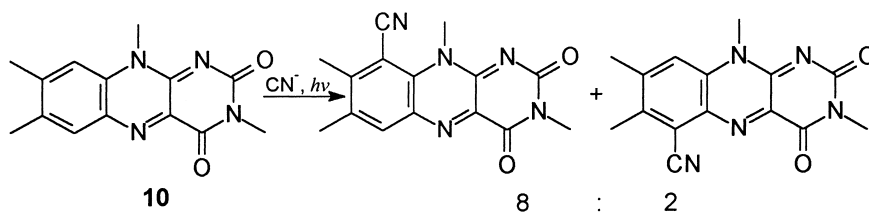


Fig. 1. Pathways of photocyanation of 1-methoxynaphthalene.

Formation of 11% of 1-methoxy-4-cyanonaphthalene from **7** would be explained by incomplete oxygen removal by the use of a nitrogen purge. This mechanism is not consistent with the idea already stated that the regioselectivity of photocyanations is determined by the initial site of attack of CN^- . Alternatively, attack of CN^- may occur at C-4 under both nitrogen and air. In air, the initial 1-methoxynaphthalene-4-cyano adduct (or its protonated form) is oxidized to 1-methoxy-4-cyanonaphthalene, whereas under N_2 protonation and loss of MeOH gives an apparent ipso substitution. Ipso (or apparent ipso) photocyanation is also seen for 1-nitronaphthalene, which produces 1-naphthonitrile in high yield (α substitution) [22], whereas 2-nitronaphthalene is almost unreactive.

Photocyanation of heteroaromatic compounds, especially nitro-substituted compounds such as 2-nitrofurans [23], 2-nitrothiophene [24], and 5-nitroimidazoles [25], has been studied extensively. Among heterocyclic $\text{S}_{\text{N}}\text{Ar}^*$ reactions, photocyanation of 2-nitrofurans appears to be exceptional in that loss of the NO_2 group is reported to precede attack of cyanide ion, (the only example reported so far of an $\text{S}_{\text{N}}1\text{Ar}^*$ mechanism).



Photocyanations in flavins (e.g., **10**) offer a rare example of unassisted hydrogen replacement by cyanide in heterocycles and are of great synthetic value for isoalloxazine chemistry [26]. This reaction is strictly an addition-elimination process rather than a true photosubstitution; it was found to proceed through the intermediacy of cyanodihydroflavins, the latter being oxidized by oxygen to the cyanoflavins.

Photocyanations exhibit significant solvent effects, not all of which are understood. Polar solvents are needed to dissolve alkali cyanide salts and also to promote photoche-

mical electron transfer in the case of the dicyanoarene-assisted reactions. Satisfactory solvent systems include aqueous *t*-butyl alcohol as used by Havinga et al. [20], aqueous acetonitrile, and polar aprotic solvents such as acetonitrile and dimethylformamide, in which cyanide ion is weakly solvated and hence more nucleophilic. Although methanol (and to a lesser extent ethanol) are good solvents for cyanide salts, yields of photocyanation products from phenanthrene and naphthalene are lower in methanol and methanol-water than in DMF-water or acetonitrile-water [15,27], an effect attributed to strong solvation of CN^- by the hydroxylic solvent [27]. Photocyanation of unsubstituted arenes such as biphenyl and naphthalene was not observed in EtOH [27], and was less efficient in dry methanol than in aqueous acetonitrile, although addition of water to methanol greatly enhanced the reaction [16]. A similar effect was noted in the photocyanation of anisole derivatives [28].

The reactivity of the weakly solvated cyanide ion in aprotic organic solvents compared with protic organic solvents can be enhanced by the addition of phase transfer agents, such as 18-crown-6 [29] or polyethylene glycol [30]. This effect parallels the use of phase-transfer catalysts for the thermal synthesis of aliphatic nitriles [31].

The foregoing results suggest that the proton-transferring and salt-dissolving properties of water are beneficial for photocyanations, but that excess water sometimes leads to lower product yields. The reasons are not completely clear: it could be that excessive solvation of the cyanide ion limits its nucleophilicity, but the possible explanation that hydrolysis of CN^- to $\text{HCN} + \text{OH}^-$ lowers the yields of nitriles through competing photohydrolysis seems to be untenable. With unsubstituted arenes, in the absence of electron acceptors, photohydrolysis does not occur (with the exception of phenanthrene [19]), and even in other systems hydroxide is a weaker nucleophile than cyanide. For example, the maximum quantum yields of photohydrolysis of 4-fluoroanisole

and 4-chloroanisole in *t*-butanol-water at 280 nm are both ~ 0.5 , the same as the maximum quantum yields of photocyanation. This suggests that at sufficiently high nucleophile concentration, both OH^- and CN^- trap the same proportion of excited states. However, photohydrolysis is negligible when $[\text{CN}^-] > 0.1 \text{ M}$ [11], showing that CN^- out-competes the solvent for the substrates' excited states.

The efficiency of photocyanation of unsubstituted arenes such as naphthalene and biphenyl [16], anthracene, pyrene, phenanthrene [15], and 9-phenylanthracene [32], increases in the presence of electron acceptors such as the dicyano-

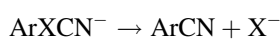
benzenes, methyl-*p*-cyanobenzoate, 1-cyanonaphthalene, 9-cyanophenanthrene, 9,10-dicyanoanthracene [15], dicyanoethylene [33], and persulphate ion [16]. Chemical yields of these assisted photocyanations are also solvent-dependent: in acetonitrile–water, the yield of carbonitrile products from naphthalene and biphenyl, assisted by 1,4-dicyanobenzene (DCB), decreased as the water content of the solvent increased from 10% to 50% [15,16]. In the corresponding reaction with phenanthrene, the quantum yield of photocyanation increased with increased concentration of water in the presence of oxygen, but decreased when the photolysis was done under nitrogen [21]. Attempts to use DMF–water in assisted cyanations of unsubstituted arenes were complicated by competing dark reactions [15].

2. Mechanistic summary

The major mechanisms of S_NAr^* reactions relevant to photocyanations are S_N2Ar^* , $S_{R+N}Ar^*$, Photoionization, and Excimer.

S_N2Ar^* reactions involve the attack of the nucleophile on the excited state of the aromatic partner, and show typical photochemical bimolecular kinetics, with $\phi_{diss}^{-1} \propto [Nucleophile]^{-1}$, and are interpreted in terms of a σ -bonded intermediate. Electron transfer reactions can involve the photoexcited aromatic compound either as an electron donor ($S_{R+N}1Ar^*$) or as an electron acceptor ($S_{R-N}1Ar^*$) [34]. In the $S_{R+N}1Ar^*$ reaction, electron transfer is followed by attack of nucleophile on the aromatic radical cation, whereas in the $S_{R-N}1Ar^*$ reaction the electron donor normally participates also as the “nucleophile” by attacking the radical anion of the aromatic compound. However, the $S_{R-N}1Ar^*$ mechanism is never followed in photocyanations, on account of the high oxidation potential of CN^- (+1.3 V in pure acetonitrile [35], +1.95 V in methanol [36] and reportedly +1.7 V [35] and +2.26 V [36] in water). By comparison, the oxidation potentials of primary amines in acetonitrile and water are in the range of 0.54–1.35 V [37].

3. S_N2Ar^* mechanism



Photocyanations of methoxynitroarenes are triplet state reactions that are proposed to be S_N2Ar^* by analogy with photohydrolysis, for which time-resolved studies have allowed the identification of reaction intermediates [38–40]. Van Eijk et al. [40] showed by laser spectroscopy that the *meta* photosubstitution of 4-nitroveratrole with OH^- is a triplet state reaction, whereas the corresponding substitution with methylamine involves the singlet state. Detailed laser

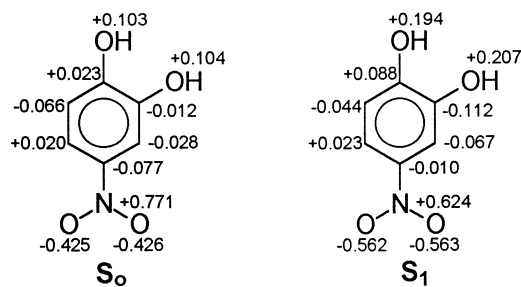


Fig. 2. Charge distribution in ground and singlet excited states of 4-nitrocatechol [4].

flash photolysis studies of photocyanations of methoxynitrobenzenes do not yet appear to have been carried out, but the parallel between photohydrolysis and photocyanation in these systems makes it likely that the mechanisms are also comparable.

The earliest attempts to understand the mechanisms of S_N2Ar^* reactions involved correlating the charge densities at the various ring positions of the nitroanisoles and nitroveratroles with their susceptibility to photosubstitution. For example, Cornelisse and Havinga [4] correlated the *meta* orientation by nitro substituents and the *para* orientation of methoxy with the charge distribution in the π , π^* excited state. Photosubstitution occurred preferentially at positions carrying the least negative charge in the lowest π , π^* singlet, and sometimes triplet, excited state (Fig. 2), but this theory failed to account for the fact that nitroaromatic compounds invariably react from triplet excited states because of high intersystem crossing quantum yields. This theory also did not explain the *ortho* orientation observed with electron donating substituents and the “reversed” effects with certain nucleophiles, such as the substitution of 4-nitroveratrole at the 3-methoxy group with cyanide, hydroxide, ammonia, and methylamine, but at the 4-methoxy group with secondary and aromatic amines. This change in orientation was later shown to be due to a change in mechanism from S_N2Ar^* to $S_{R-N}1Ar^*$ with “nucleophiles” of lower ionization potential, as demonstrated in a series of intramolecular photosubstitutions (Smiles rearrangements) [41,42]. Frontier orbital energy diagrams (Fig. 3) illustrate the difference between the two mechanisms. Regioselectivity in S_N2Ar^* reactions is governed by the interaction between the nucleophile’s HOMO and the aromatic substrate’s ground state HOMO (described by Mutai [41] as HOMO-controlled); the nucleophile attacks the aromatic substrate at the positions where the molecular orbital coefficient is highest. In the LUMO-controlled $S_{R-N}1Ar^*$ reaction, the interaction between the aromatic substrate’s ground state LUMO and the HOMO of the nucleophile controls the regioselectivity; following electron transfer from the “nucleophile” to the substrate, the nucleophile’s radical cation attacks the position bearing the highest LUMO coefficient.

Mutai’s rules were successfully applied to photosubstitutions of *meta*-alkoxynitrobenzenes, 3,4-dialkoxynitroben-

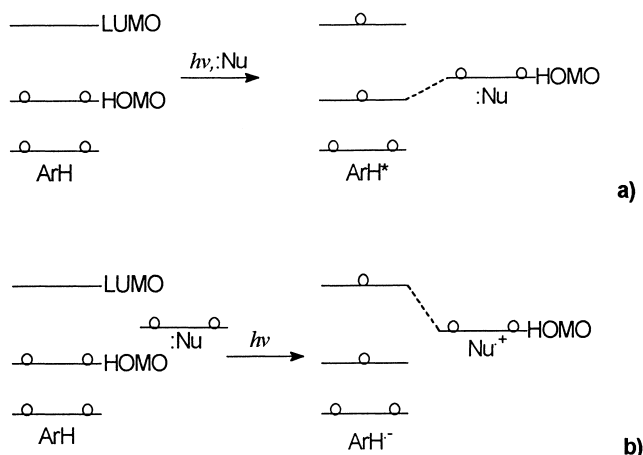


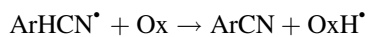
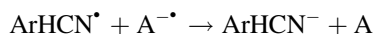
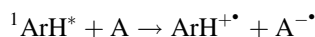
Fig. 3. Schematic illustration of the orientation-determining step, σ -complex formation after (a) direct interaction of an excited molecule and nucleophile ($S_{N2}Ar^*$), and (b) photoinduced electron transfer [41].

zenes and chloronitrobenzenes [41]. Their application to $S_{R-N}1Ar^*$ reactions was criticized by Cantos et al. [43], who argued that the regioselectivity of substitution of 4-nitroanisole by primary amines is explained by the relative stabilities of the intermediate σ -complexes formed when the radical-ion pair collapses, rather than by frontier orbital coefficients or net charge densities.

A point that has never been completely resolved in the $S_{N2}Ar^*$ mechanism is the disposition of the electrons following the attack of the nucleophile on the photoexcited aromatic substrate. The HOMO and LUMO are both singly occupied, so placing an electron pair into a vacant MO would lead to a highly excited state. The σ -complex is generally written as an electron-paired species, implying that at this stage the intermediate has returned to the ground state potential surface. Van Riel, Lodder, and Havinga [13] postulated that the regioselectivity in photocyanations of compounds bearing electron withdrawing groups is controlled by the size of the energy gap between the excited (triplet) state substrate-nucleophile encounter complex and the ground state σ -complex. Therefore the *meta* orientation of the nitro group arises because the ground state σ -complex is not stabilized by the nitro group, and the energy gap between the excited (triplet) state substrate-nucleophile encounter complex and the ground state σ -complex is smaller than those arising from *ortho* or *para* attacks [13]. Cornelisse [2] suggested that other electron withdrawing groups do not lower the triplet energy to the same extent as NO_2 ; we may further postulate that these other electron-withdrawing groups give less stabilization than NO_2 to the ground state *o*- and *p*- σ -complexes, relative to the *m*-. Hence the gap between the excited state and the ground state σ -complex is particularly small for attack *meta* to a nitro group. For example, photocyanation of 3,4-dimethoxybenzonitrile and 3,4-dimethoxyacetophenone led to mixtures of *meta* and *para* displaced products [12], so to date, clean *meta* photosubstitutions governed by an electron withdrawing

group have been reported only for nitro compounds. In the 3,4-dimethoxy-1,X-benzene series, the nitro group has the highest activating power, and relative quantum yields of photocyanation were 1:1.5:6:1000 for X=H, CN, $COCH_3$, and NO_2 , respectively [12].

4. $S_{R+N}Ar^*$ mechanism



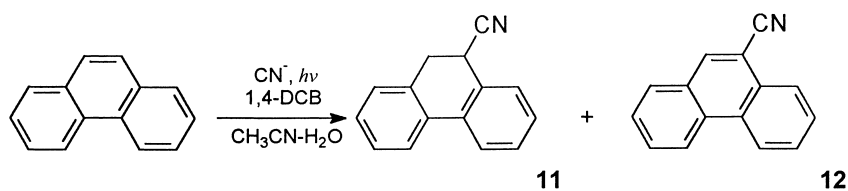
The role of the electron acceptor in assisted photocyanations is to oxidize the aromatic component to its radical cation, which is then more susceptible to attack by the nucleophile ($S_{R+N}1Ar^*$). This requires the free energy change for electron transfer from the photoexcited arene to the electron acceptor to be negative; for example, 1,4-dicyanobenzene ($E_{1/2} = -1.64$ V [44]) in the photocyanation of anthracene [15] and naphthalene [18]. Since the nitrile products of photocyanation are usually good electron acceptors, autocatalytic effects are observed in the unassisted photocyanations of phenanthrene [15], naphthalene [16] and biphenyl [16]. This was demonstrated for the photocyanation of phenanthrene; the gradual acceleration of the reaction by the 9-cyanophenanthrene produced was shown by studying the rate of reaction in the presence of different concentrations of 9-cyanophenanthrene [17].

Autocatalysis was observed recently by Konstantinov and Bunce [45] in the photocyanation of a variety of highly chlorinated aromatic compounds, this time in the context of the $S_{N2}Ar^*$ mechanism. Hexachlorobenzene, for example, gave pentacyanophenol, 4-chloro-2,3,5,6-tetracyanophenol and a dichlorotricyanophenol on irradiation with sodium cyanide. The lack of mono- and dicyanated products implied autocatalysis, with each successive cyanation proceeding with increasing quantum yield [46].

The experimental consensus is that photocyanation of unsubstituted arenes in the presence of electron acceptors is a singlet state reaction (unlike NO_2 -containing substrates such as 4-nitroanisole that undergo rapid intersystem crossing and react from the triplet [47]). *p*-Dicyanobenzene strongly quenches the fluorescence of naphthalene and biphenyl; kinetic experiments with naphthalene have shown that the reaction is first order in CN^- and *p*-dicyanobenzene, but independent of the concentration of naphthalene under conditions that all incident light is absorbed by naphthalene [16]. Singlet state reactivity in the presence of electron acceptors has also been suggested for the photocyanation of anisole [30], anthracene [15], methoxy-substituted

naphthalenes [15], phenanthrene [15,21,29], and 9-phenylanthracene [32].

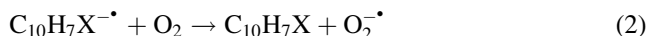
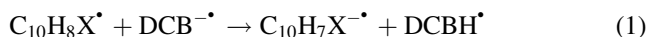
In polar solvents, electron transfer leads to the radical ion pair rather than an exciplex. Addition of cyanide ion to the aromatic radical cation forms an uncharged σ -intermediate ArH-CN^\cdot that can disproportionate into substitution and addition products. Other possible routes to these products are back electron transfer from the radical anion of 1,4-dicyanobenzene and proton addition, leading to the dihydronitrile, or oxidation with oxygen or other oxidant to the arene nitrile. The first two reactions are important under anaerobic conditions; the latter pathway becomes predominant in the presence of oxidizing agents like O_2 or N_2O [17].



The importance of an oxidizing agent for achieving high yields of nitriles is illustrated by the photocyanation of phenanthrene in aqueous acetonitrile, assisted by 1,4-dicyanobenzene. Under N_2 , 9,10-dihydrophenanthrene-9-carbonitrile (**11**) and 9-cyanophenanthrene (**12**) were formed in 55% and 16% yields, respectively [15]. Under aerobic conditions, **12** was the only product, isolated in 78% yield. In dry acetonitrile, in the absence of oxygen, formation of **12** was completely suppressed [19].

Yasuda et al. [15] noted that recovery of the electron acceptors from photocyanations is often low; this shows that back electron transfer from $\text{A}^{\cdot-}$ to regenerate the electron acceptor is far from quantitative. Electrochemical studies have shown that proton capture and dimerization are alter-

native reactions of the radical anion of DCB $^{\cdot-}$ [48,49]. The same process is implied by the results of Niranen et al. [19] who studied photochemical cyanation and hydroxylation of naphthalene assisted by 1,4-dicyanobenzene. They suggest that attack of X^- on naphthalene radical cation is followed by proton transfer, and oxidation to give the final product.



Cornelisse's group [18] studied the photocyanation of naphthalene in aerated acetonitrile in the presence of various electron acceptors (see Fig. 4). The ratio of 1- and 2-

cyanonaphthalenes was 7:1, consistent with the calculated charge distribution in naphthalene radical cation: +0.09 at position 1, -0.05 at position 2, and also with the relative stabilities of the two σ -complexes: $\alpha\text{-C}_{10}\text{H}_8\text{CN}^\cdot$ is calculated to be more stable than $\beta\text{-C}_{10}\text{H}_8\text{CN}^\cdot$ ($\Delta H_f = 93.8$ vs. 97.5 kcal/mol) due to more extensive resonance. The absolute quantum yield of disappearance of naphthalene varied with the electron acceptor (and reached the maximum with 1,4-dicyanobenzene), but the ratio of 1- and 2-cyanonaphthalenes was constant. Photocyanation under these conditions required only a catalytic amount of 1,4-dicyanobenzene, which was not consumed during the reaction [18] because DCB radical anion was reoxidized to DCB by O_2 , yielding oxygen radical anion (Fig. 4). At low $[\text{O}_2]$ the

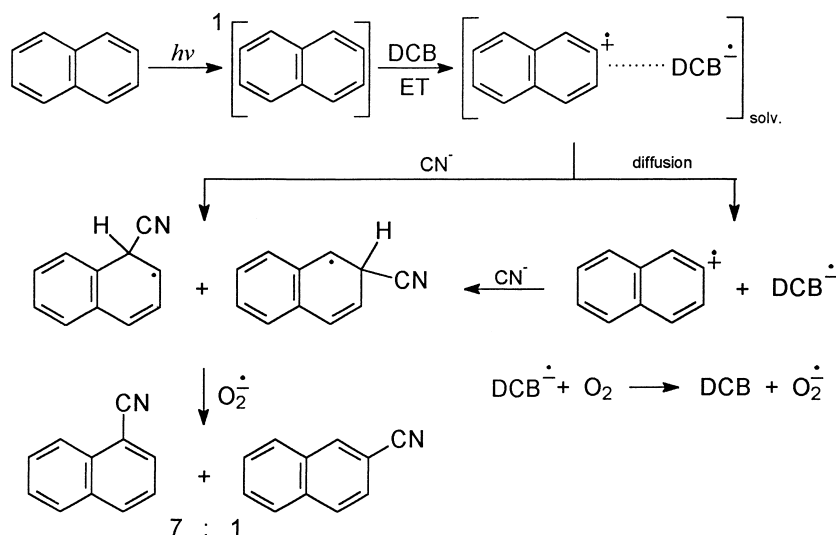


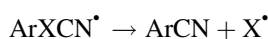
Fig. 4. Mechanism for the photocyanation of naphthalene in the presence of 1,4-dicyanobenzene [18].

reaction with $C_{10}H_8$ and $C_{10}D_8$ had k^H/k^D 1.6–2.5, indicating that C–H bond cleavage is rate-limiting under these conditions. Although either O_2 or its radical anion could in principle act as the hydrogen abstractor, the authors suggest that $O_2^{\cdot-}$ is chiefly responsible, despite its low concentration, based on calculations suggesting that the activation energy for hydrogen atom transfer from α - $C_{10}H_8CN^{\cdot-}$ to $O_2^{\cdot-}$ (<2 kcal/mol) is much smaller than to O_2 (28 kcal/mol) [18].

For photocyanations of simple arenes, flash photolysis studies by Lemmetyinen et al. [17,21,29] showed the formation of two photoinduced transients, both of which are quenched by oxygen. Products are formed by interaction of O_2 with the second transient, which is believed to be the σ -complex. Oxygen quenching of the initially formed intermediate is unproductive, but is more rapid. Consequently, high concentrations of O_2 inhibit photocyanation while low concentrations promote the reaction, and also promote formation of the nitrile rather than the corresponding dihydro compound [29].

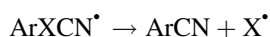
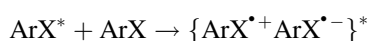
Although many reagents may act as oxidants not all combinations lead to substitution when CN^- is present. For example, both H_2O_2 and di-*t*-butyl peroxide quench naphthalene fluorescence; but in the presence of CN^- , H_2O_2 causes rapid destruction of naphthalene and di-*t*-butyl peroxide retards photocyanation [16]. Nitrous oxide and $(NH_4)_2S_2O_8$ were found to be efficient oxidants for the photocyanation of anisole and its *meta*-substituted derivatives, and also of benzene [11]. For photocyanations in aqueous media, $(NH_4)_2S_2O_8$ is preferred over oxygen because of its higher solubility. Nitrous oxide was found to behave similarly to oxygen in that a maximum rate of cyanation was obtained at low N_2O concentrations and the rate decreased with increasing N_2O concentrations [17]. In reactions where substituents like halogens and methoxy are displaced by cyanide, no oxidation step is necessary and oxygen, N_2O or $(NH_4)_2S_2O_8$ do not influence the efficiency of photocyanation [11].

5. Photoionization mechanisms



In aromatic systems substituted with electron donating groups such as methoxy, there is the possibility of photoionization as the initial step, implicating the $S_{R+N}Ar^*$ mechanism [50]. Photoionization has been seen also for 9-phenylanthracene under conditions of two-photon photon absorption [32], and has been implied in laser spectroscopic studies of the photocyanation of 4-chloroanisole and 4-fluoroanisole by observing solvated electrons [33]. The latter photosubstitutions, which occur in the absence of electron acceptors, proceed via the triplet excited state for anisole [30], haloanilines [51], 4-fluoroanisole [11,33] and 4-chloroanisole [11,33], whose triplet energies are ~ 80 kcal/mol [52]. The reactions are sensitized by acetone ($E_T=82$ kcal/mol [52]) and quenched by *trans*-1,3-pentadiene ($E_T=59$ kcal/mol [52]). The quantum yields for photocyanation show a very strong dependence on water concentration [11] consistent with an ionization process. For 4-fluoroanisole ϕ increased from 0.01 to 0.69 on going from 64% to 99% (mol/mol) water in *tert*-butanol/water mixture (a similar dependence of ϕ on water concentration was reported for photosubstitutions of 4-chloro- and 4-fluoroanisoles in acetonitrile/water solvent [33]). 4-Fluoroanisole has $\phi_{isc}=0.75$ [52], indicating that nearly every triplet molecule that is formed leads to the substitution product via ionization in highly aqueous media. The order of reactivity in photosubstitution of haloanisoles by cyanide ion ($F>Cl>Br>I$) is probably due to the heavy atom effect of the halogen in increasing the rate of intersystem crossing from the triplet to the ground state: see Fig. 5 [11]. Further evidence for the photoionization mechanism is provided by the similarity of the products obtained by photocyanation and anodic cyanation of the haloanisoles [11]. We can note in passing that this similarity is not observed for $S_{N2}Ar^*$ reactions [13].

6. Excimer reactions



When $X=H$: $2ArHCN^{\cdot-} \rightarrow ArCN + HArHCN$ (a dihydro product). The Reactive excited state is triplet for $X \neq H$; singlet for $X=H$.

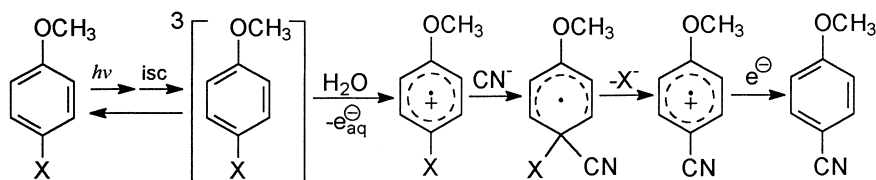


Fig. 5. Mechanism of nucleophilic substitution of anisoles with KCN in aqueous *t*-BuOH [11].

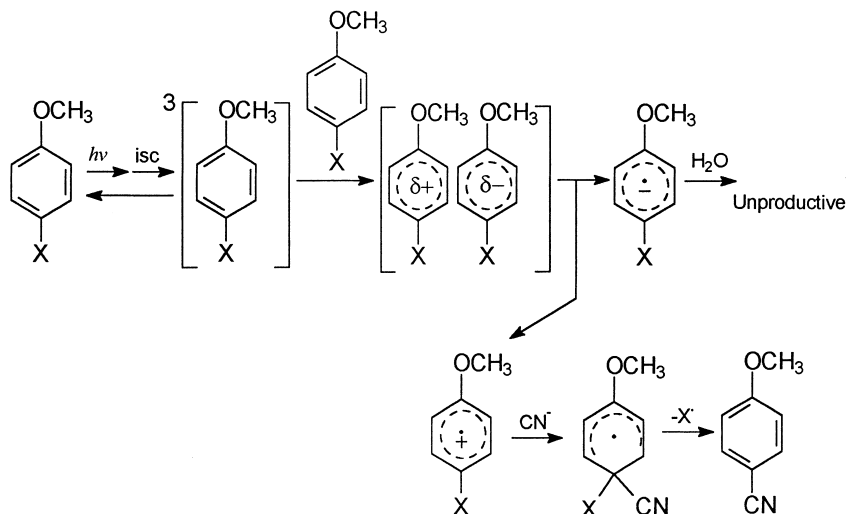
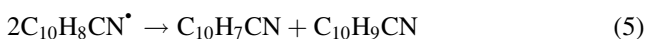


Fig. 6. Mechanism of photocyanation of haloanisoles involving the radical ion pairs.

Photocyanations by an excimer mechanism have been suggested at both substituted and unsubstituted positions of aromatic compounds. In aqueous acetonitrile, Lemmetyinen et al. [33] found that the formation of the radical-cation of 4-chloroanisole was first order in the concentration of ground state 4-chloroanisole. This suggests that the interaction between the excited and ground state molecules produces the ion pair which dissociates into radical cation and radical anion (Fig. 6). Attack of the nucleophile on the radical anion yields neutral radicals of type ArXCN^{\bullet} , which were observed by laser spectroscopy. The authors [33] argued that the next step is the departure of the halogen atom rather than the halide ion, since no radical cations of the type $\text{ArCN}^{+\bullet}$ were observed by flash photolysis, and the measured lifetime of solvated electrons is too short to allow for the back electron transfer. The released halogen atom X^{\bullet} yields the halide anion upon recombination with the negative species formed in the reaction of water and radical anion of 4-fluoroanisole.

Dependence of the quantum yield on the substrate concentration has also been noticed in photocyanations of unsubstituted arenes, such as naphthalene and biphenyl [28]. These reactions were proposed to proceed through the singlet excimer. Attack of CN^- on the excimer or the radical ion pair affords the ArHCN . σ -complexes, which can disproportionate (Eqs. (4) and (5)).



This mechanism allows no exchange of hydrogen with the solvent, and when photocyanation was carried out in $\text{CH}_3\text{CN}-\text{D}_2\text{O}$ there was no incorporation of deuterium into the products [28]. On the basis of analysis of Stern–Volmer quenching for the reaction between the excited singlet state of naphthalene and electron acceptor Lemmetyinen [17] suggested that the unassisted photocyanation of naphthalene

is a triplet state process, however, no direct experimental evidence of the triplet reaction has yet been reported. Vink et al. [20] observed that photocyanation of biphenyl could be sensitized by benzophenone and proposed a triplet state mechanism. However, there is disagreement on this point; based on the results from sensitization (benzophenone, acetophenone derivatives, acetone) and quenching (dienes, biacetyl) of the photocyanations of naphthalene and biphenyl, Bunce et al. [16] concluded that photocyanation of these substrates proceeds via a singlet excimer.

The photocyanation of phenanthrene [21,29,53,54] takes place via a triplet excited state in the absence of electron acceptors, as demonstrated by sensitization and flash photolysis methods [21]. It was formerly suggested that the radical cation of phenanthrene is formed by electron transfer to a cyanide ion [29]. However, CN^- does not quench the singlet or triplet excited states of phenanthrene [54] so the radical cation of phenanthrene must be formed either through the excimer or by electron photoejection. The excimer mechanism is supported by flash photolysis experiments, which showed the formation of a transient whose yield increased with increasing concentration of the substrate [21]. The authors suggested a mechanism similar to that of naphthalene, but involving the triplet rather than the singlet excited state.

In conclusion, we may say that photocyanation remains a promising but hitherto unexploited synthetic procedure. Sufficient is now known about the mechanisms of these reactions that it would be realistic to design synthetic procedures that would give high yields of products with good regioselectivity.

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