Direct Cyanation of Aromatic Compounds

II.[1] A Comparison of Isomer Distributions from Different Cyanation Methods

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The isomer distributions of aromatic nitriles formed in five direct cyanation reactions have been determined and are discussed in terms of the possible reaction mechanisms. The reactions investigated are anodic cyanation, photolysis of aromatic compounds in cyanide solution, photolysis of halogen cyanide, diazotation of cyanamide in the presence of aromatic compounds, and cyanation of aromatic compounds with cyanogen chloride/aluminium chloride. In the first two of these reactions the cyano group attacks the aromatic ring as a nucleophile, the two following are radical reactions, whereas the last reaction is best described as an electrophilic aromatic substitution reaction.
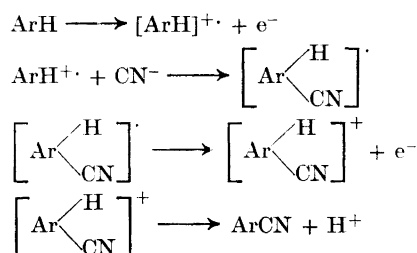
RESULTS AND DISCUSSION

Anodic cyanation was first described by Koyama *et al.*[2] in 1965 and has been the subject of numerous investigations since then. The fact that cyanide ions are oxidixed at a lower potential than most aromatics made it theoretically possible that cyanide ions were oxidized to cyano radicals which reacted with aromatic compounds in the solution *via* a homolytic mechanism. Evidence from controlled potential experiments,[3,4] isomer distribution determination of aromatic nitriles formed[4] and the observation that cyanide ion has a high overpotential on platinum due to formation of cyanide compounds as a film on the electrode surface[5] have ruled out this mechanism. Anodic cyanation is now best described as a nucleophilic attack by cyanide ion on a cation radical formed by an initial one-electron transfer from the substrate to the anode (see Scheme 1). The isomer distribution of nitriles formed in anodic cyanation reaction with some selected aromatic compounds are shown in Table 1.

Photolysis of aromatic compounds in the presence of cyanide ions. In 1961, Havinga published some interesting results on the hydrolysis of phosphate esters of nitrophenols.[6] The hydrolysis rate was strongly enhanced when an

Table 1. Isomer distributions of aromatic nitriles formed in anodic cyanation.

| Compound | Isomer distributions of nitriles, % | | |
	ortho or α-	*meta* or β-	*para*
Anisole	53	0.1	47
Chlorobenzene	50	0.5	50
Biphenyl	24	0.4	76
Toluene	40	8	52
Isopropylbenzene	4	9	87
t-Butylbenzene	41	13	46
Naphthalene	90	10	

$$ArH \longrightarrow [ArH]^{+\cdot} + e^-$$

$$ArH^{+\cdot} + CN^- \longrightarrow \left[Ar{\overset{H}{\underset{CN}{\diagup\!\diagdown}}} \right]^{\cdot}$$

$$\left[Ar{\overset{H}{\underset{CN}{\diagup\!\diagdown}}} \right]^{\cdot} \longrightarrow \left[Ar{\overset{H}{\underset{CN}{\diagup\!\diagdown}}} \right]^{+} + e^-$$

$$\left[Ar{\overset{H}{\underset{CN}{\diagup\!\diagdown}}} \right]^{+} \longrightarrow ArCN + H^+$$

Scheme 1.

alkaline solution of the ester was placed in the sunlight.[7,8] This observation was during the 60's followed by others which can be collected under the heading "Light Induced Heterolytic Reactions in Solution". The reactions follow the general equation:

$$ArX + Y^- \xrightarrow{h\nu} ArY + X^-$$
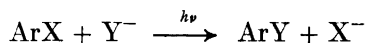
where X^- is OPO_3^-, OCH_3^-, *etc.*, and Y^- is OH^-, $NHCH_3^-$, CN^-, *etc.* Thus Letsinger and McCain[8] reported that photolysis of aromatic nitro compounds in cyanide solution gave 3-nitrobenzonitriles. We have independently found that aromatics (not necessarily nitroaromatics) can be cyanated in this way.* The isomer distributions from some of these reactions are shown in Table 2.

Table 2. Isomer distributions of aromatic nitriles formed in photolysis of aromatic compounds in the presence of cyanide ions.

| Compound | Isomer distributions of nitriles, % | | |
	ortho or α-	*meta* or β-	*para*
Anisole	53	0.2	47
Biphenyl	30	3	67
Naphthalene	90	10	

* This reaction was also reported recently by Vink, J. A. J., Lok, C. M., Cornelisse, J. and Havinga, E. *Chem. Commun.* **1972** 710.

The reaction mechanisms for these light induced reactions are not known with certainty. Havinga [9] proposed a mechanism for the hydrolysis of nitrophenolate esters that proceeds *via* the singlet state:
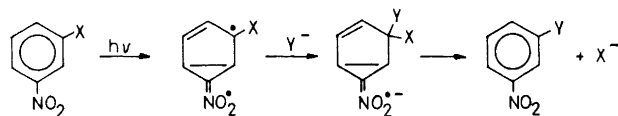
This mechanism may be valid when X^- is a good leaving group and the singlet state (that here is written as a diradical according to Bryce-Smith and Gilbert [10]) is stabilized by a substituent like the nitro group. When the leaving grouop is H^- (as in direct cyanation) it appears more probable that the reaction starts with a photoionisation of the aromatic compound. The reaction sequence would then be (Scheme 2):
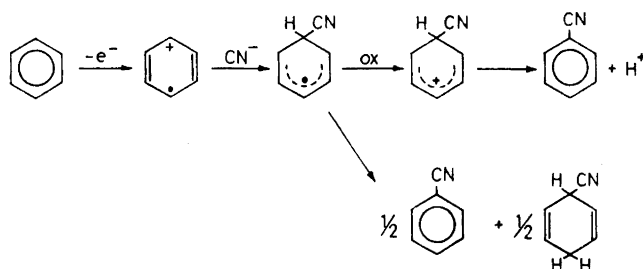
Scheme 2.

The second oxidation to a Wheland-type intermediate may occur with oxygen.[8] The other possibility is disproportionation to an aromatic nitrile and a dihydro compound. In the photolysis of naphthalene we actually found a dihydro compound, 1,4-dihydro-1-cyanonaphthalene, which may have been formed in this way. It is, however, possible that this compound has been formed from reaction between 1-cyanonaphthalene and solvated electrons. 1-Cyanonaphthalene reacts faster than naphthalene with solvated electrons [11] by a factor of 4.

Photolysis of halogen cyanide in the presence of aromatic compounds. Photolysis of iodine, bromine, and chlorine yields free halogen radicals. It is not possible to get cyano radicals in the same way from cyanogen due to its instability and tendency to polymerize. A homolytic dissociation of a halogen cyanide depends on the bond strength and polarity of the carbon-halogen bond. The determination of bond lengths [12] and bond energy [12-14] (dissociation energy) of different halogen cyanides together with determination of the ionisation potential of the cyano group [15] and calculations of the electronegativity of the cyanide ion [16,17] and the electron affinity of the cyano radical [17-19] make it possible to arrange the cyano group in these respects in a series of halogens
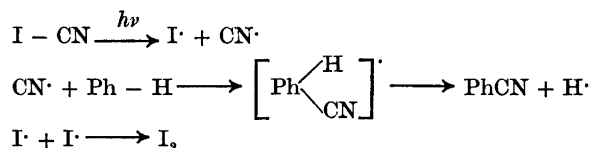
and pseudo-halogens: F, ONC, OCN, Cl, Br, CN, SCN, ClO_2, I. The names of the halogen cyanides should according to this be cyanogen fluoride, cyanogen chloride, cyanogen bromide, and iodine cyanide. The first three of them should give a positive cyano ion and a halogenide ion while iodine cyanide should give iodonium ion and cyanide ion when subjected to heterolytic dissociation. This prediction is confirmed by the results from hydrolysis of halogen cyanides.[20] A homolytic dissociation should give cyano and halogen radicals and should be easiest to perform with cyanogen bromide or iodine cyanide.

When a solution of iodine cyanide and an aromatic compound in carbon tetrachloride or methanol was photolysed, a mixture of aromatic nitriles was formed. The isomer distributions (Table 3) indicate that the reaction starts

Table 3. Isomer distributions of aromatic nitriles formed in photolysis of iodine cyanide in the presence of aromatic compounds.

Compound	Solvent	Isomer distributions of nitriles, %		
		ortho or α-	*meta* or β-	*para*
Anisole	CH_3OH	58	14	28
Anisole	CCl_4	51	16	33
Chlorobenzene	CCl_4	27	27	46
Nitrobenzene	CCl_4	22.5	63	14.5
Biphenyl	CH_3OH	44	28	28
Toluene	CH_3OH	47.5	31.5	21
Naphthalene	CH_3OH	61	39	

with homolytic dissociation of iodine cyanide and that the cyano radical attacks the aromatic ring (Scheme 3). The intermediate radical looses a hydrogen radical either by oxidation, disproportionation, or by a second attack by another cyano radical. The iodine radicals dimerize to iodine which is observed by its colour. Aromatic iodination could not be detected. It is, however, possible that aromatic iodides formed in this reaction were destroyed during the photolysis.[21]
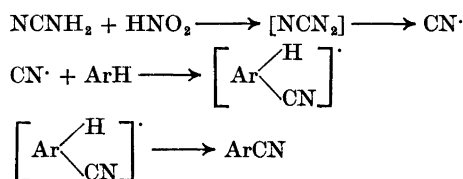
$$I - CN \xrightarrow{h\nu} I\cdot + CN\cdot$$

$$CN\cdot + Ph - H \longrightarrow \left[Ph\overset{H}{\underset{CN}{<}} \right]^{\cdot} \longrightarrow PhCN + H\cdot$$

$$I\cdot + I\cdot \longrightarrow I_2$$

Scheme 3.

Diazotation of cyanamide in the presence of aromatic compounds. When photolysis of halogen cyanide is used as a source of cyano radicals, the result may become complicated due to photorearrangement. In Part I of this series[1] a thermal method of generating cyano radicals is described. The reaction mech-

anism discussed therein (Scheme 4) implies a radical attack on the aromatic ring, and the isomer distributions of aromatic nitriles formed in the reaction are in accordance with this mechanism (Table 4).
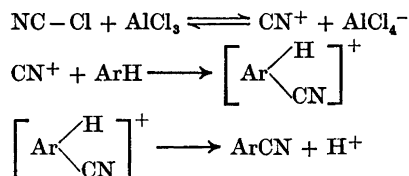
Table 4. Isomer distributions of aromatic nitriles formed by diazotation of cyanamide in the presence of aromatic compounds.

Compound	Isomer distributions of nitriles, %		
	ortho or α-	*meta* or β-	*para*
Anisole	44	13	43
Chlorobenzene	41	9	50
Biphenyl	54	29	17
Toluene	50	27	23
Ethylbenzene	14	10	76
Isopropylbenzene	29	0	71
Naphthalene	60	40	

$$NCNH_2 + HNO_2 \longrightarrow [NCN_2] \longrightarrow CN\cdot$$

$$CN\cdot + ArH \longrightarrow \left[Ar\begin{smallmatrix}H\\CN\end{smallmatrix} \right]\cdot$$

$$\left[Ar\begin{smallmatrix}H\\CN\end{smallmatrix} \right]\cdot \longrightarrow ArCN$$
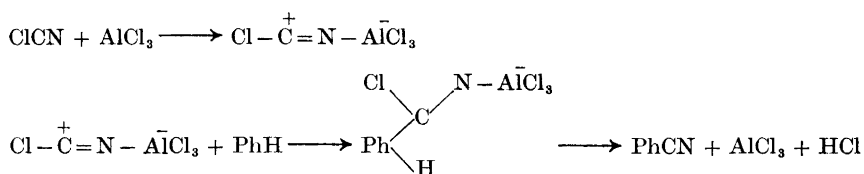
Scheme 4.

Cyanation of aromatic compounds with cyanogen chloride/aluminium chloride. Cyanogen chloride or bromide reacts with aromatic compounds in the presence of aluminium chloride to give aromatic nitriles. The method has been known since the end of the last century [22,23] but has not received wide attention due to side reactions. In the light of the earlier discussion, it is evident that a heterolytic dissociation of cyanogen chloride would give a cyano cation and a chloride ion. The cyanation reaction has also been described to proceed *via* formation of cyanogen cations [24,25] (Scheme 5).

$$NC-Cl + AlCl_3 \rightleftharpoons CN^+ + AlCl_4^-$$

$$CN^+ + ArH \longrightarrow \left[Ar\begin{smallmatrix}H\\CN\end{smallmatrix} \right]^+$$

$$\left[Ar\begin{smallmatrix}H\\CN\end{smallmatrix} \right]^+ \longrightarrow ArCN + H^+$$

Scheme 5.

It is, however, not necessary to postulate "free" cyano cations. An investigation of the infrared spectra of adducts of antimony(V) chloride and cyanogen halogenides [26] makes it probable that these have a structure like

$X - \overset{+}{C} = N \longrightarrow \bar{S}bCl_5$. The infrared spectrum of cyanogen chloride also changes when aluminium chloride is added but the bathochromic shifts of the frequencies of the nitrile group and the carbon-halogen bond are less pronounced. From these facts it is possible to propose a modified mechanism for this Friedel-Crafts resembling reaction (Scheme 6).

$$ClCN + AlCl_3 \longrightarrow Cl - \overset{+}{C} = N - \bar{Al}Cl_3$$

$$Cl - \overset{+}{C} = N - \bar{Al}Cl_3 + PhH \longrightarrow Ph\underset{H}{\overset{Cl}{\diagdown}}\underset{}{\overset{N - \bar{Al}Cl_3}{C}} \longrightarrow PhCN + AlCl_3 + HCl$$

Scheme 6.

Both of the mechanisms are in accordance with the isomer distributions observed in the reaction (Table 5).

Table 5. Isomer distributions of aromatic nitriles formed in reaction with cyanogen chloride/aluminium chloride.

Compound	Isomer distributions of nitriles, %		
	ortho or α-	*meta* or β-	*para*
Anisole	11	0	89
Toluene	28	0	72
Naphthalene	92	8	

As is evident from the preceding discussions and can be seen in the experimental part it is possible to introduce a cyano group into an aromatic ring under very different reaction conditions. Heterolytic cyanation can take place at the electrode surface in an anodic cyanation reaction, under influence of ultraviolet light in solution or in the presence of a strong Lewis acid. The isomer distributions of nitriles formed follow the same general pattern. The reaction conditions of the two radical cyanations are very much different. In one of them, ultraviolet light is used, in the other, diazotation in acid solution generates the cyano radical. Here too the isomer distributions are similar although not identical. The preparative possibilities of the reactions are promising but not fully investigated yet.

EXPERIMENTAL

General. Solvents and starting materials were purified and checked before use by VPC. Reference substances were prepared by standard methods if not commercially available (see Part I[1]). Analyses were made with VPC (Perkin-Elmer 880 equipped with 5 % neopentylglycol succinate on Chromosorb P) and the retention times of the products from

the reactions were compared with reference substances. In some cases IR, UV, NMR, and mass spectra were used as additional proof of the structures.

Anodic cyanation. A solution of 0.1 mol aromatic compound and 0.2 mol sodium cyanide in 300 ml methanol was electrolysed af the half-wave potential of the aromatic compound. After 10 % of the theoretically calculated amount of charge had passed, the electrolyte was evaporated, extracted with ether and the ether solution analysed by VPC.

Photolysis of aromatic compounds in cyanide solution. A solution of 0.1 mol aromatic compound and 0.2 mol sodium cyanide in 120 ml methanol was photolysed for 50 min with a high pressure mercury lamp mounted in the reaction flask. The solution was worked up as before.

Photolysis of iodine cyanide in the presence of aromatic compounds. A solution of 0.1 mol aromatic compound and 0.5 g iodine cyanide in 120 ml methanol was photolysed as described. Use of the less polar solvent carbon tetrachloride gave approximately the same results.

Diazotation of cyanamide in the presence of aromatic compounds. See Part I.[1]

Cyanation with cyanogen chloride/aluminium chloride. A solution of 0.01 mol aromatic compound and 1.0 g aluminium chloride in 50 ml carbon disulfide was stirred during inlet of cyanogen chloride in the cold. After reflux for 15 min and distillation the rest was poured on ice and extracted. A preparative run with 0.5 mol toluene and equivalent amount of cyanogen chloride (precondensed in a cooling trap) gave a yield of 39 % tolunitriles.

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