Photochemical Production of the Electrophilic Cyano-radical: Homolytic Aromatic Cyanation

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The reaction of cyano-radicals, produced by the photolysis of cyanogen iodide, with aromatic compounds afforded aromatic nitriles. The isomer ratios and the relative reactivities were determined for a variety of monosubstituted benzenes and the results indicated that the cyano-radical preferably attacks relatively electronegative sites. The partial rate factors for the *meta*- and *para*-positions correlate with σ^+ to give a slope of $-0{\cdot}42$. It is concluded that cyano-radical possesses a slight electrophilic character.

AROMATIC substitutions can be effected by carbon free radicals whatever the hybridization of the carbon atom holding the unpaired electron may be; aromatic substrates can thus be substituted by aromatic [1,2] as well as by aliphatic [3,4] radicals and examples are known of reactions carried out with ethylenic [5] and acetylenic [1] radicals. Although all these substitutions retain their essential homolytic characteristics, the various radicals do not behave in exactly the same way but can present electrophilic or nucleophilic properties.

Results are here reported concerning the chemical behaviour in aromatic substitution reactions of the *sp*-hybridized carbon radical cyano, ·CN. In view of the results obtained with the PhC≡C· radical,[1] the cyano-radical is expected to exhibit slight electrophilic character; this can also be predicted from the low value of the electron affinity and very high ionization potential of this radical.[6] Moreover the steric requirements in the substitution step can be predicted to be less for the cyano-radical than for the other previously reported carbon radicals.

Few examples have been reported in which cyano-radicals have been postulated as reaction intermediates. Cyano-radicals from the photolysis of mercury(II) cyanide react with organic solvents by addition and abstraction, and sometimes give isonitriles as well as nitriles.[7] Mercury(II) cyanide is not, however, photolysed in aromatic solvents. Cyanation of several monosubstituted benzenes has been carried out by anodic oxidation of cyanide ions;[6] although cyano-radicals could be involved in these reactions the orientation and reactivity data obtained were not the results of an homolytic aromatic cyanation, but could rather be interpreted as resulting from the generation of an aromatic ion radical at the anode by the loss of a π-electron from the aromatic substrate.[8] In a comprehensive study by N. Kharasch and his co-workers [9] on the photolysis of iodo-derivatives, cyanogen iodide was also investigated. The reaction in benzene afforded, after hydrolysis, benzoic acid in 50% yield, indicating that aromatic cyanation had occurred. In view of the ready availability of the material and of the expected homolytic nature of the reaction the photolysis of cyanogen iodide was employed throughout this work to study the character of the cyano-radical.

From the irradiation of ICN in benzene iodine was released; benzonitrile could be isolated and a detailed analysis of the mixture was carried out by g.l.c. to detect other possible products. In view of the results of the photolysis of mercuric cyanide in cyclohexene,[7] particular care was paid to the possible presence of phenyl isocyanide but no trace of it could be detected; the possible isomerization to nitrile was also tested, the starting isocyanide being however recovered unchanged after irradiation, no nitrile being formed.

The study was then carried out with the competitive method; the photolysis of ICN was effected in equimolar benzene–monosubstituted benzene mixtures and the reactions were analysed by g.l.c. The values of the relative reactivities thus determined (${}^{X}_{H}K$) are reported

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[1] G. Martelli, P. Spagnolo, and M. Tiecco, *J. Chem. Soc.* (*B*), 1970, 1413.

[2] D. H. Hey, Arylation of aromatic compounds, in G. H. Williams, 'Advances in Free-Radical Chemistry,' Logos Press Ltd., London, **1967**, vol. II, p. 47; R. Ho, T. Migita, N. Morikawa, and O. Simamura, *Tetrahedron*, 1965, **21**, 955.

[3] G. E. Corbet and G. H. Williams, *J. Chem. Soc.*, 1964, 3437; 1966, 877; B. Cowley, R. Norman, and W. Waters, *ibid.*, p. 1959, 1799; E. Eliel, K. Rabindran, and S. Wilan, *J. Org. Chem.*, 1957, **22**, 859.

[4] J. R. Shelton and G. W. Uzelmeier, *J. Amer. Chem. Soc.*, 1966, **88**, 5222.

[5] P. Spagnolo and M. Tiecco, *Tetrahedron Letters*, 1968, 2313.

[6] K. Koyama, T. Susuki, and S. Tsutsumi, *Tetrahedron*, 1966, **23**, 2675.

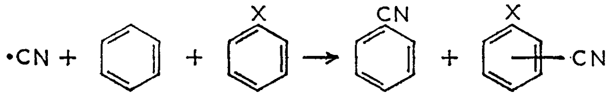
[7] K. Yoshida and S. Tsutsumi, *J. Org. Chem.*, 1966, **31**, 3635.

[8] T. Susuki, K. Koyama, A. Omori, and S. Tsutsumi, *Bull. Chem. Soc. Japan*, 1968, **41**, 2663.

[9] N. Kharasch, W. Wolf, T. Erpelding, P. G. Naylor, and L. Tokes, *Chem. and Ind.*, 1962, 1720.

in the Table 1 which also contains the isomer ratios and the partial rate factors (k) for the *ortho-*, *meta-*, and *para*-positions. The polar character of the cyano-radical was tested by employing as substrates aromatic compounds holding activating and deactivating substituents; moreover from the gradual variation of the bulk of the substituents along the series of alkylbenzenes and halogenobenzenes the steric requirements of the substitution could be investigated.

$$ICN \xrightarrow{h\nu} I\cdot + \cdot CN$$



X = OMe, Me, Et, Pr^i, Bu^t, F, Cl, Br, CO_2Me

With all the alkylbenzenes the percentage of *ortho*-substitution, as well as k_{ortho}, remain substantially unchanged; only with t-butylbenzene is a slight decrease observed. This situation is unlike that observed with all the other carbon free radicals studied where a gradual decrease of the proportion of *ortho*-substitution is observed as the steric bulk of the substituent increases.[1,2] Considerable variations of the *ortho*-substitutions were not observed along the series of the halogenobenzenes. The steric requirement in the substitution step is thus, as expected, lower for the cyano-radical than for other radicals and indeed the percentage of *ortho*-substitution by the cyano-radical in t-butylbenzene is considerably higher than those for substitution by other radicals.

TABLE 1

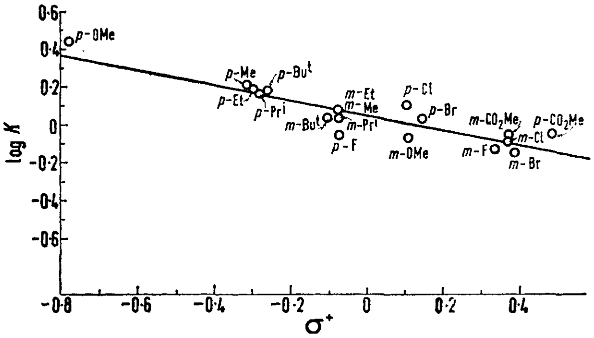
Isomer ratios, *meta* : *para*-ratios, relative reactivities ($\frac{X}{H}K$) and partial rate factors (k) for substitution of cyano-radical in monosubstituted benzene derivatives

	Isomer ratios/%							
Substrate	*ortho*	*meta*	*para*	m/p	$\frac{X}{H}K$	k_{ortho}	k_{meta}	k_{para}
Anisole	46·5	20·2	33·3	0·61	1·4	1·99	0·85	2·79
Toluene	42·3	34·4	23·3	1·48	1·15	1·45	1·19	1·60
Ethylbenzene	42·3	34·9	22·8	1·54	1·13	1·43	1·18	1·54
Cumene	44·1	33·0	22·9	1·44	1·07	1·41	1·05	1·46
t-Butylbenzene	38·5	36·5	25·0	1·44	0·98	1·13	1·06	1·47
Fluorobenzene	36·9	39·5	23·6	1·68	0·62	0·68	0·73	0·87
Chlorobenzene	37·5	35·3	27·2	1·30	0·78	0·87	0·82	1·27
Bromobenzene	38·7	34·8	26·5	1·31	0·68	0·78	0·71	1·08
Methyl benzoate	36·0	41·8	22·2	1·9	0·67	0·72	0·84	0·89

In the alkylbenzenes and halogenobenzenes, the values of the *meta* : *para*-ratios do not greatly differ; in every case however they are lower than the corresponding values[1] for reaction with the phenyl radical, indicating that the extent of *para*-substitution is greater for the cyano- than for the phenyl radical. This is further verified with anisole where the *meta* : *para*-ratio is very low and the variations are more apparent. The value of the *meta* : *para*-ratio for the cyanation of methyl benzoate is instead very high and is considerably higher than that reported for the phenyl radical. The proportion of *para*-substitution is thus increased by groups which increase the electron density at that position and *vice versa*; this indicates that the cyano-radical seeks to react at the relatively electronegative sites of the aromatic substrates.

This electrophilic behaviour of the ·CN radical is also supported by the relative reactivities. These values are not very widely spread indicating that the cyanation is not very selective; nevertheless it is apparent that anisole and the alkylbenzenes are more reactive than benzene, while methyl benzoate and the halogenobenzenes are less reactive. Thus the qualitative considerations of both the isomer ratios and the relative reactivities are in agreement with the expectation that the cyano-radical should be slightly electrophilic.

The partial rate factors for *meta-* and *para*-substitution correlate with σ^+ parameters according to the Hammett relationship giving a line of slope —0·42 (correlation coefficient 0·91) (see Figure). The negative value of the slope in the present case lends further support to the idea of the electrophilicity associated with the cyano-radical discussed above. The use of σ parameters leads to a line with slope of —0·52 (correlation coefficient 0·81) but with the point of *p*-methoxy significantly deviating from the plot; the better correlation of the results of the homolytic aromatic cyanation with σ^+ rather than σ probably indicates that, among the structures which could contribute to the transition state of this substitution, polar structures should not be neglected.



EXPERIMENTAL

Cyanogen iodide, *o*-, *m*-, and *p*-bromobenzonitrile, *o*-, *m*-, and *p*-chlorobenzontrile, *p*-fluorobenzonitrile, and *m*-, and *p*-toluonitrile were commercial products, *o*-Toluonitrile,[10]

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[10] L. Friedman and H. Shechter, *J. Org. Chem.*, 1961, **26**, 2522.

o-,[10] *m*-,[11] and *p*-ethylbenzonitrile,[12] *m*-isopropylbenzonitrile,[13] and *p*-[14] and *m*-t-butylbenzonitrile[13] were prepared as in the literature. All the other substituted benzonitriles were prepared by the method of Friedman and Shechter[10] from the corresponding iodides. The general procedure was as follows: a mixture of the iodo-aromatic compound (0·01 mol), cuprous cyanide (0·015 mol) and dimethylformamide (40 ml) was stirred and refluxed for 6 h. The resulting reaction mixture was poured into a solution of hydrated ferric chloride (40 g), conc. hydrochloric acid (10 ml), and water (60 ml) and warmed at 60—70°C for 20 min. After cooling, benzene was added and the two layers separated; the benzene solution was dried and evaporated. The residue was chromatographed through a silica gel column; elution with light petroleum (b.p. 40—60°) afforded the unchanged iodo-aromatic compound. The crude nitrile was obtained by passage through the column of a mixture (1 : 9) of diethyl ether and light petroleum; after evaporation of the solvent the product was purified by distillation or crystallization. The following substituted benzonitriles were prepared in this way (% yields and m.p. or b.p./mm are given in that order); *o*-F, 64, 90—92°/15 (lit.,[15] 130°/35); *m*-F, 74, 90°/15 (lit.,[16] 89°/40); *o*-OMe 78, 140°/18 (lit.,[17] m.p. 21·5—22°); *m*-OMe, 60, 128—130°/18 (lit.,[18] 111—112°/13); *p*-OMe, 71, 60° (lit.,[19] 61); *o*-$CHMe_2$, 70, 103—105°/15 (lit.,[20] 101—104°/15); *p*-$CHMe_2$, 50, 126°/17 (lit.,[21] 122—124°/9); *p*-CMe_3, 75, 132—134°/15 (lit.,[21] 126°/14).

Photolysis of Cyanogen Iodide in Benzene.—A solution of cyanogen iodide (2 g) in benzene (300 ml) was put in a cylindrical vessel, surrounded by a water-jacket, with a central neck from which the lamp (Hanau P.L. 368) was immersed. The solution was magnetically stirred and irradiated for 24 h. The mixture was washed with sodium thiosulphate and dried and the solvent distilled off; the residue was chromatographed through a silica gel column using a mixture (9 : 1) of light petroleum (b.p. 40—60°) and diethyl ether as eluant. After a few fractions containing cyanogen iodide, benzonitrile was collected (0·7 g) and purified by distillation; it was identified by comparison of its i.r. spectrum with that of the authentic compound. G.l.c. of the reaction mixture, under several experimental conditions, showed the presence of benzonitrile as the sole product.

Determination of Isomer Distributions and Relative Reactivities for Homolytic Cyanation.—Solutions (*ca.* 0·1M) of cyanogen iodide in an equimolecular mixture of benzene and a monosubstituted benzene were put in a stoppered 5 ml quartz conical flask and immersed in a water-bath at 15—20 °C. The mixtures were irradiated for 24 h with the mercury lamp, also immersed in the bath, *ca.* 1 cm from the conical flask. The mixtures were then analysed by g.l.c. without manipulation. Three independent reactions were carried out with each substrate (only two with methyl benzoate). Results are in Table 2; the averaged values of the isomer ratios and of the reactive reactivities are in Table 1. The yields of substitution products were 30—50%. In some case, besides substituted benzonitrile, small amount of other products were detected by g.l.c.; their retention times were identical with those of the iodo-derivatives of the monosubstituted benzenes. The benzonitriles were identified by comparison of their retention times with those of authentic compounds; from experiments on a preparative scale, the single isomers were also isolated by a combination of column chromatography and preparative g.l.c. and their i.r. spectra compared with those of the independently prepared benzonitriles.

TABLE 2

Isomer ratios and relative reactivities for homolytic cyanation

Substrate	Isomer ratios/% *ortho*	*meta*	*para*	Relative reactivities	Column
Anisole	46·25	20·55	33·20	1·40	A
	47·00	19·91	33·09	1·38	A
	46·20	20·31	33·49	1·41	A
Toluene	43·34	34·06	22·60	1·17	B
	40·61	36·23	23·16	1·15	B
	42·95	33·00	24·05	1·13	B
Ethylbenzene	42·42	34·57	23·01	1·12	A
	42·02	35·54	22·44	1·14	A
	42·59	34·66	22·75	1·13	A
Cumene	43·76	33·10	23·14	1·05	A
	43·97	33·34	22·69	1·09	A
	44·65	32·56	22·79	1·06	A
t-Butylbenzene	38·48	36·37	25·15	0·95	B
	38·44	36·40	25·16	1·02	B
	38·64	36·21	25·15	0·97	B
Fluorobenzene	39·45	41·79	18·76	0·59	A
	38·72	41·28	20·00	0·61	A
	38·42	41·22	20·36°	0·66	A
Chlorobenzene	37·14	35·31	27·55	0·77	B
	37·71	35·02	27·77	0·78	B
	37·53	35·73	26·74	0·80	B
Bromobenzene	38·53	35·64	25·83	0·63	A
	38·59	36·21	25·20	0·69	A
	38·99	32·60	28·41	0·73	A
Methyl benzoate	35·07	42·61	22·32	0·67	C
	36·00	41·82	22·18	0·67	C

The g.l.c. analyses were carried out with a Varian Aerograph 1520 instrument equipped with flame ionization detector; a calibration for area-response differences between benzonitrile and substituted benzonitriles was made for every reaction with an internal standard. The following columns were employed on Aeropak 30 (80—100 mesh): (A) 5% Bentone 34 + 5% poly(phenyl ether) (3 m); (B) 5% LAC (3 m); (C) 10% FFAP (3 m).

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[11] G. Baddeley, *J. Chem. Soc.*, 1949, **5**, 229.

[12] E. R. Bissel and R. E. Spenger, *J. Org. Chem.*, 1959, **24**, 1146.

[13] H. S. Newman and E. K. Easterbrook, *J. Amer. Chem. Soc.*, 1955, **77**, 3763.

[14] T. Hayashi, K. Watanabe, and K. Hata, *Nippon Kagaku Zasshi*, 1962, **83**, 348; *Chem. Abs.*, 1963, **59**, 3826g.

[15] G. C. Finger, D. R. Dickerson, Tourady Adl, and T. Hodgins, *Chem. Comm.*, 1965, 430.

[16] R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. J. Davies, *J. Amer. Chem. Soc.*, 1963, **85**, 709.

[17] W. A. Lees and A. Buraway, *Tetrahderon*, 1963, **19**, 419.

[18] W. H. Carothers, C. F. Bickford, and G. J. Hurwitz, *J. Amer. Chem. Soc.*, 1927, **49**, 2908.

[19] M. F. Grundon and H. D. Scott, *J. Chem. Soc.*, 1964, 5674.

[20] P. A. S. Smith and E. P. Antoniades, *Tetrahedron*, 1960, **9**, 210.

[21] T. L. Brown, *J. Amer. Chem. Soc.*, 1959, **81**, 3232.