283. *The Mobility of Groups in Certain Benzonitriles.*

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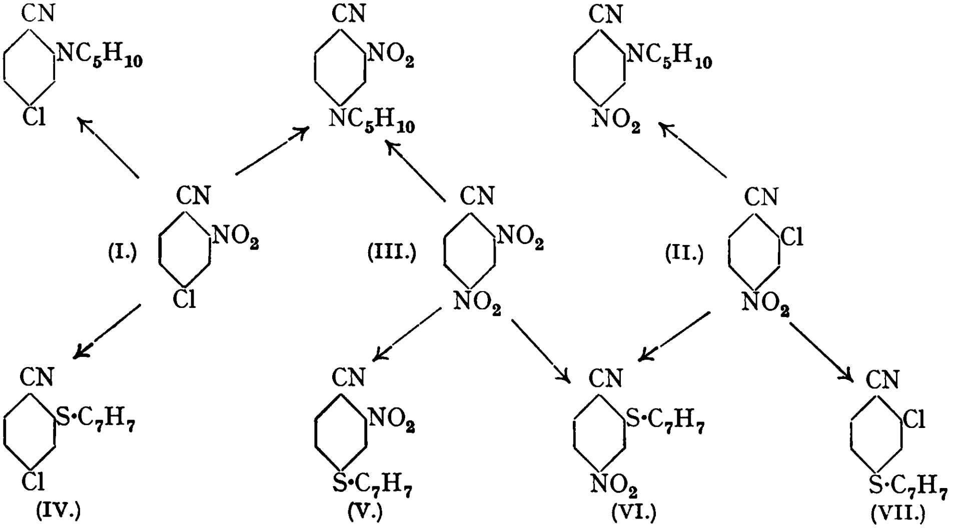
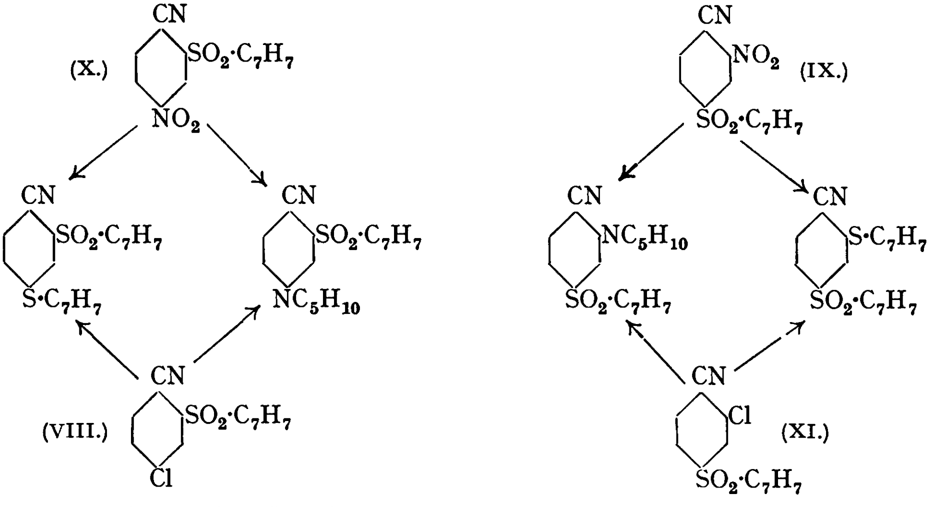
In a series of seven *op*-disubstituted benzonitriles it is shown that a chloro- or nitro-substituent is replaced in reactions with piperidine and with the sodium salt of thio-*p*-cresol. The topic is related to some general considerations on cationoid nuclear reactivity.

A HIGH degree of mobility in a potential anion attached to a benzene ring is associated in the great majority of cases with the presence of an *o*- or *p*-nitro-group (*op*-orienting towards anionoid reagents). It is well known, however, that other cationoid groups are individually capable of producing a similar, though much less powerful, effect and that combinations of cationoid groups sometimes produce, at centres where their orienting influences are cumulative, a degree of mobility comparable with that which results from the concerted action of nitro-groups. The significance of the latter fact is clarified by the pronounced mobility of nitro- and chloro-substituents in 2 : 4- and in 4 : 2-chloronitrodiphenylsulphones (Loudon and Robson, J., 1937, 242), where the orienting influences of the cationoid groups (*viz.*, NO_2 and SO_2Ph) are not cumulative, and where again the mobility is not solely attributable to the effect of the sulphonyl group as measured in the less reactive chlorodiphenylsulphones or even in nitrodiphenylsulphones. Clearly the common factor promoting the efficiency of weak cationoid groups is the presence of electron-restraining substituents in the nucleus. Kenner (J., 1914, **105**, 2717) includes the " negative " condition of the nucleus among factors contributing to cationoid reactivity, but, as a practical aid for the study of uncatalysed reactions oriented by individual cationoid groups, its consequences have been neglected. The work described below illustrates the effect of the cyano-group operating in a suitably tempered nucleus.

In selecting the nitriles (I), (II), and (III) for investigation we were influenced by several more specific considerations. First, Baudet (*Rec. Trav. chim.*, 1924, **43**, 707) has shown that 1-chloro-2-cyano-4-nitrobenzene approaches 1-chloro-2 : 4-dinitrobenzene in rate of reaction with sodium methoxide; whence it may be argued that the cyano-group does exert a powerful influence in a suitable environment. Secondly, it may be anticipated that the stability of the carbon linkage with the nucleus will assist the cyano-group to secure directive control in the systems by blocking the competitive orienting influence of the nitro-group. Moreover, both considerations receive some measure of support from the recorded replacement of the nitro-group in *o*- or *p*-nitrobenzonitrile by the action of sodium methoxide (Reinders and Ringer, *ibid.*, 1899, **18**, 326, 330), and from the similar reactions probably implicit in the formation of 2-nitro-6-alkyloxybenzonitriles from *m*-dinitrobenzene, or of the corresponding 3-chloro-derivatives from 1-chloro-2 : 4-dinitrobenzene, by the action of potassium cyanide in methyl or ethyl alcohol (Van Heteren, *ibid.*, 1901, **20**, 107; Blanksma, *ibid.*, 1902, **21**, 424).



Attention was for the present confined to the reactions with two reagents, *viz.*, piperidine and the sodium salt of thio-*p*-cresol. It was found advantageous to employ the latter reagent in an aqueous medium, *e.g.*, aqueous alcohol, since reduction processes intervened in the absence of water : Richardson (J., 1926, 522) has found a similar behaviour in the interaction of alcoholic potassium hydroxide and *p*-chloronitrobenzene. All three nitriles reacted very readily, a chloro- or nitro-substituent, but in no case the cyano-group, being replaced. The relationships between the various products are shown in the diagram : in several cases indications were also found of concurrent replacements not represented in the products isolated; *e.g.*, (I) ⟶ (V) was indicated by the formation of chloride ions, but such reactions were not extensive. The *thio-ethers* (IV)—(VII) yielded the respective *sulphones* (VIII)—(XI) when oxidised with hydrogen peroxide in acetic acid, although in one case partial hydrolysis of the nitrile occurred, the product being a mixture of the cyano-sulphone (VIII) and the corresponding *benzamide*. These sulphones, which differ from the original nitriles in having a sulphonyl in place of a nitro-group, were employed



in a second set of experiments with the piperidine and the mercaptide. Here again, the ensuing reactions were very rapid and it is noteworthy that, in each case, the sulphonyl as well as the cyano-group has survived in the products obtained (diagram, p. 1522). With all the nitriles examined, the thiol reactions were indistinguishably rapid under the conditions employed, but those nitriles, *viz.*, (VIII) and (XI), which contain no nitro-substituent, reacted more slowly than the others with piperidine.

Reactions of the type under consideration are in many respects the complement of those occurring at nuclear anionoid centres. Both types are subject to the *op*-directive influences of appropriate substituents graded in power, but the innate behaviour of the benzene ring is anionoid and must supplement the effect of an anionoid substituent and oppose that of a cationoid group. It remains to be seen in how far an effective orientation by other cationoid groups can be secured by the provisions made here, but it may be noted that the main difference in behaviour between these nitrobenzonitriles and the nitrodiphenylsulphones previously studied (*loc. cit.*, and J., 1939, 1618) arises from the mobility of the sulphonyl group, which in the latter compounds is itself occasionally replaced.

EXPERIMENTAL.

2-Chloro-4-nitroaniline was prepared by the following modification of a patent (*Centralbl.*, 1905, **76**, I, 415). Nitric acid (18 c.c., *d* 1·42) was added to *p*-toluenesulphon-2-chloroanilide (60 g.) dissolved in hot acetic acid (600 c.c.) in a 3-l. flask fitted with an efficient reflux condenser. Even at the b. p., nitration seldom occurred, but on allowing the solution to cool quietly a brown patch appeared on the surface of the liquid, and the violence of the ensuing reaction was diminished by shaking the flask at this stage. After boiling to remove oxides of nitrogen, the solution was diluted to about 1 l. with hot water, and on cooling, the 4-nitro-derivative, m. p. 165—166°, separated. This yielded the required aniline, m. p. 105°, on hydrolysis with 80% sulphuric acid. Further dilution of the mother-liquor from the nitration furnished a small quantity of p-*toluenesulphon-2-chloro-4 : 6-dinitroanilide,* m. p. 141° (from alcohol) (Found: N, 11·3. $C_{13}H_{10}O_6N_3ClS$ requires N, 11·3%). From this, 2-chloro-4 : 6-dinitroaniline, m. p. 157° (cf. Ullmann, *Ber.*, 1911, **44**, 3734), was obtained by hydrolysis.

2-*Chloro-4-nitrobenzonitrile* (II).—The following method (cf. preparation of 2 : 4-dinitrobenzonitrile; Storrie, J., 1937, 1746) was worked out in collaboration with Dr. Storrie. A diazotised solution of 2-chloro-4-nitroaniline [from the amine (6·9 g.), dissolved in acetic acid (40 c.c.), added to sodium nitrite (3·1 g.) in concentrated sulphuric acid (22 c.c.)] was slowly stirred into a cooled solution of nickelocyanide [from potassium cyanide (14 g.) in water (60 c.c.), added to a hot solution of nickel chloride (6·6 g.) in water (40 c.c.)] mixed with sodium carbonate (38 g.) in water (200 c.c.). When addition was complete (30 mins.) the temperature was slowly raised to 60—70° and maintained thereat for about 30 mins. After cooling, the solid *product* was filtered off, distilled in steam, and crystallised from alcohol, forming almost colourless needles, m. p. 81° (Found: N, 15·3. $C_7H_3O_2N_2Cl$ requires N, 15·3%). 4-Chloro-2-nitrobenzonitrile, m. p. 97—98° (cf. Claus and Kurz, *J. pr. Chem.*, 1888, **37**, 197), was prepared similarly except that the steam-distillation was omitted.

4-*Chloro*-2-p-*tolylthiobenzonitrile* (IV).—Aqueous sodium hydroxide (3 c.c.; 10% solution) was added gradually to a solution of 4-chloro-2-nitrobenzonitrile (1 g.) and thio-*p*-cresol (0·7 g.) in alcohol at 70°. A transient brown colour developed at each addition and was allowed to fade before another addition was made. The oily precipitate, which appeared towards the end of the reaction, solidified on cooling and was purified from alcohol, yielding thick colourless needles, m. p. 117° (Found: N, 5·6. $C_{14}H_{10}NClS$ requires N, 5·6%). Chloride ions were present in the reaction solution, but *p*-tolyl disulphide was the only other organic product found.

4-*Chloro*-2-p-*toluenesulphonylbenzonitrile* (VIII) was obtained when (IV) was oxidised by hydrogen peroxide in acetic acid at 100°. It crystallised from the reaction liquid in lustrous plates, m. p. 187° (Found: N, 4·9. $C_{14}H_{10}O_2NClS$ requires N, 4·8%), and yielded 4-*chloro*-2-p-*toluenesulphonylbenzoic acid,* m. p. 155° (Found, after heating at 100° in a high vacuum: C, 54·2; H, 3·5. $C_{14}H_{11}O_4ClS$ requires C, 54·1; H, 3·5%), when hydrolysed with 70% sulphuric acid. Dilution of the oxidation mother-liquor gave a fraction distinct from (VIII) and melting at 196° after crystallisation from acetic acid. This was shown to be 4-*chloro*-2-p-*toluenesulphonylbenzamide* (Found: N, 4·6. $C_{14}H_{12}O_3NClS$ requires N, 4·5%) by its conversion (*a*) into the acid of m. p. 155° when treated in warm sulphuric acid (30%) with sodium nitrite

(5% aqueous solution), and (*b*) into the nitrile (VIII) when heated with phosphoric oxide at 200°.

4-*Nitro*-2-p-*tolylthiobenzonitrile* (VI) formed the main product when aqueous sodium hydroxide (2 c.c.; 10% solution) was slowly added to 2 : 4-dinitrobenzonitrile (1 g.) and thio-*p*-cresol (0·64 g.) dissolved in hot alcohol. The solid which separated on cooling (filtrate A) crystallised from alcohol (filtrate B) in fine yellow needles, m. p. 156° (Found: N, 10·6. $C_{14}H_{10}O_2N_2S$ requires N, 10·4%). The structure is established by the formation of the same compound from 2-chloro-4-nitrobenzonitrile (cf. below). Oxidation with hydrogen peroxide in the usual way gave 4-*nitro*-2-p-*toluenesulphonylbenzonitrile* (X) in plates, m. p. 176° (Found: C, 55·4; H, 3·4; N, 9·4. $C_{14}H_{10}O_4N_2S$ requires C, 55·6; H, 3·3; N, 9·3%).

2-*Nitro*-4-p-*tolylthiobenzonitrile* (V) was obtained when the filtrates A and B (above) were cautiously diluted with water. After repeated crystallisation from alcohol, it formed pale yellow plates, m. p. 115° (Found: N, 10·5. $C_{14}H_{10}O_2N_2S$ requires N, 10·4%). Since considerable loss is involved in the purification of (V), 2-*nitro*-4-p-*toluenesulphonylbenzonitrile* (IX) was prepared by direct oxidation of the crude material obtained from the filtrates A and B. The oxidation product was extracted with boiling alcohol, in which the isomer (X) is much the more soluble, leaving the required compound. It formed colourless needles, m. p. 201°, from acetic acid (Found: C, 55·4; H, 3·4; N, 9·4. $C_{14}H_{10}O_4N_2S$ requires C, 55·6; H, 3·3; N, 9·3%).

When the method described for (IV) was applied to 2-chloro-4-nitrobenzonitrile, the transient coloration suddenly gave place to a permanent bright crimson, and a red sulphur-free solid separated when about half the alkali had been added. The same product was rapidly formed when an alcoholic solution of the nitrile was treated with a mercaptide solution prepared from the thiol and alcoholic sodium ethoxide, and it was also obtained when the nitrile was subjected to Nisbet's procedure for preparing azoxy-compounds (J., 1927, 2081). In different preparations the colour shade of the product varied from orange to red, suggesting a mixture of azoxy- and azo-compounds, and one sample which crystallised from dioxan in red needles had m p. 221—223° (Found: C, 55·6; H, 2·1; N, 17·8. $C_{14}H_6ON_4Cl_2$ requires C, 53·0; H, 1·9; N, 17·7%. $C_{14}H_6N_4Cl_2$ requires C, 55·8; H, 2·0; N, 18·6%).

2-*Chloro*-4-p-*tolylthiobenzonitrile* (VII).—2-Chloro-4-nitrobenzonitrile (1 g.) and an excess of thio-*p*-cresol (1·1 g.), dissolved in alcohol at 40°, were slowly treated with 10% aqueous sodium hydroxide, the developed colour being allowed to fade between each addition. The appearance of a permanent crimson colour (no solid was precipitated under these conditions) when 4—4·2 c.c. of the alkali had been added was taken as the end-point of the reaction. The oil obtained on cooling was separated from the mother-liquor by decantation and became solid when shaken with a little alcohol. The solid crystallised from alcohol as a mixture of colourless prisms and fine yellow needles, which were separated by hand. The latter were identified as (VI), m. p. and mixed m. p. 156°, and the prisms, after further purification, gave the *product* (VII), m. p. 95° (Found: C, 64·75; H, 3·8. $C_{14}H_{10}NClS$ requires C, 64·7; H, 3·85%). 2-*Chloro*-4-p-*toluenesulphonylbenzonitrile* (XI), plates m. p. 175°, was obtained by oxidising (VII) with hydrogen peroxide in acetic acid (Found: C, 56·6; H, 3·6. $C_{14}H_{10}O_2NClS$ requires C, 56·3; H, 3·4%).

2-p-*Toluenesulphonyl*-4-p-*tolylthiobenzonitrile*.—Sodium hydroxide (10% aqueous solution) was added to a boiling solution of thio-*p*-cresol and the sulphone (VIII) or (X) in alcoholic dioxan. After a few minutes' refluxing, the solution was cooled and diluted with water, and the resulting solid was crystallised from alcohol; in each case it formed plates, m. p. 132°, rising to 136° after some weeks (Found: N, 3·9. $C_{21}H_{17}O_2NS_2$ requires N, 3·7%).

4-p-*Toluenesulphonyl*-2-p-*tolylthiobenzonitrile* was similarly prepared from the sulphones (IX) and (XI). It was very soluble in alcohol but crystallised from benzene–ligroin in colourless needles, m. p. 170° (Found: C, 66·6; H, 4·6. $C_{21}H_{17}O_2NS_2$ requires C, 66·5; H, 4·5%).

4-*Chloro*-2-*piperidinobenzonitrile*.—4-Chloro-2-nitrobenzonitrile (I) was refluxed for a few minutes with piperidine (3 c.c. per g.). After cooling, ether was added, and the solid (A) was filtered off and washed with ether. The ethereal filtrate and washings were concentrated, excess of piperidine removed by shaking with water, and the residue crystallised first from ligroin and then from alcohol. The product was obtained in pale yellow plates, m. p. 77° (Found: N, 12·8. $C_{12}H_{13}N_2Cl$ requires N, 12·8%).

2-*Nitro*-4-*piperidinobenzonitrile*.—(*a*) The solid (A) was freed from piperidine salts by washing with water and then crystallised several times from alcohol, yielding red needles, m. p. 143° (Found: N, 18·25. $C_{12}H_{13}O_2N_3$ requires N, 18·2%). (*b*) 2 : 4-Dinitrobenzonitrile was heated as above with piperidine; the gum which was precipitated by addition of water solidified when shaken with dilute hydrochloric acid. Crystallisation from alcohol gave the red needles, m. p. and mixed m. p. 143°, but subsequent fractions could not be obtained crystalline.

4-*Nitro*-2-*piperidinobenzonitrile*.—2-Chloro-4-nitrobenzonitrile was heated for a few minutes with piperidine, and the tar which resulted from addition of water was extracted with concentrated hydrochloric acid. Dilution of the extract with water gave the crude product, which, after several crystallisations from alcohol, separated in bright yellow plates, m. p. 107° (Found : N, 18·15. $C_{12}H_{13}O_2N_3$ requires N, 18·2%). Nitrite as well as chloride ions were detected in the reaction mixture.

2-p-*Toluenesulphonyl*-4-*piperidinobenzonitrile*.—The sulphones (X) and (VIII) were refluxed with piperidine for 3 and for 30 mins. respectively. In each case the product obtained on cooling and addition of water crystallised from alcohol in plates, m. p. and mixed m. p. 198° (Found : N, 8·4. $C_{19}H_{20}O_2N_2S$ requires N, 8·2%).

4-p-*Toluenesulphonyl*-2-*piperidinobenzonitrile* was similarly prepared from the sulphones (IX) and (XI) and formed colourless needles, m. p. 150°, from alcohol (Found : N, 8·4. $C_{19}H_{20}O_2N_2S$ requires N, 8·4%).

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