the ideal case. The ionic radii are as follows[9]: $NH_4^+ = 1.43$ Å., $Tl^+ = 1.44$ Å., and $K^+ = 1.33$ Å. Thus difference in size of the substituting ion is very important in determining deviations from ideality with respect to Vegard's law, but seems of little importance from the standpoint of the distribution ratios between liquid solutions and solid solutions. The data on the system potassium alum–ammonium alum,[3] where the maximum deviation from Vegard's law is -0.003 Å. for a_0 in the neighborhood of 50–50 mole per cent., bear this out.

In the chrome alum series both the A and B members of a duplicate pair gave the same diffraction pattern with identical lattice constants. The relative intensities were also alike indicating that the coördination of the chromium in the final mixed alum was the same regardless of the direction from which equilibrium was reached.

The authors wish to express their thanks and appreciation to Professor J. E. Ricci for his kindness in making the solid solution samples available. They also wish to acknowledge with gratitude a grant from the Graduate School of the

(9) Stillwell, "Crystal Chemistry," McGraw-Hill Book Co., New York, N. Y., 1938, p. 417.

University of Minnesota under which this study was carried out.

Summary

1. Solid solutions of the following pairs of alums have been studied by means of X-rays: $TlAl(SO_4)_2 \cdot 12H_2O$–$NH_4Al(SO_4)_2 \cdot 12H_2O$, $TlAl(SO_4)_2 \cdot 12H_2O$–$KAl(SO_4)_2 \cdot 12H_2O$, and $NH_4Cr(SO_4)_2 \cdot 12H_2O$–$KCr(SO_4)_2 \cdot 12H_2O$.

2. The thallium–ammonium alum pair follows Vegard's law perfectly, while the other two pairs deviate slightly from the law.

3. The difference in size of the substituting ions is important in determining deviations from Vegard's law, but seems to have little bearing on the distribution ratios between liquid solutions and solid solutions and their deviation from the ideal case.

4. No change in the coördination of the chromium was noted in the chrome alum series for final mixed alums which approached equilibrium from opposite directions.

5. The following new values are reported for the lattice constants of the pure alums at $25 \pm 0.1°$:

$NH_4Al(SO_4)_2 \cdot 12H_2O$	$a_0 = 12.215 \pm 0.001$ Å.
$TlAl(SO_4)_2 \cdot 12H_2O$	$a_0 = 12.206 \pm 0.001$ Å.

The Steric Inhibition of Resonance. II.[1] Rates of Reaction of Nitro- and Cyano-aryl Halides

By William Carl Spitzer[2] and George Willard Wheland

Wheland and Danish[1] recently presented chemical evidence confirming the hypothesis[3] that resonance in aromatic nitro compounds could be partially inhibited by methyl substituents ortho to the nitro groups. However, the effect which they observed was rather small in magnitude, and its interpretation was made somewhat uncertain by the lack of quantitative data. For that reason, it seemed desirable to examine the problem in greater detail and in a more quantitative manner. The present paper describes the results of such an investigation.

(1) For the first paper of this series, see G. W. Wheland and A. A. Danish, This Journal, 62, 1125 (1940).

(2) Abstract of a thesis presented by W. C. Spitzer to the Faculty of the Division of Physical Sciences of the University of Chicago in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1940.

(3) R. H. Birtles and G. C. Hampson, J. Chem. Soc., 10 (1937); C. E. Ingham and G. C. Hampson, ibid., 981 (1939).

As is well known, the reaction of an aromatic halide with an anionoid[4] or nucleophilic[5] reagent, such as hydroxide ion, alkoxide ion, ammonia, or the like, is greatly accelerated by the presence of one or more nitro groups ortho or para to the halogen atom. This activating effect of the nitro group is exerted also, but to a smaller extent, by a number of other meta-directing groups, including the carboxyl, aldehyde, and cyanide groups.[6] On the other hand, methyl substituents appear to exert the opposite effect and, especially when in the ortho and para positions, to make the reaction more difficult.[7] In accordance with the theory

(4) A. Lapworth, Nature, 115, 625 (1925).

(5) C. K. Ingold, J. Chem. Soc., 1120 (1933); Chem. Rev., 15, 225 (1934).

(6) M. Schöpff, Ber., 22, 3281 (1889); 23, 3440 (1890); 24, 3771 (1891).

(7) H. Lindemann and A. Pabst, Ann., 462, 24 (1928); N. Campbell, W. Anderson and J. Gilmore, J. Chem. Soc., 446 (1940).

of reactivity which has been developed principally by Robinson[8] and by Ingold,[9] these various effects are to be related to alterations in the distribution of electric charge within the aromatic ring. In p-nitrobromobenzene, for example, resonance with a quinoid structure of the type A tends to produce an open sextet of electrons upon the
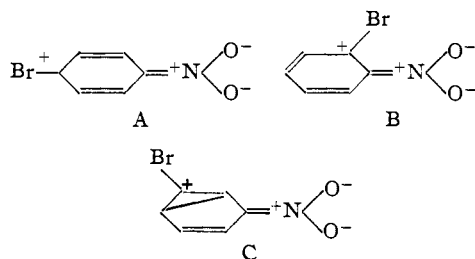
carbon atom carrying the halogen. As a result of this, the substance reacts more easily with such reagents as the ones mentioned above, since these, having unshared pairs of electrons, presumably require an open sextet at the point of attack. In o-nitrobromobenzene, resonance with the structure B activates the molecule in the same way as in the para derivative. In the meta compound, on the other hand, little if any activation occurs, in consequence of the relative instability of the meta quinoid structure C. The carboxyl, aldehyde and cyanide groups introduce possibilities for resonance similar to those just mentioned in connection with the nitro group, and consequently their activating effect can be interpreted along similar lines. The deactivation caused by a methyl substituent, on the other hand, is presumably to be referred to an inductive effect initiated by the methyl group moment.[10]

In view of the above discussion, it is evident that the activating effect of an ortho or para nitro, carboxyl, aldehyde, or cyanide group should be greatly decreased if the resonance of the type described were inhibited in some way. The work of Birtles and Hampson[3] and of Wheland and Danish[1] suggests that, in the case of the nitro compounds, this inhibition could be achieved by the placing of methyl or other bulky substituents in the two positions ortho to the nitro group.

From analogy, a similar result would be expected with the corresponding carboxyl and aldehyde derivatives, but not with the cyanides. This follows from the fact that the inhibition of resonance is the result of a steric interaction which twists the nitro, and presumably also the carboxyl and aldehyde, groups out of the plane of the benzene ring, but which can have no such effect upon the linear cyanide group. The deactivating effect of a methyl substituent should not be subject to steric inhibition, since it probably is not due to resonance; in any case, it is comparatively small and an experimental study of it from this point of view would be difficult.

A few reactions[11] have been reported which at first sight appear to be anomalous, but which can be readily interpreted on the basis of the considerations of the preceding paragraphs. Although largely reactions of dinitro compounds instead of nitrohalogen compounds, these are of the same type as the ones discussed heretofore, since they consist of simple replacements of a nitro group by a methoxyl, amino, or alkyl amino group, as the case may be. A typical example is provided by 2,5-dinitro-m-xylene, D, which was found by Ibbotson and Kenner[11] to be transformed into
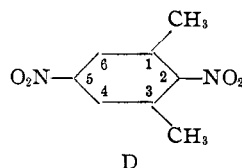
2-amino-5-nitro-m-xylene on being treated with methyl alcoholic ammonia. This result seems surprising because the nitro group which is replaced is hindered sterically (in the classical sense[12]) and also is ortho to the deactivating methyl substituents, while the nitro group which does not react is unhindered and also is merely meta to the methyl substituents. From the point of view of inhibition of resonance, however, the result is not unreasonable; the nitro group in position 5 activates, but is not effectively activated by, the one in position 2, since the former is free to assume the necessary planar configuration while the latter is not. It is to be noted that one could not have predicted in advance which of the two opposing effects would be the
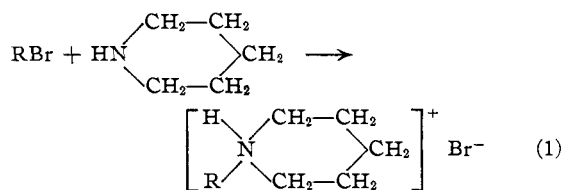
(8) R. Robinson, "Outline of an Electrochemical (Electronic) Theory of the Course of Organic Reactions," Institute of Chemistry of Great Britain and Ireland, London, 1932; *J. Soc. Dyers and Colourists*, Jubilee Journal, 65 (1934).

(9) For a discussion of the similar problem of orientation in aromatic substitution, see C. K. Ingold, *Rec. trav. chim.*, **48**, 797 (1929).

(10) This is the same effect that is supposed to account for the ortho–para orientation by methyl groups in the usual type of substitution reaction. See references 8 and 9, and also G. W. Wheland and L. Pauling, THIS JOURNAL, **57**, 2086 (1935).

(11) K. Ibbotson and J. Kenner, *J. Chem. Soc.*, **123**, 1260 (1923), and further references given there.

(12) The word "classical" is used here to avoid any ambiguity that might arise from the fact that the inhibition of resonance is also, in a sense, a steric effect. In the following, any mention of steric hindrance is to be understood as referring to the classical type.

greater: the steric hindrance combined with the direct deactivating influence of the methyl groups on the one hand, or the deactivation due to the inhibition of the resonance on the other. The experimental data show that the second is the more important here, although this need not be generally true and, in fact, is not true in the reactions reported below.

The present paper is concerned with the determination of the rates with which a series of nitrobromobenzenes and cyanobromobenzenes[13] react with piperidine in accordance with the equation

$$RBr + HN\diagup{\!\!\!\!\!\!\!}\begin{array}{c}CH_2{-}CH_2\\ \diagdown CH_2\\ CH_2{-}CH_2\end{array} \longrightarrow$$

$$\left[\begin{array}{c}H\diagdown \diagup CH_2{-}CH_2\\ N{\diagup}{\!\!\!}\diagdown CH_2\\ R\diagup \diagdown CH_2{-}CH_2\end{array}\right]^{+} Br^{-} \quad (1)$$

and the rates with which some of the same nitrobromobenzenes react with hydroxide ion in accordance with the equation

$$RBr + OH^{-} \longrightarrow ROH + Br^{-} \quad (2)$$

The simultaneous occurrence of steric hindrance and of the usual deactivating effect of methyl groups along with the inhibition of the resonance complicates the problem considerably and has made it necessary to investigate a rather extensive group of compounds, I–XII. A number of these were hitherto unknown and had to be prepared for the first time. The methods of synthesis and of proof of structure, as well as the details of the procedures used in the rate determinations, are described in the experimental part.

I II III IV V VI VII

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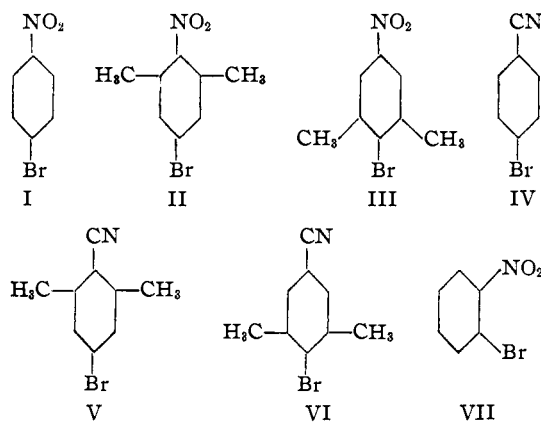
(13) It is shown later in the experimental part that the reactions of the cyanobromobenzenes are of the same type as those of the nitrobromobenzenes and that they follow the course indicated in equation (1).

VIII IX X XI XII
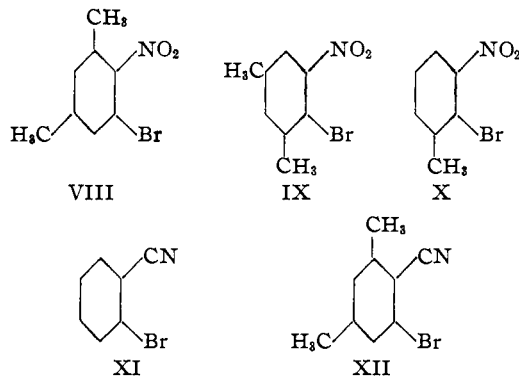
Discussion of Results

The substances studied divide themselves naturally into two sets consisting, respectively, of the ones in which the bromine atom is para, and of those in which it is ortho to the activating group (nitro or cyano). It will be convenient to discuss the two sets separately. The first consists of the compounds I–VI. As was expected, the reaction of *p*-nitrobromobenzene, I, with piperidine (Table I) was found to be considerably faster than that of 2-nitro-5-bromo-*m*-xylene,

TABLE I

REACTIONS OF NITROARYL BROMIDES WITH PIPERIDINE
Solvent: benzene, 10 cc.

Compound	Moles of compound	Moles of piperidine	Per cent. reaction in 8 hr.	Velocity constant $(k \times 10^3)$[a]
p-Nitrobromo-	0.001789	0.05084	52.8	94
benzene[b] (I)	.001783	.05084	51.9	92
	.001769	.05092	54.8	99
	.001785	.05081	55.2	100
	.001793	.05093	53.4	96
	.001803	.05096	54.2	98
2-Nitro-5-bromo-	.001789	.05081	2.4	3.1
m-xylene (II)	.001794	.05096	2.2	2.8
	.001782	.05098	2.0	2.5
2-Bromo-5-nitro-	.001794	.05096	0.64	0.81
m-xylene (III)	.001794	.05096	.43	.55
	.001793	.05091	.36	.43
o-Nitrobromoben-	.001796	.05096	82.2	1730
zene (VII)[c]	.001801	.05094	81.7	1700
4-Nitro-5-bromo-	.001793	.05096	12.3	16
m-xylene (VIII)	.001799	.05100	12.4	16
4-Bromo-5-nitro-	.001801	.05101	2.4	3.1
m-xylene (IX)	.001790	.05093	2.3	2.9
2-Bromo-3-nitro-	.001801	.05097	8.3	11
toluene (X)	.001794	.05098	8.4	11

[a] Pseudo first order constants in hours^{-1}. The lack of strict constancy in the concentration of piperidine, which is present in large excess, introduces an uncertainty small compared with the experimental error. [b] The results for this compound agree only fairly well with those reported by Sandin and Liskear.[19] [c] Reaction time one hour.

TABLE II

REACTIONS OF CYANOARYL BROMIDES WITH PIPERIDINE

Solvent: ethylbenzene, 10 cc.

Compound	Moles of compound	Moles of piperidine	Per cent. reaction in 8 hr.	Velocity constant ($k \times 10^5$)[a]
p-Cyanobromoben-	0.001791	0.05100	13.0	17
zene (IV)	.001782	.05095	12.2	16
2-Cyano-5-bromo-	.001798	.05093	3.54	4.5
m-xylene (V)	.001800	.05096	4.15	5.3
2-Bromo-5-cyano-	.001800	.05094	0.13	0.16
m-xylene (VI)	.001798	.05097	0.13	0.16
o-Cyanobromoben-	.001801	.05095	13.3	18
zene (XI)	.001795	.05096	12.9	17
4-Cyano-5-bromo-	.001800	.05097	4.64	5.9
m-xylene (XII)	.001801	.05092	4.43	5.7

[a] See note a, Table I.

TABLE III

REACTIONS OF NITROARYL BROMIDES WITH HYDROXIDE ION

Reagent: NaOH in aqueous dioxane, 65 cc.

Compound	Moles of compound	Moles of NaOH	Time in hours	Per cent. reaction	Velocity constant ($k \times 10^4$)[a]
p-Nitrobromoben-	0.001800	0.01919	24	7.23	31
zene (1)	.001797	.01920	24	7.51	33
2-Nitro-5-bromo-	.001802	.01921	48	1.95	4.1
m-xylene (11)	.001800	.01921	48	1.71	3.6
2-Bromo-5-nitro-	.001799	.01921	48	1.20	2.5
m-xylene (111)	.001801	.01921	48	1.63	3.4

[a] Pseudo first order constants in hours^{-1}. The excess of NaOH is only about ten-fold, but the extent of reaction is so small that no appreciable error is introduced.

II, the ratio of the rate constants being about 35:1. While this difference might be due merely to the recognized deactivating effect of methyl substituents,[7] such an explanation seems improbable since the methyl groups in the latter compound are meta to the bromine atom and hence should have only a comparatively small effect upon it. Little is known, however, about the magnitude to be expected for such a deactivating effect, and, consequently, the study was extended to include 2-bromo-5-nitro-m-xylene, III. In view of the results obtained by Ibbotson and Kenner[11] with 2,5-dinitro-m-xylene (see above) one might anticipate that compound III would react more rapidly than 2-nitro-5-bromo-m-xylene, II. The opposite, however, proved to be the case, so that here the combined effects of the steric hindrance and the deactivation by the methyl groups outweigh the inhibition of the resonance.

An attempt was made to discover whether this discrepancy could be explained on the basis of an unusually great steric hindrance in the reaction with piperidine. Such an explanation seems reasonable since the large piperidine molecule might be expected to be more subject to steric influences than the much smaller ammonia molecule used by Ibbotson and Kenner. For this purpose, the reaction was studied between the same set of three compounds, I, II and III, on the one hand, and hydroxide ion in aqueous dioxane on the other. This choice of reagent and solvent was made (at the expense of not duplicating exactly the conditions of Ibbotson and Kenner) in order to avoid the difficulty of carrying out kinetic measurements with a reagent as volatile as ammonia, and in order to remove the possibility of reduction of the nitro compound in a basic alcoholic medium. The results of these determinations (Table III) were not entirely conclusive. While the rate of reaction of the 2-bromo-5-nitro compound, III, did increase in comparison with that of the 2-nitro-5-bromo compound, II, the change was not sufficient to remove the discrepancy with the work of Ibbotson and Kenner. The data are of considerable interest, nevertheless, since the observed approximate equality of the velocity constants is difficult to account for except on the basis of an inhibition of resonance. The comparison of p-nitrobromobenzene, I, and 2-bromo-5-nitro-m-xylene, III, is also of some interest since it provides further evidence regarding the magnitude of the effect due to the steric hindrance. In the reactions with piperidine, the ratio of the velocity constants for these two compounds is about 160:1, while, in the reactions with hydroxide ion, the ratio is only about 11:1. Thus the total deactivation due to the two methyl groups ortho to the bromine atom has been materially reduced by the use of the smaller reagent molecule. This phase of the problem was not investigated further.

Greater success was achieved from an investigation of the reactions of piperidine with the cyanides, IV, V and VI, corresponding in structure to the nitro compounds, I, II and III, respectively. The importance of these compounds is that, as already has been pointed out, an inhibition of their resonance is impossible. Consequently, from a study of them, an estimate can be made of the magnitude of the combined effects of the classical steric hindrance and of the direct deactivation by the methyl substituents. Comparison of p-cyanobromobenzene, IV, and 2-cyano-5-bromo-m-xylene, V (Table II), shows that in this case the two methyl groups meta to

the bromine atom in compound V lower the rate constant to about one-third of its value in the unmethylated compound, IV. In view of the close similarity of the reactions involved, one might have expected to find approximately the same ratio of 3:1 in the rate constants for the analogous nitro compounds, I and II. The fact that the observed ratio for this pair of substances is instead approximately 35:1 can be taken as evidence for an appreciable effect resulting from inhibition of resonance. With 2-bromo-5-cyano-*m*-xylene, VI, the rate of reaction is again very small, in agreement with the large effect of steric hindrance plus direct deactivation observed in the corresponding nitro compound. No study was made of the reaction of these compounds with hydroxide ion since the hydrolysis of the cyanide group would have made the interpretation of the results difficult if not impossible.

The ortho series of compounds, VII–XII, provides data in quite satisfactory agreement with those obtained in the para series. The rate constant for the reaction of *o*-nitrobromobenzene, VII, with piperidine (Table I) is about one hundred times as great as that for the reaction of 4-nitro-5-bromo-*m*-xylene, VIII, with the same reagent. This difference is again presumably due largely to the inhibition of resonance, since in the latter compound the nitro group is surrounded by two bulky substituents, and since neither steric hindrance nor the direct deactivation by the methyl groups is adequate to account for such a large effect. Indeed, a comparison of the corresponding cyanide compounds, XI and XII, respectively (Table II), shows that, just as in the para series, the steric hindrance and the deactivation by the methyl groups are capable of producing a ratio of velocity constants of only about 3:1 instead of the required 100:1. That substituents ortho to the bromine atom can exert a large steric hindrance is again shown by the fact that 4-bromo-5-nitro-*m*-xylene, IX, reacts with piperidine even more slowly than does 4-nitro-5-bromo-*m*-xylene, VIII.

The direct deactivating effect of a para methyl group is shown by a comparison of 2-bromo-3-nitrotoluene, X, with 4-bromo-5-nitro-*m*-xylene, IX. These differ only in the presence in the latter of a methyl group which is para to the bromine atom and so situated that it can be involved in neither steric hindrance nor the inhibition of resonance. The rate constants for their reactions

with piperidine (Table I) are in the ratio of about 4:1. This result supports the conclusion, reached from a consideration of the cyano compounds, that the direct deactivating effect of the methyl substituents is insufficient to account for the comparative unreactivity of 2-nitro-5-bromo-*m*-xylene, II, and of 4-nitro-5-bromo-*m*-xylene, VIII. In each of these, the two methyl groups meta to the bromine atom produce a much greater effect upon the rate of reaction with piperidine than could have been anticipated in view of the comparatively small effect of the para methyl group in 4-bromo-5-nitro-*m*-xylene, IX. This is especially true since meta substituents are known in general to be considerably less effective in this way than para substituents. The existence of a further factor, the inhibition of resonance, is thus strongly indicated.

Conclusion

From the above discussion it is evident that the inhibition of resonance can be detected in the aromatic nitro compounds by its effect upon the chemical, as well as upon the physical, properties of the substances involved. This effect, however is rather small in magnitude, and its existence can be established beyond question only with the aid of extensive quantitative data. This conclusion is in excellent agreement with the qualitative results reported by Wheland and Danish.[1]

The smallness of the observed effect suggests that the inhibition of the resonance is only partial. In this connection, it is interesting to note that the dipole moment data of Birtles and Hampson[3] seem to indicate that the inhibition is nearly if not entirely complete. This difference between the conclusions reached by the two methods of attack may be real and not merely due to experimental errors, inasmuch as the chemical reactivity may possibly be, for reasons that are not apparent, less sensitive to a moderate inhibition of resonance than is the dipole moment. The evidence at present available, however, is not sufficient to allow a decision on this point to be made.

The authors wish to express their appreciation to Mr. Kurt Eder and to Dr. T. S. Ma for the micro analyses reported in this paper.

Experimental

Preparation of Compounds.—Aside from the compounds discussed below, all materials needed in this investigation, having already been described by previous investigators,

were prepared in accordance with the directions in the literature. All melting points given below are uncorrected.

2-Nitro-5-bromo-*m*-xylene, (II), was prepared by the method of Hantzsch and Blagden.[14] Ten grams of 2-amino-5-bromo-*m*-xylene was dissolved in a mixture of 400 cc. of water and 25 g. of concentrated sulfuric acid. The amine was diazotized below 5° with 5.5 g. of potassium nitrite in 10 cc. of water. The diazonium solution was made just alkaline to litmus by the dropwise addition of concentrated sodium hydroxide, the temperature being held constant. It was then made very faintly acid by the addition of two or three drops of concentrated sulfuric acid. Cuprocuprisulfite, prepared from 20 g. of copper sulfate and 16.5 g. of sodium sulfite, was then added and the mixture poured into 150 cc. of water containing 80 g. of potassium nitrite. The mixture was heated to boiling and then steam distilled. The product was extracted from the aqueous distillate with ether and recovered by evaporation of the ether. The residue was recrystallized from alcohol and was obtained in colorless needles melting at 65.5–66.5°. The yield ranged from 20 to 35% of the theoretical. The compound turns yellow on long standing in the light, and samples were recrystallized before use.

Anal. Calcd. for $C_8H_8O_2NBr$: C, 41.74; H, 3.48; N, 6.09. Found: C, 41.83; H, 3.48; N, 6.15.

The structure of the nitro compound was confirmed by reduction to the original amine with the use of acid stannous chloride. The identity of the two samples of amine was shown by melting point and mixed melting point.

2-Bromo-4-acetylamino-5-nitro-*m*-xylene.—This substance and the following one were prepared as intermediates in the synthesis of 2-bromo-5-nitro-*m*-xylene, (III). Seventy grams of 2-bromo-4-acetylamino-*m*-xylene was added in 10-g. lots to a mixture of 350 cc. of concentrated nitric acid and 250 cc. of red fuming nitric acid at 5–10°. The temperature was then allowed to rise to 20°, where it was held for fifteen minutes. The solution, now bubbling faintly, was poured into ice water. The precipitate was collected, washed with water and crystallized from alcohol. The product formed colorless needles melting at 191–192°. Yields of 55–70% of the theoretical were obtained. That the substance is the 5-nitro derivative is indicated by the fact that the 6-nitro derivative, the only likely isomer, is known to have different properties, as is reported elsewhere.[15] A more conclusive proof of structure is given below.

Anal. Calcd. for $C_{10}H_{11}O_3N_2Br$: N, 9.76. Found: N, 9.76.

2-Bromo-4-amino-5-nitro-*m*-xylene.—A mixture of 45.4 g. of the above acetyl derivative and 350 g. of concentrated sulfuric acid was heated for ten minutes at 110–115°. The dark red solution was then poured on ice. A light orange precipitate was collected, washed with water, and recrystallized from alcohol. It formed orange-red needles which were only slightly soluble in cold alcohol, and which melted at 141–142°. The yield was 37.5 g. or 97% of the theoretical.

Anal. Calcd. for $C_8H_9O_2N_2Br$: N, 11.43. Found: N, 11.60.

(14) A. Hantzsch and J. W. Blagden, *Ber.*, **33**, 2544 (1900).
(15) W. C. Spitzer, THIS JOURNAL, **62**, 2884 (1940).

2-Bromo-5-nitro-*m*-xylene, III, by Deamination of the 4-Amino Compound.—Thirty grams of the above 2-bromo-4-amino-5-nitro-*m*-xylene was suspended in 600 cc. of alcohol containing 25 cc. of concentrated sulfuric acid. The amine was then diazotized at 10–13° with 18 g. of sodium nitrite in a little water. After four hours, the diazonium solution was carefully heated to boiling. Aldehyde and excess alcohol were removed by fractionation. The residue was diluted with water and steam distilled. The white solid material which passed over was collected, washed with water, and recrystallized from alcohol. It formed colorless needles melting at 102.5–103°. The yield was 18 g. or 64% of the theoretical.

Anal. Calcd. for $C_8H_8O_2NBr$: N, 6.09. Found: N, 6.14.

2-Bromo-5-nitro-*m*-xylene, III, by the Sandmeyer Reaction.—A few milligrams of 2-amino-5-nitro-*m*-xylene was prepared by the action of aqueous ammonia upon 2-hydroxy-5-nitro-*m*-xylene. The reaction, which was carried out in a sealed tube at 180°, proved to be very unsatisfactory, and only small yields were obtained. The substance formed yellow needles melting at 159–160°, in agreement with the value reported by Ibbotson and Kenner.[11] This amino compound was converted into the bromo compound by a Sandmeyer reaction in the usual way. The compound was isolated by steam distillation and, after one crystallization from alcohol, it melted at 100–103°. Since only a very small quantity of material was available, no attempt was made to purify it further. However, there can be little doubt of its identity with the 2-bromo-5-nitro-*m*-xylene prepared by the method previously described, since mixtures of the two samples melted at 100–103° and 100–102°, respectively. This establishes the structure of the compound, and shows that 2-bromo-4-acetylamino-*m*-xylene is nitrated at position 5 under the conditions described above.

2-Cyano-5-bromo-*m*-xylene, V, was prepared from 2-amino-5-bromo-*m*-xylene by a Sandmeyer reaction. The product was isolated by steam distillation of the reaction mixture and was purified by crystallization from alcohol. It formed long colorless needles melting at 70–71.5°.

Anal. Calcd. for C_9H_8NBr: N, 6.67. Found: N, 6.64.

2-Bromo-5-amino-*m*-xylene was desired as an intermediate in the synthesis of 2-bromo-5-cyano-*m*-xylene, VI. It was prepared from the corresponding nitro compound, III. Ten grams of 2-bromo-5-nitro-*m*-xylene was suspended in 250 cc. of alcohol and gradually added to a stirred solution of 36.5 g. of stannous chloride in 32.5 cc. of concentrated hydrochloric acid. After an hour, the alcohol was removed by distillation. The residue was made alkaline with aqueous sodium hydroxide and distilled with steam. A yellowish oil was obtained which crystallized on standing for two days. This was dissolved in concentrated hydrochloric acid. The acid solution was boiled for a few minutes, quickly filtered, and allowed to cool. The amine hydrochloride, which precipitated, was collected, suspended in water and treated with an excess of sodium hydroxide. The white precipitate was collected and recrystallized from alcohol. It was obtained in colorless needles melting at 75.5–76°. The yield was 7 g. or 80% of the theoretical.

Anal. Calcd. for C₈H₁₀NBr: N, 7.00. Found: N, 7.19.

2-Bromo-5-cyano-*m*-xylene, VI, from the Amine.—
The above 2-bromo-5-amino-*m*-xylene was transformed into the corresponding cyano compound by the Sandmeyer reaction. The product was separated from the reaction mixture by steam distillation and then recrystallized from alcohol. It formed very long colorless prisms melting at 145° with some sublimation. The yield was very poor: only 0.4 g. of pure material from 7 g. of amine. Doubtless the yield could be greatly improved, but no attempt was made to do so since the amount obtained was enough for the purpose at hand and since the starting material was not readily available.

Anal. Calcd. for C₉H₈NBr: C, 51.43; H, 3.84; N, 6.67. Found: C, 51.68; H, 3.73; N, 7.00.

4-Bromo-3,5-dimethylbenzamide was prepared as an intermediate in an independent synthesis of the above 2-bromo-5-cyano-*m*-xylene, VI. Two grams of *p*-bromo-mesitylenic acid was refluxed with an excess of thionyl chloride until all had dissolved. The cooled solution was treated carefully with concentrated ammonia. The white precipitate was collected, washed with water, and recrystallized from alcohol. The product was obtained as colorless needles and square platelets with a pearly luster. It melted at 205–206°. The yield was 1.5 g. or 75% of the theoretical.

Anal. Calcd. for C₉H₁₀ONBr: N, 6.15. Found: N, 6.40.

2-Bromo-5-cyano-*m*-xylene, VI, from the Amide.—
An intimate mixture of 1.5 g. of the above amide and 2 g. of phosphorus pentachloride was heated on the steam-bath for twelve hours in a loosely stoppered flask. The mixture was cooled, cautiously treated with water, and steam distilled. The solid product was collected and recrystallized from alcohol. It formed colorless prisms melting at 144–145°. A mixed melting point with the material prepared by the previous method showed no depression. The yield was 0.5 g.

4-Bromo-5-nitro-*m*-xylene, IX.—The method of Blanksma[16] for the preparation of this compound proved unsatisfactory and was modified as follows: Ten grams of 4-amino-5-nitro-*m*-xylene was suspended in 40 cc. of 18% hydrobromic acid and diazotized with 5 g. of sodium nitrite at 20°. The diazonium solution was poured into a suspension of cuprous bromide prepared by passing sulfur dioxide through a solution of 13 g. of potassium bromide, 11 g. of copper sulfate, and 30 cc. of 36% hydrobromic acid in 55 cc. of water. The reaction product was isolated by steam distillation and recrystallized from alcohol. The melting point was 55.5–56.5°, in agreement with the value of 56° reported by Blanksma.

***p*-Piperidino-benzonitrile.—**Since little seems to be known about the behavior of piperidine toward cyano-aryl halides, it seemed desirable to examine the reaction in some detail in order to show that it actually does follow the course indicated above in equation (1). For this purpose, *p*-bromobenzonitrile, IV, was chosen as the most suitable compound on account of both its availability and its reactivity. Ten grams of *p*-bromobenzonitrile was refluxed with 20 cc. of piperidine for eight hours.

The mixture was poured into water, just neutralized with hydrochloric acid, and then made slightly basic with sodium carbonate. The heavy oil which separated solidified on long standing. This solid was dissolved in benzene, and the solution was extracted with 20% hydrochloric acid. The benzene solution was dried and the solvent was evaporated off. The residue, which weighed 3.10 g., was dissolved in a small quantity of alcohol, diluted with water, and steam distilled. The solid distillate was crystallized from dilute alcohol. The purified product, which weighed 2.8 g. was shown to be unchanged *p*-bromobenzonitrile by melting point and mixed melting point.

The hydrochloric acid extracts from above were neutralized with aqueous ammonia. The yellow precipitate which formed was collected and washed with water. The filtrate yielded a further small quantity of material upon extraction with ether. The combined weight of this *p*-piperidino-benzonitrile was 6.75 g. After several recrystallizations, first from 95% and then from more dilute alcohol, it was obtained in light yellow leaflets melting at 55°. The weight of pure material was 5.8 g.

Anal. Calcd. for C₁₂H₁₄N₂: N, 15.06; mol. wt., 186. Found: N, 15.04; mol. wt. (benzene), 182, 188.

In this experiment, the amount of the original *p*-bromobenzonitrile which was recovered either as unchanged starting material or as *p*-piperidino-benzonitrile was equivalent to 97% of the amount taken initially on the basis of the crude products obtained, or to 84% on the basis of the purified materials. It is evident, therefore, that the reaction is a clean one, and that no appreciable quantity of side products is formed.

***p*-Piperidinobenzoic Acid by Hydrolysis of the Nitrile.—**In order to show that the substance prepared as above actually was *p*-piperidino-benzonitrile, a sample was hydrolyzed to the corresponding acid. One gram of the nitrile was refluxed with 40 cc. of 20% hydrochloric acid for two and one-half hours. The clear solution was then cooled and made neutral to litmus by the addition of the requisite amount of dilute potassium hydroxide. The almost white precipitate was collected, washed with water, decolorized with Norit in alcohol solution, and finally recrystallized from alcohol. The pure acid formed white leaflets melting at 224–224.5°.

Anal. Calcd. for C₁₂H₁₅O₂N: N, 6.83. Found: N, 6.93.

Scholtz and Wassermann[17] reported the melting point of this compound as 188°. Their synthesis was accordingly repeated in order to clear up the discrepancy.

***p*-Piperidinobenzoic Acid by the Method of Scholtz and Wassermann.—**The directions given by these authors were too scanty to be duplicated exactly. In the present work, the following procedure was followed. Five grams of pentamethylene bromide and 10.5 g. of *p*-aminobenzoic acid were dissolved in 30 cc. of methyl alcohol and refluxed for forty-eight hours. About 2 g. of a white crystalline precipitate formed in the solution after prolonged cooling. This was filtered off and crystallized from dilute alcohol. The purified product melted at 220–223°, and mixtures of it with the acid obtained from the nitrile melted at 220–222° and at 221–223°, respectively. There

(16) J. J. Blanksma, *Rec. trav. chim.,* **25,** 165 (1906).

(17) M. Scholtz and E. Wassermann, *Ber.,* **40,** 852 (1907).

is thus no question that the melting point given by the earlier workers is in error.

Solvents and Stock Sodium Hydroxide Solution

Benzene.—Thiophene-free benzene was distilled from sodium and stored over sodium wire. The fraction taken boiled at 79.5–80°.

Ethylbenzene.—The Eastman Kodak Co. product was distilled from sodium and stored over sodium wire. The fraction taken boiled at 134–135°.

Piperidine.—The Eastman product (highest grade) was distilled from sodium and stored over sodium wire. The fraction taken boiled at 105–106°. The piperidine purified in this way gave the same results as some purified through the benzoyl derivative.

Dioxane.—Commercial dioxane was purified by the method of Eitel and Lock.[18] It gave only a faint test for halogen after it had been refluxed for four hours with aqueous sodium hydroxide.

Stock Sodium Hydroxide Solution.—Mallinckrodt sodium hydroxide of low chlorine content (assay, 0.001% Cl, 67–70% NaOH) was used. Forty-three and one-half grams was dissolved in as little distilled water as possible, filtered from the precipitated carbonates and silicates, and diluted to 1100 cc. with freshly boiled distilled water. To this solution was added 1300 cc. of dry dioxane. The solution was standardized against potassium acid phthalate and was found to be 0.2957 N.

Kinetic Measurements. Reactions Employing Piperidine.—The procedure was essentially the same as that used by Sandin and Liskear[19] and by McLeish and Campbell.[20] The nitrobromo- or cyanobromo- compound (approximately 0.0018 mole) and piperidine (approximately 0.051 mole) were weighed out and transferred to a 100-cc. round-bottom flask, which could be attached to a reflux condenser by means of a ground glass joint. Ten cc. of benzene or ethylbenzene, as the case might be, was pipetted into the flask and the mixture gently refluxed for eight hours (for one hour in the case of o-nitrobromobenzene). At the end of this time, the contents of the flask was rapidly cooled by an external cold water-bath, while 15 cc. of water was added through the condenser. The benzene or ethylbenzene layer was separated from the aqueous layer and washed several times with water. The combined aqueous extracts were analyzed for bromide ion by the Volhard method.

(18) A. Eitel and G. Lock, *Monatsh.*, **72**, 392 (1939).

(19) R. B. Sandin and M. Liskear, THIS JOURNAL, **57**, 1304 (1935).

(20) N. McLeish and N. Campbell, *J. Chem. Soc.*, 1103 (1937).

For the benzene solutions, a negligible blank was found. For the ethylbenzene solutions, a blank of 0.0016 milliequivalent was found, and the percentage reaction was corrected by this amount.

Reactions Employing Sodium Hydroxide.—The nitroaryl halide (approximately 0.0018 mole) was refluxed for twenty-four or forty-eight hours with 65 cc. of the stock sodium hydroxide solution, which was delivered from a buret. After this time, the cooled solution was treated with 25 cc. of benzene, which was added through the condenser. The aqueous layer was separated and the benzene solution was extracted several times with water. The combined aqueous extracts were analyzed for bromide ion by the Volhard method.

A blank of 0.0168 milliequivalent was found for the twenty-four hour period, and of 0.0221 milliequivalent for the forty-eight hour period. The analytical figures were corrected by these amounts.

These determinations were rendered difficult by the separation of much siliceous material, resulting from the reaction of the hot sodium hydroxide solution with the glass reaction vessel. However, a blank determination on a weighed quantity of potassium bromide, approximately the same in bromide content as the final reaction mixture, gave an analysis correct to 1%.

Summary

1. Determinations have been made of the rates with which a series of nitroaryl and cyanoaryl bromides react with piperidine and/or hydroxide ion.

2. The data so obtained have been interpreted as demonstrating that the resonance can be inhibited in suitably substituted aromatic nitro compounds but not in the corresponding cyano compounds.

3. The effect of the inhibition of resonance is somewhat smaller in magnitude than one would be led to expect from the results of the dipole moment measurements of Birtles and Hampson.

4. The reaction between p-bromobenzonitrile and piperidine has been studied and the structure of the product has been established.