

ORIENTATION IN NITRATION OF
AROMATIC NITRILES

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INTRODUCTION

Reactions involving substitution in the benzene ring have long been of particular interest to the organic chemist. It was early recognized that the position taken by an incoming group was directly dependent on the nature of the substituent already in the ring. Thus the different substituent groups were divided into ortho- and para- or meta-directing groups depending on whether they caused further substitution to occur in the ortho and para or in the meta position. On the basis of rough work it was possible to make this distinction for many of the common substituent groups and to set up tables of groups depending on their directing influence. As the listed groups increased and the electronic interpretations of organic chemistry began to take shape, it was pointed out that the ortho- and para-directing groups were electron repelling groups and that they activated the ring; that is, they increased the ease of entrance of the incoming group. The meta-directing groups, on the other hand, were classified as electron withdrawing or attracting groups and deactivating groups for they were found to render the substitution of the incoming group more difficult.

The traditional substitution reactions all involve the entrance into the ring of an electrophilic group. In some cases this group has been shown to be actually a positive ion. Thus if the group already present could increase the electron density of the ring further substitution would be made easier and the ring would be "activated". Likewise any group that tended to decrease the electron density of the ring would cause "deactivation" of the ring. In this type of classification little attention was paid to other than electronic factors and steric factors were largely neglected.

In a consideration of the ratio of ortho- to para-substitution both in the reactions of ortho- and para-directing compounds and of predominantly meta-directing compounds the finer points of influence must be considered. The steric effects as well as electronic effects must be considered and the nature of the incoming group can no longer be neglected.

The most widely studied of the aromatic substitution reactions and that one most frequently employed in investigating isomer ratios obtained in substitution reactions is the nitration reaction. This reaction is particularly well suited to these studies for it is an irreversible reaction and, even under widely different conditions, can be made to give mono-substitution only.

The present investigation was undertaken in order to obtain data which would help clarify the general problem of the ortho to para-ratio obtained in the nitration of compounds containing a meta-directing group. Many of the meta-directing groups have been found to be to some extent ortho-directors. These groups are the non-linear, unsaturated groups such as $-\text{NO}_2$, $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{R}$, $-\text{COR}$ and $-\text{SO}_3\text{H}$. Only one experiment has been reported in which an attempt was made to determine the isomer ratio of nitrobenzonitriles obtained on the mono-nitration of benzonitrile. Because of the difference in geometry and steric requirements of the nitrile group and of the non-linear groups which are supposed to have the same electronic influences, it seemed important to determine very carefully the ortho to para-ratio obtained in the mono-nitration of aromatic nitriles. This has been done in the case of benzonitrile. The isomer ratio has been obtained by an infrared analytical method.

It was also desired to obtain similar data from the mono-nitration of 2,5-dichlorobenzonitrile so that the results might be compared to those obtained from the mono-nitration of 2,5-dichloronitrobenzene. This was not accomplished, however, due to the difficulty encountered in attempting to obtain a pure sample of 2,5-dichloro-3-nitrobenzonitrile. Qualitative evidence that was obtained

implied that this nitration would give results similar to those obtained from the nitration of benzonitrile and the isomer ratio, while not being quantitatively the same, would follow the trend established by benzonitrile.

HISTORICAL REVIEW

The Mechanism of Aromatic Nitration

There has been much speculation concerning the mechanism of aromatic nitration. For a long time the most widely accepted theory was the "addition-elimination" theory, according to which the elements of nitric acid were added across a double bond of the Kekule structure and then the elements of water were eliminated¹. Nitration is now believed to be an electrophilic displacement reaction and it has recently been shown that in most cases the nitrating agent is the nitronium ion, NO_2^+ .

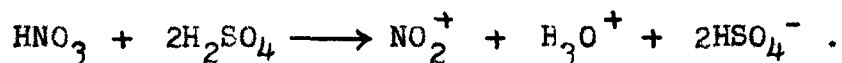
That the nitronium ion was actually the attacking species was first suggested by Euler². It was not until relatively recently, however, that the existence of this species was actually demonstrated. The presence of the nitronium ion in solutions identical or very similar to those used in aromatic nitration has now been proved in four ways which are not dependent on the nitration reaction. The existence

¹For a review of this and the more modern theory see R. J. Gillespie and D. J. Millen, Quart. Rev., **2**, 277 (1948).

²H. Euler, Ann., **330**, 280 (1903); Z. angew. Chem., **35**, 580 (1922).

of this species has greatly clarified the mechanism of the nitration reaction.

The first type of evidence is obtained from cryoscopic measurements. Hantzsch³ was a pioneer in this field and found the value of the Van't Hoff *i* factor to be three for solutions of nitric acid in sulfuric acid. By means of improved cryoscopic techniques it has been found that the depression of the freezing point is not three times but four times that of an ideal solute⁴. From this information it is concluded that nitric acid ionizes in sulfuric acid in accordance with the following equation:



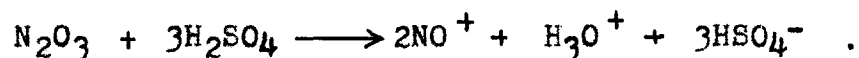
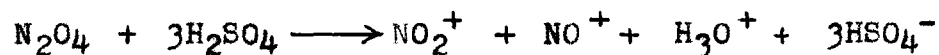
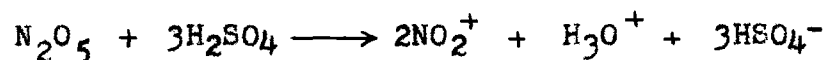
In no other way could a four-fold depression of the freezing point of sulfuric acid be produced. Cryoscopic work with oxides of nitrogen in sulfuric acid has shown that these solutes give six-fold depressions of the freezing point⁵ and

³A. Hantzsch, Z. physik. Chem., **65**, 41 (1908).

⁴R. J. Gillespie, J. Graham, E. D. Hughes, C. K. Ingold, and E. R. A. Peeling, Nature, **158**, 480 (1946).

⁵R. J. Gillespie, J. Graham, E. D. Hughes, C. K. Ingold, and E. R. A. Peeling, J. Chem. Soc., 2504 (1950).

has led to the conclusion that these oxides are quantitatively converted into nitronium and nitrosonium ions:



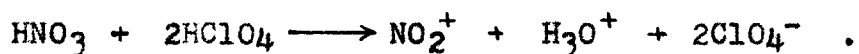
The second type of evidence for the existence of the nitronium ion is the identification of this ion by spectroscopic means. Medard⁶ observed two frequencies, 1400 and 1050 cm.⁻¹, in the Raman spectra of certain mixtures containing nitric acid. Chedin⁷ investigated these two frequencies extensively and concluded that they were due to dinitrogen pentoxide in a special form. More recent spectroscopic work has shown that only the 1400 cm.⁻¹ frequency could be attributed to the nitronium ion, and that the 1050 cm.⁻¹ frequency was due to other species present in the solutions.⁸ The presence of this frequency then gave a

⁶L. Medard, Compt. rend., 199, 1615 (1934).

⁷J. Chedin, Compt. rend., 200, 1397 (1935); 201, 552, 714 (1935); 202, 220, 1067 (1936); 203, 772, 1509 (1936); Ann. chim., 8, 243 (1937).

⁸C. K. Ingold, D. J. Millen, and H. G. Poole, J. Chem. Soc., 2576 (1950).

basis for the detection and estimation of the nitronium ion. Thus the ionization of nitric acid and of the oxides of nitrogen in sulfuric acid as shown above has been confirmed⁹. Ingold, Millen, and Poole⁸ observed in the Raman spectra of solutions of nitric acid in perchloric acid every spectral frequency which could be expected from the ionization of nitric acid according to the equation



Halberstadt, Hughes, and Ingold¹⁰, however, obtained no evidence of the nitronium ion in aqueous nitric acid solutions containing about eleven mole per cent perchloric acid.

The third line of evidence for the existence of the nitronium ion is that given by the preparation, and spectroscopic study, of crystalline nitronium salts¹¹. Hantzsch first showed that nitric and perchloric acids interact to form solid salt-like compounds. It has been shown¹² that

⁹D. J. Millen, J. Chem. Soc., 2600 (1950).

¹⁰E. S. Halberstadt, E. D. Hughes, and C. K. Ingold, J. Chem. Soc., 2441 (1950).

¹¹A. Hantzsch, Ber., 58, 958 (1925).

¹²D. R. Goddard, E. D. Hughes, and C. K. Ingold, Nature, 158, 480 (1946); J. Chem. Soc., 2559 (1950).

these solids are really mixtures of nitronium and hydroxonium perchlorates $(\text{NO}_2)^+(\text{ClO}_4)^-$ and $(\text{H}_3\text{O})^+(\text{ClO}_4)^-$. Other pure nitronium salts have been prepared and have been shown to be ionic; the Raman spectra of the crystals consist simply of the superposed, known spectra of the ions involved¹³.

Gillespie¹⁴ in a cryoscopic study of nitronium and ammonium perchlorates in sulfuric acid found that the depression of the freezing point was three, rather than two, times that of an ideal solute. He also observed that dilute solutions of either salt fumed in ordinary air even if the sulfuric acid had been pre-treated with about five hundredth molar of water, and from these data he concluded that the perchlorate ion is converted into perchloric acid by the sulfuric acid.

The fourth type of evidence for the existence of the nitronium ion has been obtained through the X-ray analysis of certain nitronium salts. Both nitronium perchlorate¹⁵ and nitronium nitrate¹⁶ have been examined and the ionic constitutions have been verified.

¹³D. J. Millen, J. Chem. Soc., 2606 (1950).

¹⁴R. J. Gillespie, J. Chem. Soc., 2537 (1950).

¹⁵F. G. Cox, G. A. Jeffrey, and M. R. Truter, Nature, **162**, 259 (1948).

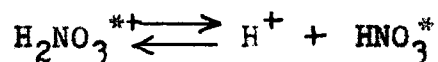
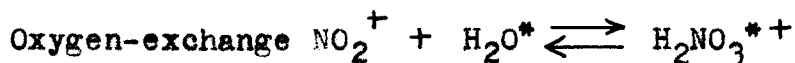
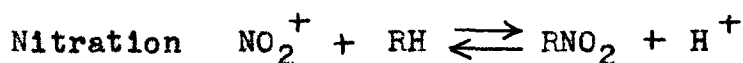
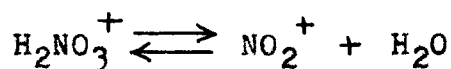
¹⁶P. E. Grison, K. Ericks, and J. L. de Vries, Acta Cryst., **3**, 290 (1950).

The fact that the nitronium ion does exist in such solutions as are used in nitration reactions makes it easier to interpret nitration rate data. In the nitration of sufficiently reactive aromatic compounds in organic solvents with a constant excess of nitric acid the nitration rate is found to be independent of the concentration of the aromatic compound. Thus the rate measured must be that of formation of some species which is consumed rapidly and the species being formed must indeed be the nitronium ion¹⁷.

The rate of nitration of less reactive aromatic compounds is found to be dependent on the concentration of the aromatic compound; that is, these reactions are first order with respect to the aromatic substrate. In a study of the nitration of arylalkanesulfonic acids Halberstadt, Hughes, and Ingold¹⁰ found that the observed first-order rate law could be explained in either of two ways: nitration by the nitracidium ion, or by formation of the nitronium ion in a very small equilibrium concentration followed by a slow reaction between it and the aromatic compound. The kinetic evidence did not allow differentiation between these two mechanisms but it did exclude the possibility of nitration

¹⁷C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, N. Y., 1953, p. 276.

by the nitric acid molecule. In a more recent study Bunton and Halevi¹⁸ compared the rates of oxygen exchange in aqueous nitric acid solutions with rates of nitration of aromatic compounds in these solutions. They considered the following equations for nitration and oxygen exchange based on the nitronium ion; the asterisk indicates the presence of radioactive oxygen.



According to these equations the rate of oxygen exchange is the rate of formation, or destruction, of the nitronium ion, and as, in a given medium, the concentration of nitronium ion is very small (kinetic "steady state"), these rates are equal. The rate of oxygen exchange should therefore give a limiting value for the rate of nitration via the nitronium

¹⁸C. A. Bunton and E. A. Halevi, J. Chem. Soc., 4917 (1952).

ion, as this rate cannot be greater than the rate of formation of the nitronium ion. Experimentally the rates of nitration are always lower than the rates of oxygen exchange although they approach this figure for reactive aromatic compounds which show approximately zero-order kinetics. It is concluded, therefore, that both nitration and oxygen exchange involve the formation and destruction of the nitronium ion. The change in kinetic order from first toward zero with increasing aromatic reactivity which was observed in aqueous nitric acid was also found in nitrations in aqueous perchloric acid-nitric acid solutions. It was not possible, because of the presence of the perchloric acid, to study the rate of oxygen exchange in these solutions but this change in kinetic form suggests that the nitronium ion is the nitrating agent in these solutions.

Two theories explaining the mechanism of attack by the nitronium ion in aromatic nitration reactions have been considered. The first is a termolecular, or single stage, introduction of the nitronium ion and simultaneous transference of the proton to an external base. The other is a two stage reaction in which the attack by the nitronium ion is the slow step and this is followed by a rapid removal of

the proton. It has been shown by Melander¹⁹ that the second is the more correct interpretation because the removal of the proton is not involved in the rate-controlling step. He nitrated aromatic compounds containing tritium in one of two or more otherwise equivalent positions and found that there was no selection of protium rather than tritium for displacement by the entering nitro group. Lauer and Noland²⁰ have extended this work to include the nitration of mono-deuterobenzene. Their work has confirmed Melander's conclusions that the loss of proton in the nitration reaction does not occur in the rate-determining step.

Orientation in Aromatic Substitution

Early in the study of aromatic substitution reactions it was recognized that the position on the aromatic ring taken by the incoming group was determined by the substituent already present. The fact that a particular substituent directed the incoming group to a particular position regardless of the identity of the incoming group led to the

¹⁹L. Melander, Nature, **163**, 599 (1949); Acta chem. Scand., **3**, 95 (1949); Arkiv Kemi, **2**, 213 (1950).

²⁰W. M. Lauer and W. E. Noland, J. Am. Chem. Soc., **75**, 3689 (1953).

study of orientation from the point of view of the already present substituent only and an almost complete disregard for the incoming group. It was early observed that certain substituents led to substitution in the positions ortho or para to this substituent whereas other groups directed the incoming group to the meta position. Thus the substituents were divided into ortho- and para- or meta-directing groups. It was observed further that the rate of substitution was influenced by the group already present in the ring and the ortho- and para-directing groups were found in general to be "activating" groups whereas meta-directing substituents were "deactivating" as compared to the ease of substitution in benzene itself. The meta-directing groups were recognized as electron attracting groups and the ortho- and para-directors as electron repelling groups. The entering groups in the substitution reactions were recognized as electrophilic reagents, although this term was not used until much later, and the orientation rules of Nolting²¹, Koerner²², and Hubner²³ were all designed to assist in the classification of a substituent group as electron attracting and thus

²¹E. Nolting, Ber., 9, 1797 (1876).

²²W. Koerner, Gazz. chim. ital., 4, 305, 446 (1874).

²³H. Hubner, Ber., 8, 873 (1875).

meta-directing or as electron repelling and thus an ortho- and para-directing group.

Later, still other rules were formulated which related the nature of the substituent group to its orienting influence. Thus the rules of Armstrong²⁴, Crum Brown and Gibson²⁵, and Vorlander²⁶ relate the influence of the group X to the ability of the acid HX to undergo direct oxidation or to the presence or absence of multiple bonds in X. All of these rules break down for certain cases and Holleman has discussed the rules and representative cases where they do not apply²⁷.

Flurscheim²⁸ formulated a theory to explain orientation based on Werner's idea of chemical affinity, but it is Holleman's criterion that must be the bases for any orientation theory. He pointed out²⁹ that, since the ortho- and para-directing groups increased the ease of aromatic

²⁴H. E. Armstrong, J. Chem. Soc., 51, 258 (1887).

²⁵H. Crum Brown and J. Gibson, J. Chem. Soc., 61, 367 (1892).

²⁶D. Vorlander, Ann., 320, 122 (1902).

²⁷A. F. Holleman, Chem. Rev., 1, 218 (1925).

²⁸B. F. Flurscheim, Chem. and Ind., 44, 246 (1925).

²⁹A. F. Holleman, "Die direkt Einfuhrung von Substituenten in den Benzolkern", Veit, Leipzig, 1910, p. 475.

substitution over that of the unsubstituted compound whereas the meta-directing groups deactivated the ring, any theory which merely explained directional influences and did not account for this activating or deactivating effect could not give a true understanding of the problem. The theory of "alternate polarity" was thus doomed from the beginning for it would allow activation of the meta position or of the ortho and para positions more or less equally by the meta- or ortho- and para-directing groups. A documented discussion of these rules and theories is given by Ingold³⁰ who shows how, with the development of the electronic theory, the problem of orientation began to fit into the general problem of constitutional effects on organic reactions.

The Ratio of Ortho- to Para-Substitution

The classification of substituents as meta- or ortho- and para-directing groups is a gross distinction, but the study of the ratio of ortho- to para-substituted side products obtained in the substitution of a compound containing a meta-directing group brings out the finer points of influence of the directing group. Both the electronic

³⁰C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, N. Y., 1953, p. 223.

and steric influences of the directing group as well as the effect of the entering group must be considered. The study of the ratio of ortho- to para-substitution was analyzed by Ingold³¹. The data led him to the conclusion that there was a steric factor, as Holleman²⁷ had already deduced, and four polar factors. The account of the evidence leading to these conclusions is reviewed by Ingold³² both from the point of view of the orienting group and of the entering group in the case of the steric influences and from the nature of the orienting group in the case of the polar factors. The evidence for the polar effects is divided into sections depending on whether the substituent group is a +I, -I, -M, or +T group. Types of orienting substituents have been classified according to their inductometric, tautomeric and mesomeric influences. A discussion of the various classifications is given to reconcile the observed meta- or ortho- and para-directing influences of the various substituent types.

³¹C. K. Ingold, Ann. Repts. on Progress Chem. (Chem. Soc. London), 23, 140 (1926).

³²C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, N. Y., 1953, p. 231.

In discussing the effect of -M substituents Ingold points out that these groups are really of the -I -M type for both the electron drifts are in the direction of the substituent group $\text{Ph} \rightarrow \text{R}$. These groups include -COR, -CO₂R, -CH, -NO₂, which are meta-orienting substituents containing a multiple bond. For these groups the chief by-product is the ortho-compound. Ingold³¹ assumed this to be the result of an interference with para-substitution due to the -M effect of the substituent. Lapworth and Robinson³³ suggested the alternative of a special facilitation of ortho-substitution. Ingold³⁴ has shown by calculations that it is more reasonable to assume a specific deactivation of the para position by the -M substituent than any particular activation of the ortho position by the groups to account for the observed large ortho to para ratio obtained. His calculation is based on a mixing law interpolation and does not explain how this proposed deactivation occurs.

³³A. Lapworth and R. Robinson, Mem. Proc. Manchester Lit. and Phil. Soc., **72**, 243 (1928).

³⁴C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, N. Y., 1953, p. 262.

Hammond, Modic, and Hedges³⁵ from their study of the ortho to para ratios obtained in the nitration of 2,5-dibromo- and 2,5-dichloronitrobenzene have suggested a mechanism by which ortho direction by non-linear, unsaturated substituents could be facilitated. According to this mechanism the negative end of the dipole in groups like NO₂, COOH, CHO attract the ortho-hydrogen and facilitate the approach of the electrophilic attacking group so that the proton is displaced in one concerted process and appears first on the neighboring group.

Recently there have been several authors who have turned to the simple L C A O molecular orbital approximation as a means of interpreting aromatic substitution. Wheland³⁶ has shown that the theory points to ortho- and para-substitution for some kinds of derivatives and meta-substitution for others, in general agreement with observation. Dewar³⁷ considered the problem of ortho to para-ratios. His results indicated that only in cases where the substituent is very electronegative would the para position be

³⁵G. S. Hammond, F. J. Modic and R. M. Hedges, J. Am. Chem. Soc., **75**, 1388 (1953).

³⁶G. W. Wheland, J. Am. Chem. Soc., **64**, 900 (1942).

³⁷M. J. S. Dewar, J. Chem. Soc., 463 (1949); J. Am. Chem. Soc., **74**, 3357 (1952).

electronically more activated than the ortho position. He points out that the electronic influence on the ortho to para-ratio may be outweighed by steric effects or hydrogen bonding. Dewar was able to account qualitatively for trends in the ortho to para-ratio as the nature of the substituent is varied but the appropriate electronegativity parameters for the various substituents are very uncertain. Brown³⁸ has shown that when the substituent is a conjugated hydrocarbon system the uncertainty about the electronegativity parameter disappears and the molecular orbital approximation provides an unequivocal prediction of the electronic activities. He as well as Dewar attributes the observed superior reactivity of the para position in biphenyl to steric effects rather than to failure in the M O theory.

Aside from the electronic influences it has long been recognized that steric factors influenced the orientation in substitution reactions. Apparently Kehrman³⁹ was the first to recognize this. LeFevre⁴⁰ explained the observed higher proportions in which para compounds are formed in

³⁸R. D. Brown, J. Am. Chem. Soc., **75**, 4077 (1953).

³⁹F. Kehrman, Ber., **23**, 130 (1890).

⁴⁰R. J. W. LeFevre, J. Chem. Soc., 980 (1933); ibid., 1501 (1934).

the nitration of the more branched side-chain homologues of toluene on the basis of steric effects. Nelson and Brown⁴¹ have determined the isomer ratios in mononitration of tert-butylbenzene and compared them to the values for toluene obtained by Jones and Russell⁴². The fact that the para to meta-ratio for toluene and tert-butylbenzene were not very different led them to conclude that the electronic effects of the two groups are similar and that the large difference in the ortho to meta- and ortho to para-ratios observed is due to steric hindrance of the ortho position by the tert-butyl group. Similar interpretation is placed on the observed substitution in para-ethyltoluene⁴³, para-cymene⁴⁴ and para-tert-butyltoluene⁴⁵. Cohn, Hughes, Jones and Peeling⁴⁶ have shown that the rates of total nitration of toluene and of tert-butylbenzene stand in the ratio

⁴¹K. L. Nelson and H. C. Brown, J. Am. Chem. Soc., **73** 5605 (1951).

⁴²W. W. Jones and M. Russell, J. Chem. Soc., 921 (1947).

⁴³O. L. Brady and J. N. E. Day, J. Chem. Soc., 114 (1934).

⁴⁴R. J. W. Le Fevre, J. Chem. Soc., 1501 (1934).

⁴⁵M. Battegay and P. Haeflery, Bull. soc. chim. (France) **35**, 981 (1924).

⁴⁶H. Cohn, E. D. Hughes, M. H. Jones, and M. G. Peeling, Nature, **169**, 291 (1952).

100:64 and that, contrary to theories of hyperconjugation, the methyl group is not the more activating group. In fact their data show that the tert-butyl group is slightly more activating than is the methyl group for substitution in all positions except the ortho-position.

EXPERIMENTAL

Materials

Perchloric acid used as solvent was Baker and Adamson reagent grade 70-72%.

Nitric acid used as the nitrating agent in all experiments was Baker and Adamson fuming nitric acid of specific gravity 1.49-1.50.

Platinum oxide catalyst was prepared according to the directions given in "Organic Synthesis"⁴⁷. If kept in a tightly covered vial it retained its activity for 10 months or more.

Benzonitrile obtained from Paragon Testing Laboratories was distilled through an E. L. Wheeler center rod column of 75 theoretical plates at atmospheric pressure. A center cut fraction boiling between 189.7° and 189.9° was used in the nitration experiments from which the quantitative data were obtained.

o-Nitroaniline, m-nitroaniline, and p-nitroaniline were obtained commercially and recrystallized from 95% ethanol. The melting points were 71.5°, 112°, and 148°, respectively.

⁴⁷ "Organic Synthesis", ed. H. Gilman and A. H. Blatt, John Wiley and Sons, Inc., New York, N. Y., 1941, Col. Vol. I, p. 463.

o-Nitrobenzonitrile, m-nitrobenzonitrile, and p-nitrobenzonitrile were prepared by Sandmeyer reactions from the corresponding nitroanilines by the method of Hodgson and Heyworth⁴⁸. The nitrobenzonitriles were separated from the reaction mixtures by steam distillation and recrystallized from 95% ethanol. The melting points were 110°, 116.5°, and 147°, respectively.

2,5-Dichloroaniline was obtained from Eastman Kodak Company and was purified by recrystallization from 95% ethanol; m.p. 53°.

2,5-Dichlorobenzonitrile was prepared from 2,5-dichloroaniline by a Sandmeyer reaction according to the procedure of Bornwater and Holleman⁴⁹ except that the diazonium sulfate solution was neutralized by pouring it over ice and calcium carbonate as suggested by Hodgson and Heyworth⁴⁸. The 2,5-dichlorobenzonitrile was separated by steam distillation to give a pure product melting at 128.5°, but the yields obtained were only about 30% of the theoretical.

⁴⁸H. H. Hodgson and F. Heyworth, J. Chem. Soc., 1131 (1949).

⁴⁹J. T. Bornwater and A. F. Holleman, Rec. trav. Chim., 31, 221 (1912).

2,5-Dichloroacetanilide was prepared from 2,5-dichloroaniline by treatment with acetyl chloride in pyridine solution. A typical synthesis utilized 32.4 g. (0.2 mole) dissolved in 200 ml. pyridine. This solution was cooled in an ice bath and 20 ml. acetyl chloride was added. The mixture was stirred 15 min. and then poured onto cracked ice. The precipitated 2,5-dichloroacetanilide was washed with cold water and dried to give 39.8 g. (97.5% yield) of pure product melting at 138°.

2,5-Dichloro-4-nitroacetanilide was prepared by the nitration of 2,5-dichloroacetanilide in concentrated sulfuric acid with concentrated nitric acid at room temperature according to the method of Whiston⁵⁰. Under these conditions mono-nitration was only 52% complete but the only nitro derivative obtained was the desired 4-nitro compound. This was easily purified by recrystallization from 95% ethanol to give pure product melting at 145°.⁵¹

2,5-Dichloro-6-nitroacetanilide was prepared in very low yields by the nitration of 2,5-dichloroacetanilide in fuming nitric acid at 0°. The main product under these conditions was the 4-nitro derivative but appreciable amounts

⁵⁰J. R. H. Whiston, J. Soc. Chem. Ind., 43, 370 T (1925).

⁵¹A. F. Holleman and F. E. van Haften, Rec. trav. chim., 40, 70 (1921).

of the 6-nitro compound was obtained. The separation of these two was effected by fractional recrystallization from benzene. The purified 2,5-dichloro-6-nitroacetanilide melted at 204-206°. ⁵¹

2,5-Dichloro-4-nitroaniline and 2,5-dichloro-6-nitroaniline were prepared from the corresponding acetanilides by hydrolysis in sulfuric acid solution at about 100°. These compounds melted at 153.5-154° and 65°, respectively ⁵¹. 2,5-Dichloro-4-nitroaniline was obtained as a yellow powder which on heating changed to a crystalline structure at approximately 135°; this material then melted sharply at 153.5°.

2,5-Dichloro-4-nitrobenzonitrile and 2,5-dichloro-6-nitrobenzonitrile were prepared from the corresponding anilines by the procedure used for the preparation of 2,5-dichlorobenzonitrile. These compounds were recovered by steam distillation and purified by recrystallization from Skelly solvent B. The yields were never greater than 18.7%. These compounds melted at 143° and 118°, respectively. The infrared spectra of these compounds were obtained and compared with the spectra of the corresponding dichlorodinitrobenzenes reported by Hammond, Modic and Hedges³⁵. The spectrum of 2,5-dichloro-4-nitrobenzonitrile is identical with that of 2,5-dichloro-1,4-dinitrobenzene except that

the 11.85μ band in the dinitro compound is shifted to 12.2μ in the nitrile. The spectrum of 2,5-dichloro-6-nitrobenzonitrile is very similar to that of 2,5-dichloro-1,6-dinitrobenzene except that the 11.05μ band in the dinitro compound is missing from the spectrum of the nitrile and the 9.0μ and 12.81μ bands in the dinitro compound are shifted to 8.83μ and 13.1μ , respectively, in the nitrile.

2,5-Dichloro-1,4-dinitrobenzene was prepared from 2,5-dichloro-4-nitroaniline by means of a Sandmeyer reaction using a procedure similar to that employed in the preparation of 2,5-dichloro-4-nitrobenzonitrile⁵². The product was recovered by steam distillation and recrystallized from 95% ethanol. The yield was poor but the pure product melted sharply at 117.5° . The infrared spectrum of this product was identical with the spectrum reported by Hammond, Modic, and Hedges³⁵ for 2,5-dichloro-1,4-dinitrobenzene obtained from the nitration of 2,5-dichloronitrobenzene.

2,5-Dichloro-3-nitrobenzonitrile could not be prepared by the methods tried. Attempted nitrations of 2,5-dichloroaniline in fuming sulfuric acid gave only tarry products which because of their extreme instability were assumed to be the result of N-nitration.

⁵²H. H. Hodgson and F. Heyworth, J. Chem. Soc., 1624 (1949).

Several attempts were made to recover this compound by fractional recrystallization of the product obtained by the nitration of 2,5-dichlorobenzonitrile under various conditions. Although this compound was expected to be the major product of such a nitration reaction no pure material having the properties expected of 2,5-dichloro-3-nitrobenzonitrile could be obtained.

Nitration Experiments with 2,5-Dichlorobenzonitrile

Many attempts to nitrate 2,5-dichlorobenzonitrile without hydrolysis of the nitrile group were carried out. In a typical experiment the acid nitration medium was prepared and cooled in an ice bath. The weighed sample of 2,5-dichlorobenzonitrile was added and the mixture stirred and kept at the desired temperature for the specified period of time. The solution was then poured onto a mixture of cracked ice and sodium carbonate. The mixture was stirred and the solid product was filtered off. The presence of appreciable amounts of unnitrated 2,5-dichlorobenzonitrile in the product mixture was detected by its pronounced odor. The extent of nitration was estimated roughly by the weight relation of product mixture and original compound. The infrared spectrum of the product was determined and the

presence of absorption bands at 6μ and at 6.5μ were taken as indicative of the presence of a carboxyl or carbamide group and of a nitro group, respectively. The presence of a strong absorption band at 6.0μ was therefore an indication that hydrolysis of the nitrile group had occurred whereas the presence of such an absorption band at 6.5μ indicated that nitration had taken place. Table 1 gives a list of some of the nitration experiments run.

Table 1. Nitration experiments with 2,5-dichlorobenzonitrile

Nitration Medium	Temp. °C	Time hrs.	Results
Fuming HNO_3	0	5	No nitration
Fuming HNO_3	25	$2\frac{1}{2}$	Very little nitration
Fuming HNO_3 + 10% HClO_4	24	22	Very little nitration
Fuming HNO_3	80	2	Hydrolysis and nitration
Fuming H_2SO_4 + NaNO_3	100	$1\frac{1}{2}$	Hydrolysis and nitration
Fuming HNO_3 + HClO_4	63	6	Nitration and hydrolysis
70% HClO_4 + HNO_3	25	$\frac{1}{2}$	Neither hydrolysis nor nitration
70% HClO_4 + HNO_3	37-40	11	Little or no nitration
70% HClO_4 + HNO_3	76	6	Nitration, some hydrolysis

Nitration in 70% HClO_4 seemed the most promising but even under carefully controlled conditions hydrolysis occurred. The indications were that hydrolysis of the nitrated compounds was more rapid than that of the unnitrated 2,5-dichlorobenzonitrile. It would not be possible to prove this point even if the rate of hydrolysis of the three nitrated isomers were determined in the nitration medium because it would not be possible to determine this value for 2,5-dichlorobenzonitrile.

The reaction product from one nitration experiment in 70% HClO_4 and HNO_3 yielded on repeated recrystallizations a small quantity of a white crystalline material which melted at 221° and appeared to be 2,5-dichloro-3-nitrobenzoic acid, m.p. 220° . The only other pure compound isolated from a nitration product was 2,5-dichloro-6-nitrobenzonitrile, m.p. $118-118.5^\circ$.

Since under no conditions tried could nitration of 2,5-dichlorobenzonitrile be effected without hydrolysis of the nitrile group, attention was turned to the study of the nitration of benzonitrile.

Hydrolysis Studies

In order to determine if benzonitrile would be hydrolyzed in cold, fuming sulfuric acid, four separate samples were studied. Four tubes each containing 7.5 ml. of fuming sulfuric acid were cooled to about -16° in an ice-salt bath. To each tube 0.5 ml. of benzonitrile was added and the solutions were stirred mechanically for one half hour, one hour, one and one half hours, and two hours, respectively. At the end of the designated times the tubes were removed from the cold bath and the solutions were poured onto crushed ice. Each mixture was extracted with ether and after the ether had evaporated the residue was dissolved in carbon disulfide and the infrared spectrum of this solution was studied. In none of the four cases was there any solid material in the residue from the ether extraction. All of the spectra showed recovery of the benzonitrile as judged by the strong absorption at 3.2μ characteristic of benzonitrile and none of them showed any indication that hydrolysis had occurred as judged by the absence of absorption at 6μ .

A similar hydrolysis test in 70% perchloric acid was made with benzonitrile at $24-25^{\circ}$. Two samples of benzonitrile were treated for one hour and three hours, respectively. In neither case did the infrared spectrum indicate that

hydrolysis had occurred, but in both cases benzonitrile was recovered unchanged.

o-Nitrobenzonitrile was treated with fuming sulfuric acid in an ice-salt bath at -15° for only 15 minutes. The mixture became dark red, and, when the solution was poured over ice and extracted, only a very small amount of the original o-nitrobenzonitrile was recovered.

This compound was also treated with 70% perchloric acid at 25° for slightly more than two hours. The solution was poured onto crushed ice and sodium carbonate and the o-nitrobenzonitrile was recovered unchanged.

m-Nitrobenzonitrile was treated with 70% perchloric acid at 25° for two and one half hours. The solution was then poured over crushed ice and sodium carbonate and the m-nitrobenzonitrile was recovered unchanged.

In a similar manner p-nitrobenzonitrile was treated with 70% perchloric acid and recovered unchanged after two and one half hours.

Nitration of Benzonitrile with Fuming Nitric Acid

One nitration run was made following the procedure of Baker, Cooper, and Ingold⁵³. Five grams of benzonitrile were added to 75 g. of fuming nitric acid at 0°. The solution was kept at 0° and stirred mechanically for two and one half hours. At the end of this time the solution was poured onto crushed ice and potassium carbonate. The mixture was extracted with ether and the product obtained from this extract was crystallized from 95% ethanol. A complete separation of isomers was not effected but one fraction melting at 110-112° appeared, from the infrared spectrum which showed maxima at 11.1 μ and 13.6 μ , to be mostly m-nitrobenzonitrile. A second fraction melting at 107-109° and a third melting in the range 55-75° were obtained. The infrared spectra of these fractions showed maxima at 11.7 μ and 13.4 μ indicating that they contained o-nitrobenzonitrile and p-nitrobenzonitrile. The 4.45 μ absorption band characteristic of the CN group and the 6.5 μ band characteristic of the NO₂ group were present in each of the spectra and

⁵³J. W. Baker, K. E. Cooper, and C. K. Ingold, J. Chem. Soc., 430 (1928).

bands characteristic of the CO, NH₂, and OH groups were absent.

Attempts to nitrate benzonitrile in fuming nitric acid at other temperatures failed. Infrared spectrophotometry was used as a means of determining whether nitration or hydrolysis or both had occurred. At -5° and at -2° nitration did not occur to an appreciable extent in two and one half hours. Another nitration run carried out at 0-1° gave a product whose infrared spectrum showed absorption maxima at 4.45 μ and at 13.2 μ , as does benzonitrile, at 7.41 μ , as do aromatic nitro compounds, and a weak band at 13.6 μ . A weak band at 5.85 μ indicated that some carbonyl function was present and, therefore, that some hydrolysis of the nitrile group must have occurred.

A similar nitration run carried out at about 20° gave a product whose infrared spectrum showed absorption maxima at 4.45 μ (weak), 6.5 μ , 13.6 μ , and 13.2 μ which indicated that while some nitration had occurred it had not been complete. The data concerning the other nitration experiments in fuming nitric acid are listed in Table 2.

Table 2. Preliminary nitration experiments with benzonitrile

Run	Medium	Temp. °C	Time hrs.	Spectral data							% Yield
				4.45 μ	6.0 μ	6.5 μ	13.6 μ	13.4 μ	11.75 μ	13.2 μ	
1	Fuming HNO ₃	0	2½								
2	Fuming HNO ₃	-5	2½	+	-	-	-	-	-	+	
3	Fuming HNO ₃	-2	2½	+	-	-	-	-	-	+	
4	Fuming HNO ₃	1-3	2½	+	-	+	+	-	-	+	
5	Fuming HNO ₃	10-15	2½	+	-	+	+	-	-	+	
6	Fuming HNO ₃	20	3	+	-	+	+	-	-	+	
7 ^a	Fuming HNO ₃	23	2½	+		+	+	+	-	-	40
8 ^a	Fuming HNO ₃	23	4	+		+	+	+	-	-	46
9 ^b	Fuming H ₂ SO ₄ NaNO ₃	Room	10 min.								
10 ^b	Fuming H ₂ SO ₄ NaNO ₃	0	2½								

^aThese show a little peak at 3.23 μ .

^bOnly tarry materials were obtained from these runs. No spectra were run.

Table 2. (Continued)

Run	Medium	Temp. °C	Time hrs.	Spectral data							% Yield
				4.45 μ	6.0 μ	6.5 μ	13.6 μ	13.4 μ	11.75 μ	13.2 μ	
11	Fuming H_2SO_4 NaNO_3	-10	2	+	-	+	+	+	+	-	55
12	10% HClO_4 HNO_3	0	5 $\frac{1}{2}$	+	-	+	+	+	+	-	36
13 ^c	20% HClO_4 HNO_3	0	1 $\frac{1}{2}$								
14	70% HClO_4 NaNO_3	-16	4 $\frac{1}{2}$	+	-	-	-	-	-	+	36
15	70% HClO_4 NaNO_3	0	6	+	-	+	+	-	-	-	
16	70% HClO_4 HNO_3	25	1	+	-	+	+	+	+	+	

^cLittle solid product was obtained in this run. No spectrum was run.

Table 2. (Continued)

Run	Medium	Temp. °C	Time hrs.	Spectral data							% Yield
				4.45 μ	6.0 μ	6.5 μ	13.6 μ	13.4 μ	11.75 μ	13.2 μ	
17	70% HClO_4 HNO_3	25	2	+	-	+	+	-	+	+	
18	70% HClO_4 HNO_3	25	18	+	-	+	+	+	+	-	95
19	70% HClO_4 HNO_3	25	24	+	-	+	+	+	+	-	93
20	70% HClO_4 HNO_3	40-42	6	+	-	+	+	+	+	-	86
21	70% HClO_4 HNO_3	52-53	8	+	-	+	+	+	+	-	46
22	70% HClO_4 HNO_3	62.5	6	-	+	+	+	+	+	-	93

Nitration of Benzonitrile in Sulfuric Acid or Perchloric Acid

In these experiments the same general nitrating procedure was followed. The acid nitrating medium was prepared and cooled in an ice or ice-salt bath. The benzonitrile sample was added and the mixture was stirred to effect solution of the benzonitrile. The reaction tube was then fitted with its cold finger condenser and transferred to a constant temperature bath which was maintained at the desired temperature. After the designated time interval the tube was removed from the bath and the solution was poured over crushed ice and sodium carbonate. When all the carbonate had dissolved the solid product was filtered, washed with water and dried. The aqueous mother liquor was extracted with ether to recover a small additional portion of the product. The ether was evaporated and the residue was added to the solid which was collected in the filtration. The combined solids were homogenized by trituration in an agate mortar. Infrared spectra of the products were run with Nujol mulls or carbon disulfide solutions. In a few cases the spectrum was also run on chloroform or bromoform solutions.

All of the preliminary nitration experiments are shown in Table 2. The nitration medium, time, and temperature are

listed for each run. The pertinent data from the infrared spectra of the products are also listed. In cases in which the product showed appreciable absorption at the wave length listed the table is marked + ; if there was little or no absorption at this wave length a - sign is given. In certain cases where it seemed warranted the per cent yield was determined by weighing the total solid product and calculating on the basis of mononitration. This and other significant information are listed for each run.

The quantitative nitration experiments were carried out following the same general procedure. It was found to be convenient and sufficiently accurate to measure the benzonitrile (s. g. = 1.01) from a calibrated syringe. The data are summarized in Table 3.

Hydrogenation Experiments

The hydrogenation experiments were carried out at room temperature and atmospheric pressure. In all the experiments the same general procedure was followed. Platinum oxide catalyst was weighed into the hydrogenation flask and a small amount of calcium carbonate was added. The solids were covered with absolute alcohol and the flask was attached to the hydrogenation apparatus. After the system

Table 3. Quantitative nitration experiments with benzonitrile

(Medium: 10 ml. 70% HClO_4 and 1 ml. fuming HNO_3)

Run	Amount of benzonitrile ^a	Temperature °C	Time (hours)
1	0.972 g.	25	8
2	1 ml.	35	1
3	1 ml.	35	2
4	0.810 g.	35	4
5	1.008 g.	35	6
6	1 ml.	35	6
7	1.033 g.	35	8
8	1 ml.	43	1
9	1 ml.	43	1

^aFrom syringe; 1 ml. = 0.997 g. \pm 0.003 g.

was swept with hydrogen for about ten minutes, the catalyst was reduced at atmospheric pressure. The sample to be hydrogenated was dissolved in absolute alcohol and the solution was added through a side arm in the hydrogenation flask. During the hydrogenation the mixture was stirred by means of a magnetic stirrer and the mercury leveling bulb was adjusted from time to time to maintain atmospheric pressure within the system. When the reaction was complete, the solution was filtered and the alcohol was removed by distillation under reduced pressure in an atmosphere of nitrogen.

The hydrogenation of o-nitrobenzonitrile gave o-aminobenzamide, m.p. 109.5-110°. (The reduction to o-aminobenzamide was complete and rapid.) In several trial runs with carefully weighed samples of o-nitrobenzonitrile a time vs. hydrogen up-take curve was made. In each case a smooth curve was obtained which leveled to zero slope when the calculated amount of hydrogen had been taken up. In no case was there a gradual rise in this curve even if the run was continued long after the calculated amount of hydrogen had been absorbed. The o-aminobenzamide was easily isolated and recrystallized. In a typical experiment 80% of pure o-aminobenzamide was obtained. It was found that this compound was sufficiently soluble in chloroform to

permit the infrared spectrum to be studied in that solvent. Samples of o-aminobenzamide were prepared and a calibration curve of optical density vs. concentration was prepared at the 6.0 μ absorption peak. Samples of o-nitrobenzonitrile were then hydrogenated as described above, the residues were taken up in chloroform and the infrared spectra were run. In no case was the recovery of o-aminobenzamide quantitative as calculated from the calibration curves but yields of 84% to 86% were typical.

Under the same hydrogenation conditions m-nitrobenzonitrile gave m-aminobenzonitrile. This product, pale yellow needles, m.p. 53^o, decomposed easily and was only isolated in low yields. A plot of time vs. hydrogen up-take gave a smooth curve that showed a definite decrease in the rate of hydrogen up-take when the amount of hydrogen required to reduce the nitro-group had been absorbed, but the curve did not level off. There was a gradual increase in hydrogen taken up. In one run which was allowed to continue after the calculated amount of hydrogen necessary to convert the nitro group to an amino group had been absorbed an additional 45 ml. of hydrogen were absorbed in 160 minutes, representing an excess of 22% of hydrogen absorbed.

When the hydrogenation product was taken up in chloroform directly, the infrared spectrum showed maxima at 4.45 μ ,

characteristic of a benzonitrile, and at 2.95μ , characteristic of the NH_2 group, but no absorption at 6μ as is observed in the spectra of benzamides or benzoic acids.

When p-nitrobenzonitrile was hydrogenated under similar conditions, p-aminobenzonitrile was obtained and isolated in low yields. On recrystallization from Skelly solvent D, pale yellow crystals of m.p. $84-85^\circ$ were obtained. In the case of this compound a plot of time vs. hydrogen up-take gave a curve which leveled off when the calculated amount of hydrogen had been absorbed. As in the case of o-nitrobenzonitrile there was no gradual absorption of hydrogen after the calculated amount was taken up.

When the hydrogenation product of p-nitrobenzonitrile was taken up directly in chloroform without any purification the infrared spectrum of the solution showed no carbonyl frequency but did show absorption maxima at 2.95μ and 4.45μ .

Several synthetic mixtures of the three nitrobenzonitriles were hydrogenated under the same conditions. The product, without any purification, was dissolved in chloroform and the infrared spectrum run on this solution. A synthetic mixture containing 22.8% o-nitrobenzonitrile was analyzed by this method and the amount of o-aminobenzamide estimated was 82% of the amount calculated. Since the error

in this experiment was of the same order as that encountered in the similar experiments with pure o-nitrobenzonitrile, it was thought that this error might be overcome by setting up the calibration curve on the basis of o-nitrobenzonitrile hydrogenated by running a series of samples and taking the hydrogenation product up directly in chloroform without purification. Such a calibration curve was made. One synthetic mixture containing 10.3% o-nitrobenzonitrile was hydrogenated and the product was dissolved directly in chloroform. The infrared spectrum of this solution was run and the o-aminobenzamide present was estimated, by comparison of the absorption at 6.01μ with the corrected calibration curve, to be 88% of the calculated amount. In two other synthetic mixtures containing 22.8% and 10.8% o-nitrobenzonitrile the amounts of o-aminobenzamide estimated by this method were 107% and 134%, respectively, of the calculated values.

Two samples of nitration products from the preliminary nitration experiments were hydrogenated and the amount of o-aminobenzamide estimated spectrophotometrically in the same manner. A sample from a run identical to Run 18 gave an estimated 6.8% o-nitrobenzonitrile but a sample from Run 18 gave so little absorption at 6μ that it was only a shoulder of the 6.19μ band, present in all these chloroform solutions

of the reduction products, and the amount of o-nitrobenzonitrile present could be estimated at only 4.1%.

The erratic results for the synthetic mixtures and the unreliable values estimated for the nitration products led to the abandoning of this method of analysis for o-nitrobenzonitrile.

Non-Aqueous Titrations of Hydrogenation Products

A sample of o-nitrobenzonitrile was hydrogenated at atmospheric pressure in absolute alcohol as before and the resultant o-aminobenzamide was taken up in a mixture of chlorobenzene and acetonitrile. A five ml. aliquot portion of this solution was titrated potentiometrically with 0.0945 N perchloric acid in glacial acetic acid. The titration curve showed a sharp break at 7.1 mv. and, based on the weight of o-nitrobenzonitrile hydrogenated, the titer showed a 1% error: 0.397 meq. of hydrogen ion being used whereas the aliquot should have contained 0.401 meq. of o-aminobenzamide.

Under the same conditions a sample of m-nitrobenzonitrile was hydrogenated and the resulting product was titrated in chlorobenzene-acetonitrile solution with perchloric acid in glacial acetic acid. The titration curve

showed a sharp break at 7.4 mv. In this experiment the titer of acid was 25% higher than that calculated from the amount of m-aminobenzonitrile. It is possible that, whereas in the case of o-nitrobenzonitrile the hydrogenation proceeded smoothly to give o-aminobenzamide, m-nitrobenzonitrile was not hydrogenated to m-aminobenzonitrile only, but that the nitrile group was also attacked. No products in which the nitrile group was completely or partially reduced were isolated, but since these compounds would be unstable their formation could account for the low yields of m-aminobenzonitrile actually isolated and for the presence of tacky, colored materials present in the hydrogenation product from m-nitrobenzonitrile. Even though this experiment points out difficulties to be expected in the hydrogenation of the mixed nitrobenzonitriles from nitration reactions, the fact that o-aminobenzamide is formed in quantitative yields under these conditions indicated that any method by which the quantity of o-aminobenzamide present could be determined accurately would, in turn, give the amount of o-nitrobenzonitrile in the mixture hydrogenated. Non-aqueous titrations could not give the amount of o-aminobenzamide present in the presence of m-nitrobenzonitrile reduction products because the values of the potential at the end points of the individual titrations were so close. This method of

determining the o-aminobenzamide formed on hydrogenation was therefore abandoned.

Metal Compounds of the Hydrogenation Products

Laboratory tests showed that none of the hydrogenation products of the three nitrobenzonitriles formed insoluble compounds with either zinc or cupric ion. On hydrolysis the hydrogenation products should give anthranilic acid, m-aminobenzoic acid, and p-aminobenzoic acid. If hydrolysis were incomplete the three aminobenzamides should be obtained. It was found that none of these compounds except anthranilic acid formed insoluble compounds with zinc or cupric ion. Inasmuch as anthranilic acid is used as a precipitating agent for the quantitative determination of zinc and copper⁵⁴ it was decided to try to use one of these metal ions as the precipitating agent to determine the anthranilic acid formed on hydrolysis of the product of hydrogenation of the mixed nitrobenzonitriles.

⁵⁴F. J. Welcher, "Organic Analytical Reagents", D. Van Nostrand Co., Inc., New York, N. Y., 1947, Vol. II, p. 195.

Attempted Potentiometric Titrations of the Metal
Anthranilates

Zinc anthranilate was prepared in 96% yield from a pure sample of anthranilic acid. A small sample was suspended in glacial acetic acid and titrated with a standard solution of perchloric acid in glacial acetic acid. The titration curve showed no break at all. It was impossible from the data to determine how much zinc anthranilate was present.

A similar titration of copper anthranilate gave a very slight break in the titration curve. An attempt to titrate anthranilic acid in glacial acetic acid with copper acetate in glacial acetic acid gave even poorer results. An attempt to titrate anthranilic acid in aqueous sodium acetate with aqueous copper sulfate gave no better results.

Attempted Determination of α -Nitrobenzonitrile as the Zinc
Anthranilate

Anthranilic acid can be determined quantitatively by the excess bromination method⁵⁵. The attempt was made to

⁵⁵A. R. Day and W. T. Taggart, Ind. Eng. Chem., 20, 545 (1928).

determine the o-nitrobenzonitrile from the nitration of benzonitrile indirectly by hydrogenation and hydrolysis of the nitration product followed by removal of the anthranilic acid as the zinc anthranilate. The zinc anthranilate was then decomposed with dilute hydrochloric acid and the anthranilic acid liberated was titrated by the excess bromination method. Each step of this sequence was tried with pure samples of anthranilic acid or with o-nitrobenzonitrile. The titration of pure samples of anthranilic acid could be carried out with errors amounting to 0.5% to 2.4%. The error increased to 10% to 15% when the anthranilic acid was first precipitated as the zinc anthranilate. When the whole sequence was tried on pure samples of o-nitrobenzonitrile the error rose to 35%. The step which seemed to cause the greatest error was the hydrolysis of the o-aminobenzamide to anthranilic acid. When sodium hydroxide was used in the hydrolysis a large amount of silicic acid was precipitated when the solution was acidified and evidently some of the anthranilic acid was adsorbed by this gel and was not extracted by the hydrochloric acid used to decompose the zinc anthranilate. When sulfuric acid was used in the hydrolysis the conversion of anthranilamide to anthranilic acid was evidently incomplete for the error from this run amounted to 98%. When a synthetic mixture of nitrobenzonitriles

was carried through the sequence, using sodium hydroxide in the hydrolysis step, the errors in the amount of o-nitrobenzonitrile calculated were from 67% to 88%. The errors were always in the same direction; the calculated amount of o-nitrobenzonitrile being always much smaller than the correct amount. One mixture obtained from the nitration of benzonitrile was carried throughout the sequence. The calculated per cent of o-nitrobenzonitrile was only 0.23%. This value was much smaller than that indicated by even the poorest spectral data.

Ultraviolet Absorption Spectra

The ultraviolet absorption spectra of the three nitrobenzonitriles, were run in 95% ethanol using a Beckmann Quartz Spectrophotometer Model DU. The optical density was read directly from the instrument and wave length range studied was 220 $m\mu$ to 370 $m\mu$. The concentrations of the three solutions were for o-nitrobenzonitrile, 1.07×10^{-4} M, m-nitrobenzonitrile, 1.13×10^{-4} M, and p-nitrobenzonitrile, 1.06×10^{-4} M. Both m-nitrobenzonitrile and o-nitrobenzonitrile showed strong absorption at 220 $m\mu$. The m-nitrobenzonitrile showed a second absorption maximum at

at 255 $m\mu$ and *o*-nitrobenzonitrile showed a weaker maximum at 260 $m\mu$. The *p*-nitrobenzonitrile sample showed only one maximum at 254 $m\mu$.

Infrared Absorption Spectra

For the qualitative work of the preliminary experiments with benzonitrile and for all the spectral work done in connection with the 2,5-dichlorobenzonitrile experiments a Baird Associates Model B infrared spectrophotometer equipped with sodium chloride optics was used. The resolution obtainable with this instrument was not sufficient for the quantitative analysis of the nitration products of benzonitrile and a Perkin-Elmer Corporation Model 13 infrared spectrophotometer also equipped with sodium chloride optics was used in this work.

The identifying absorption maxima observed in carbon disulfide solutions of benzonitrile and of the three nitrobenzonitriles are shown in Table 4. The Baird spectrophotometer tracings of these four compounds are shown in Figure 1. The data obtained from the infrared spectra of 2,5-dichloro-4-nitrobenzonitrile and 2,5-dichloro-6-nitrobenzonitrile are given above under the preparation of these compounds.

Figure 1. Infrared spectra from Baird tracings in carbon disulfide solution of benzonitrile, o-nitrobenzonitrile, m-nitrobenzonitrile, and p-nitrobenzonitrile

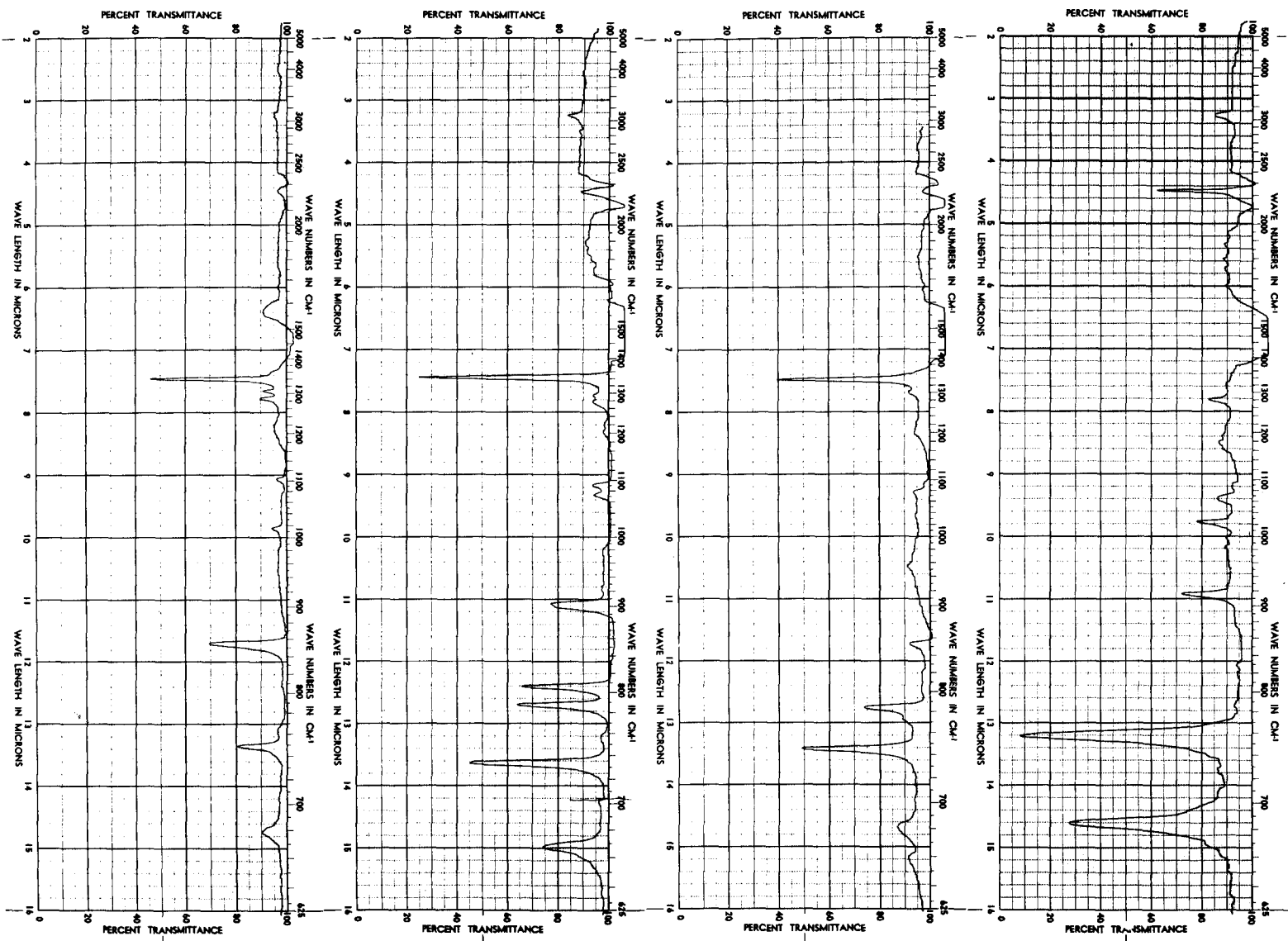


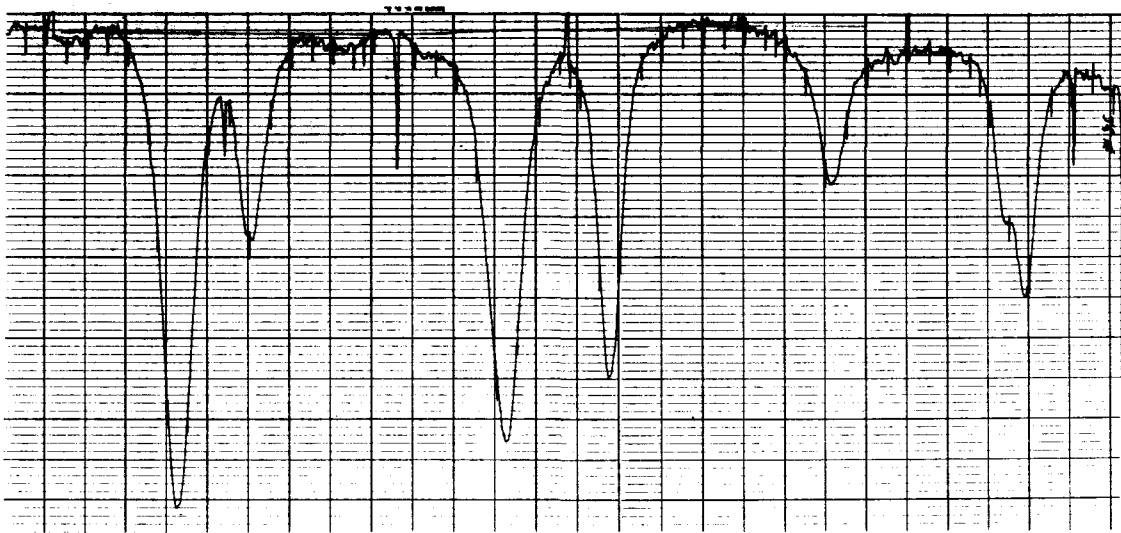
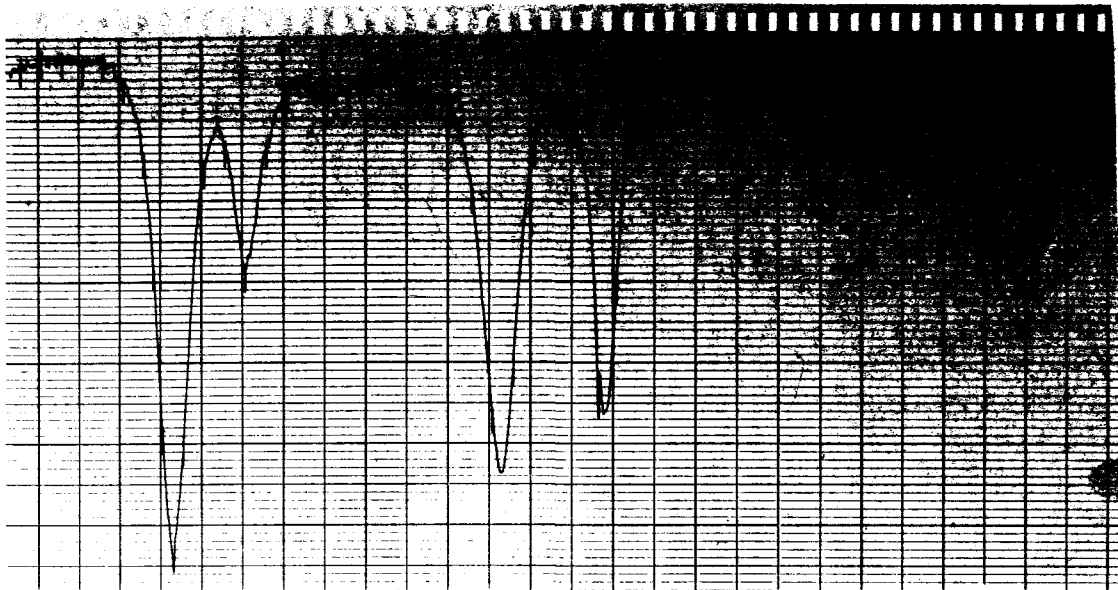
Table 4. Infrared absorption maxima

Compound	Wave length in microns					
Benzonitrile	-	-	13.22	-	-	
<u>o</u> -Nitrobenzonitrile	11.78	12.78	-	13.42	-	
<u>m</u> -Nitrobenzonitrile	-	12.72	-	-	13.63	
<u>p</u> -Nitrobenzonitrile	11.75	-	-	13.38	-	

The spectra of one synthetic mixture of the three nitrobenzonitriles and of one sample of a nitration product are reproduced in Figure 2 from the Perkin-Elmer spectrophotometer tracings. In reading the spectra for quantitative comparisons the base line technique⁵⁶ was first tried but abandoned in favor of a simpler method of compensating for differences in background level of the different spectral tracings. It was found that the point in the absorption spectrum corresponding to the counter marking 6.7, or a frequency of 12.05 , was constant in all the tracings made by means of the Perkin-Elmer spectrophotometer.

⁵⁶J. J. Heigel, M. F. Bell and J. U. White, Anal. Chem., 19, 293 (1947).

Figure 2. Infrared spectra from Perkin-Elmer tracings of synthetic mixture No. 5 and of the nitration product from Run 6



Accordingly, this point was taken to represent 100% transmission and a correction factor applied to the whole curve which would in effect raise the transmission value a constant amount at each point on the curve. In many of the spectra used in the quantitative work this correction factor was as low as 1% but in one the factor was 8.5%. This method of unifying the spectral tracings seems to be justified by the results obtained in the calibration curves of $\log(I_0/I)$ vs. concentration for m-nitrobenzonitrile. Since the points obtained at 11.2 and at 13.6 gave very good straight lines and the estimates of the m-nitrobenzonitrile content in the unknown mixtures from both calibration curves agree very well, this method gives better internal agreement than does the method of base line reading, which, in effect, gives a different correction at different frequencies. The fact that the values obtained with known mixtures of the nitrobenzonitriles fall on the same lines established by the pure m-nitrobenzonitrile samples further justifies this method for estimating the amount of m-nitrobenzonitrile in the unknowns.

DISCUSSION

The difficulties encountered in attempting to nitrate 2,5-dichlorobenzonitrile without hydrolysis led to the use of perchloric acid and fuming nitric acid as a nitrating medium. Pearce and Nelson⁵⁷ have shown that the water activity in perchloric acid is very small and Robinson⁵⁸ has mentioned the use by Müller of perchloric acid as a solvent in nitration reactions. He dismissed the possibility with the remark that the process was too dangerous to have any practical application. In this work mixtures of 70% perchloric acid and fuming nitric acid have been used in small scale nitration experiments at temperatures as high as 80° without any ill effects. Under no conditions tried could nitration of 2,5-dichlorobenzonitrile be effected without hydrolysis of the nitrile group. Indications were, however, that hydrolysis of the nitrated compounds was more rapid than hydrolysis of 2,5-dichlorobenzonitrile. No 2,5-dichlorobenzamide or 2,5-dichlorobenzoic acid was ever isolated from a reaction mixture whereas 2,5-dichloro-3-nitrobenzoic acid was isolated in very low yields from one

⁵⁷J. N. Pearce and A. F. Nelson, J. Am. Chem. Soc., **55**, 3075 (1933).

⁵⁸R. Robinson, J. Chem. Soc., 238 (1941).

product. It was not possible under the conditions employed to study the ortho to para ratio in nitration of 2,5-dichlorobenzonitrile, but the fact that 2,5-dichloro-6-nitrobenzonitrile was easily isolated from the nitration mixture points to considerable ortho direction by the nitrile group in this compound. That a small quantity of 2,5-dichloro-3-nitrobenzoic acid is isolated is probably due to a greater solubility of the acid compounds. The fact that no 2,5-dichloro-4-nitrobenzonitrile or hydrolysis product of this compound was isolated may indicate that very little was formed or that what formed was hydrolysed and escaped detection.

Since the experiments in which perchloric acid was used looked most promising, it was chosen as the solvent in the nitration experiments with benzonitrile. Preliminary experiments showed that this compound could be nitrated quantitatively without hydrolysis of the nitrile group and the problem became one of analyzing the product mixtures for the three nitrobenzonitriles.

The infrared spectra of the three nitrobenzonitriles were obtained by means of the Baird Associates infrared spectrophotometer Model 12 equipped with sodium chloride optics. The spectra of the o- and p- nitrobenzonitriles show overlapping absorption bands at 11.75 μ and 13.4 μ ,

and that of m-nitrobenzonitrile shows a strong band at 13.6 μ . Since the o- and p-nitrobenzonitriles have two absorption bands in common it might have been possible to calculate the concentrations of both of these compounds from the absorption maxima at the two wave lengths and calibration curves for the two nitrobenzonitriles. Since m-nitrobenzonitrile shows strong absorption bands at frequencies where neither o- nor p-nitrobenzonitrile absorb, the calculation of the concentration of the former in a mixture would have been easy. It was found, however, that in a mixture of the nitrobenzonitriles the absorption band characteristic of o- and p-nitrobenzonitrile at 13.4 μ was overshadowed by the strong band of the meta isomer at 13.6 μ . The resolution of these two bands was not possible with this instrument.

The hydrogenation of the nitrobenzonitriles to amines was carried out with the hope that in the spectra of the amino compounds the absorption maxima would be so shifted that an infrared method of analysis could be employed. Catalytic hydrogenation was chosen as the method of reduction because it requires the introduction of fewer chemicals than would be the case with other methods and should lead to a more easily purified product. The reduction of the nitrobenzonitriles to aminobenzonitriles has been carried

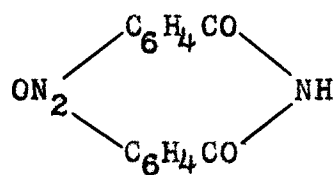
out by means of stannous chloride and hydrochloric acid and the three aminobenzonitriles have been well characterized⁵⁹.

The hydrogenations were carried out at room temperature and atmospheric pressure in absolute alcohol with a small quantity of calcium carbonate added to neutralize any acid which might have been present on the catalyst. Under these conditions m- and p-nitrobenzonitrile were hydrogenated to the corresponding aminobenzonitriles. The isolated yields of these products were low but the reduction to these compounds was unmistakable. In the case of o-nitrobenzonitrile, however, quantitative yields of o-aminobenzamide, m.p. 109-110°, were obtained. Except for the addition of calcium carbonate these conditions are the same as those reported by Cook, Heilbron, Reed and Strachan⁶⁰. They reported the reduction of o-nitrobenzonitrile to o-azoxyphenyl cyanide, m.p. 197-198°. The infrared spectrum of the product obtained in the present research gave unmistakable evidence of the presence of the amino and carbamide groups. Furthermore o-azoxyphenyl cyanide is reported to give the imide of

⁵⁹M. T. Bogert and W. F. Hand, J. Am. Chem. Soc., 24, 1038 (1902). M. T. Bogert and H. T. Beans, J. Am. Chem. Soc., 26, 469 (1904). M. T. Bogert and L. Kohnstamm, J. Am. Chem. Soc., 25, 481 (1903).

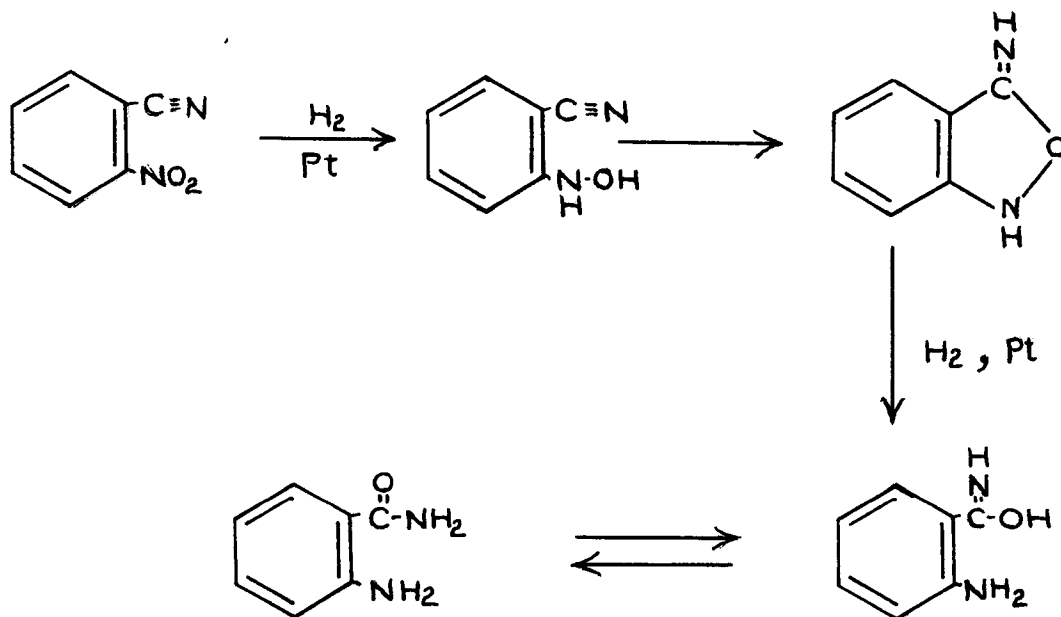
⁶⁰A. H. Cook, I. M. Heilbron, K. J. Reed and M. N. Strachan, J. Chem. Soc., 861 (1945).

o,o'-azoxybenzoic acid,



on heating with hydrochloric acid, whereas the product obtained in this work gave anthranilic acid on either acidic or basic hydrolysis.

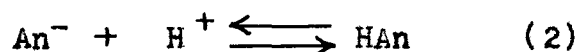
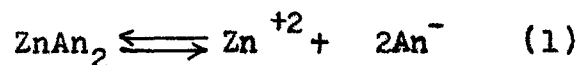
A possible mechanism for this reductive hydrolysis of o-nitrobenzonitrile is given below.



The critical point in this suggestion is the fact that the intermediate can cyclize. The first and last are the generally accepted steps in catalytic hydrogenation of an aromatic nitro compound and an aromatic hydroxyl amine.

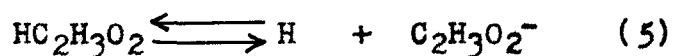
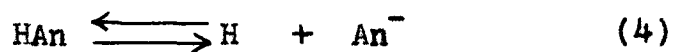
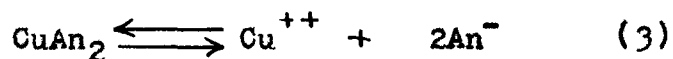
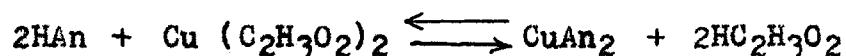
Analytical methods based on the reduction of the nitro-groups to amino groups in the product mixture have been outlined above. The failure of all of these methods must be due to the large amount of m-nitrobenzonitrile in the product since the theoretically most promising of them were methods of determining o-nitrobenzonitrile. The fact that the basicities of the three amino compounds obtained from the hydrogenation of the three nitrobenzonitriles were so nearly the same could not have been predicted but is not surprising. The titration of a suspension of zinc or copper anthranilate in glacial acetic acid with perchloric acid in glacial acetic should have been the titration of a strong base, anthranilate anion, with a strong acid, perchloric acid. By use of a potentiometric titration method with a glass indicator electrode it was expected that a sharp break in the titration curve might mark the equivalence point of the titration. No sharp break occurred during the titration indicating that zinc anthranilate, the chelate, ZnAn_2 , is very stable and the dissociation constant, for it must be

smaller than the ionization constant of anthranilic acid, HAn, in this medium.



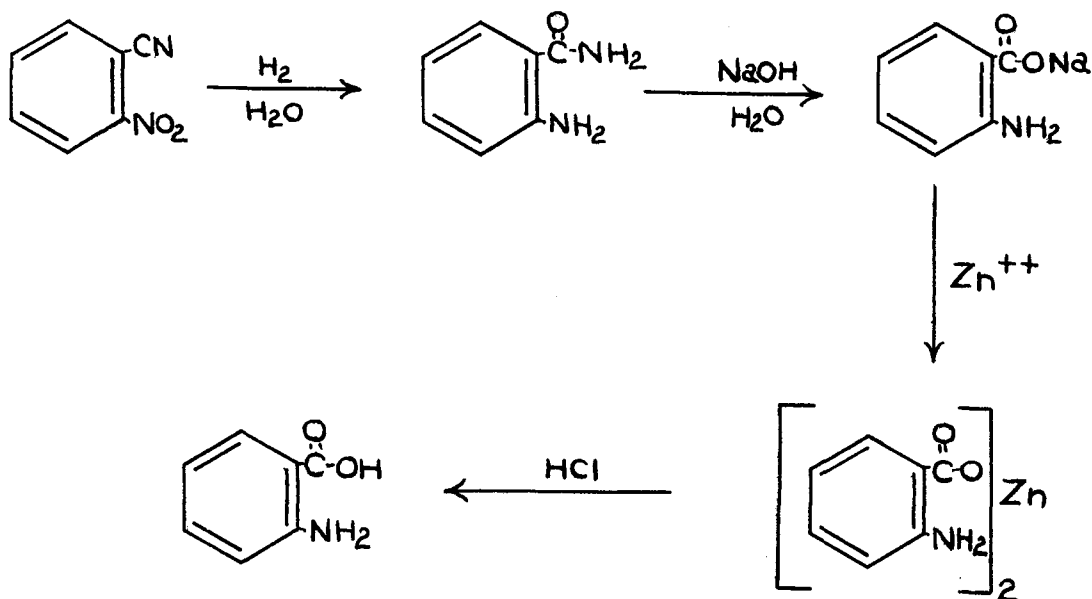
Since the zinc anthranilate was not soluble in the medium when the titration was begun and only gradually dissolved during the course of the titration another medium might have given better results. It appears, however, that this titration fails to give a sharp break at the equivalence point because the equilibrium in (1) is shifted to the right only in the presence of a large excess of hydrogen ions.

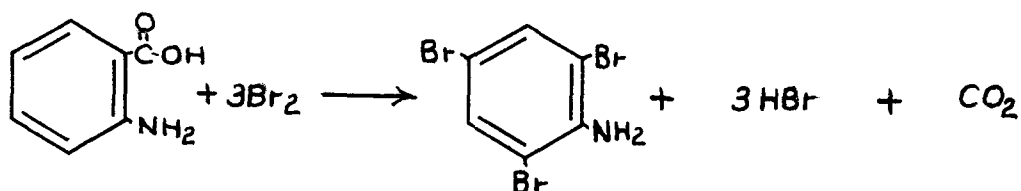
A homogeneous potentiometric titration in glacial acetic acid of anthranilic acid with copper acetate gave no better results. This titration was based on the following reactions.



Since copper anthranilate is only very slightly soluble and stable the equilibrium in (3) should be displaced to the left tying up the anthranilate ion, An^- , from the equilibrium (4). The acetate ion would combine with the hydrogen ions thus liberated. Excess copper acetate added after the equivalence point had been reached might have increased the pH sufficiently to cause a noticeable break in the titration curve.

The attempts to determine o-nitrobenzonitrile from the method depending on hydrogenation, hydrolysis, precipitation with zinc, decomposition of the zinc anthranilate, and titration of the anthranilic acid by the excess bromination method failed at the hydrolysis and precipitation steps.





That it was not the hydrogenation step that failed to be quantitative was shown by the quantitative yields of o-aminobenzamide obtained from this step alone. The precipitation of zinc anthranilate from the slightly acidified hydrolysis mixture could not be accomplished without the accompanying precipitation of silicic acid gel. Filtration of this mixture was slow and difficult. When the precipitate was treated with excess dilute hydrochloric acid to decompose the zinc anthranilate and dissolve out the anthranilic acid for the titration step, in no experiment was it certain that all the anthranilic acid had been extracted from the gel. When this step of the procedure was carried out on the hydrolysis product obtained from the sequence beginning with a mixture of nitrobenzonitriles, the precipitated silicic acid gel could have adsorbed and carried down the aromatic compounds resulting from the hydrogenation of the m- and p-nitrobenzonitriles. If these compounds were taken up with the anthranilic acid by the extracting acid

solution, they would have interfered with the bromination titration. If all the anthranilic acid and none of the other possible aromatic compounds were extracted the results would have been correct. Since erratic results were obtained it must be that in some experiments not all the anthranilic acid was extracted whereas in others some of the other aromatic compounds must have been carried down and extracted by the hydrochloric acid. When acid hydrolysis of the hydrogenation product was tried, the results were so low that it could only be concluded that hydrolysis was incomplete.

When it was certain that this sequence of reactions would not lead to an accurate determination of the o-nitrobenzonitrile in the reaction mixture, the infrared method of analysis was again tried. At this time a Perkin-Elmer Model 13 instrument was available and the resolution of this instrument was shown to be far superior to that of the Baird Associates instrument used earlier. Since the spectra of o-nitrobenzonitrile and p-nitrobenzonitrile show absorption at two common frequencies but neither shows an isolated absorption band characteristic of it alone, it was necessary to calculate ortho to para ratio from absorption at these two frequencies. The superiority of the Perkin-Elmer instrument was shown by its ability to separate the

746 cm^{-1} , 13.4 μ , absorption band characteristic of the o- and p-nitrobenzonitriles from the stronger absorption band at 735 cm^{-1} , 13.6 μ , characteristic of m-nitrobenzonitrile.

Attempts were made to work out calibration curves for the o- and p-nitrobenzonitriles using absorption at 13.4 μ and 11.7 μ so that by a method of simultaneous equations the amounts of o- and p-nitrobenzonitrile in a synthetic mixture could be calculated accurately. The calibration curves obtained by plotting $\log (I_0/I)$ at a given frequency against concentration of either o- or p-nitrobenzonitrile obtained from spectra of solutions of pure samples of these compounds run in carbon disulfide solution showed only a fair linear relationship. Slopes of the best straight lines drawn through these points were obtained. At 13.4 μ slopes for the o- and p-nitrobenzonitrile curves were 1.6×10^{-2} and 0.28×10^{-2} , respectively. At 11.7 μ the corresponding values for o- and p-nitrobenzonitrile were 0.55×10^{-2} and 1.7×10^{-2} , respectively. From these values it is seen that in a mixture absorption at 13.4 μ would be due more to the ortho isomer whereas absorption at 11.7 μ would be due more to the para isomer. Using these values of the slopes of the calibration curves, equations were set up and tested by substituting the values of $\log (I_0/I)$ from the spectra of synthetic mixtures. The amounts of the

o- and p-nitrobenzonitriles calculated in this way never agreed with the amounts present in the mixture. It could only be concluded that absorption by the two compounds at the two frequencies were not additive and that, while fair linearity was obtained in the calibration curves, the solutions did not follow Beer's law accurately.

Since the absorption at the two frequencies was due, nevertheless, to the o- and p-nitrobenzonitriles present in the mixture, the ratio of the I_0/I values at the two frequencies should be proportional to the ortho to para ratio.

A series of synthetic mixtures similar to the mixtures of nitrobenzonitriles obtained in the nitration experiments were prepared and their spectra run. The I_0/I values were calculated at the pertinent frequencies. The data for these mixtures are given in Table 5 in which $D = I_0/I$ at the frequency indicated.

The amount of m-nitrobenzonitrile in the product mixtures was determined from the log D vs. concentration calibration curves at both 13.6μ and 11.2μ shown in Figure 3. Included in this figure are data obtained from the pure samples of m-nitrobenzonitrile shown in Table 6 as well as data from the synthetic mixtures. The concentration and percentage of m-nitrobenzonitrile in nitration products estimated from both calibration curves and the calculated

Table 5. Synthetic mixtures of nitrobenzonitriles

No.	Wt. mg.	Wt. of Isomers			% of Isomers			o/p	D ^a				D _{13.4}
		mg.			o	m	p		13.4 μ	11.7 μ	13.6 μ	11.2 μ	D _{11.7}
		<u>o</u>	<u>m</u>	<u>p</u>									
1	73.8	10.4	60.5	2.9	14.1	82.0	3.9	3.59	1.51	1.31	-- ^b	-- ^b	1.153
2	39.0	8.0	28.6	2.4	20.5	73.4	6.16	3.33	1.39	1.28	2.04	1.37	1.085
3	33.6	7.9	22.8	2.9	23.5	67.9	8.64	2.72	1.40	1.34	1.82	1.31	1.045
4	51.4	7.9	40.5	3.0	15.4	78.9	5.85	2.63	1.39	1.34	2.38	1.47	1.037
5	45.9	7.3	36.5	2.1	15.9	79.6	4.58	3.48	1.33	1.25	2.50	1.51	1.064
6	37.9	11.5	23.5	2.9	30.4	62.0	7.65	3.97	1.52	1.33	1.82	1.30	1.143
7	46.7	9.7	28.5	8.5	20.7	61.0	18.3	1.14	1.46	1.61	2.01	1.36	0.906

^aD = I_0/I at the wave length given.

^bAll of the meta isomer was not in solution.

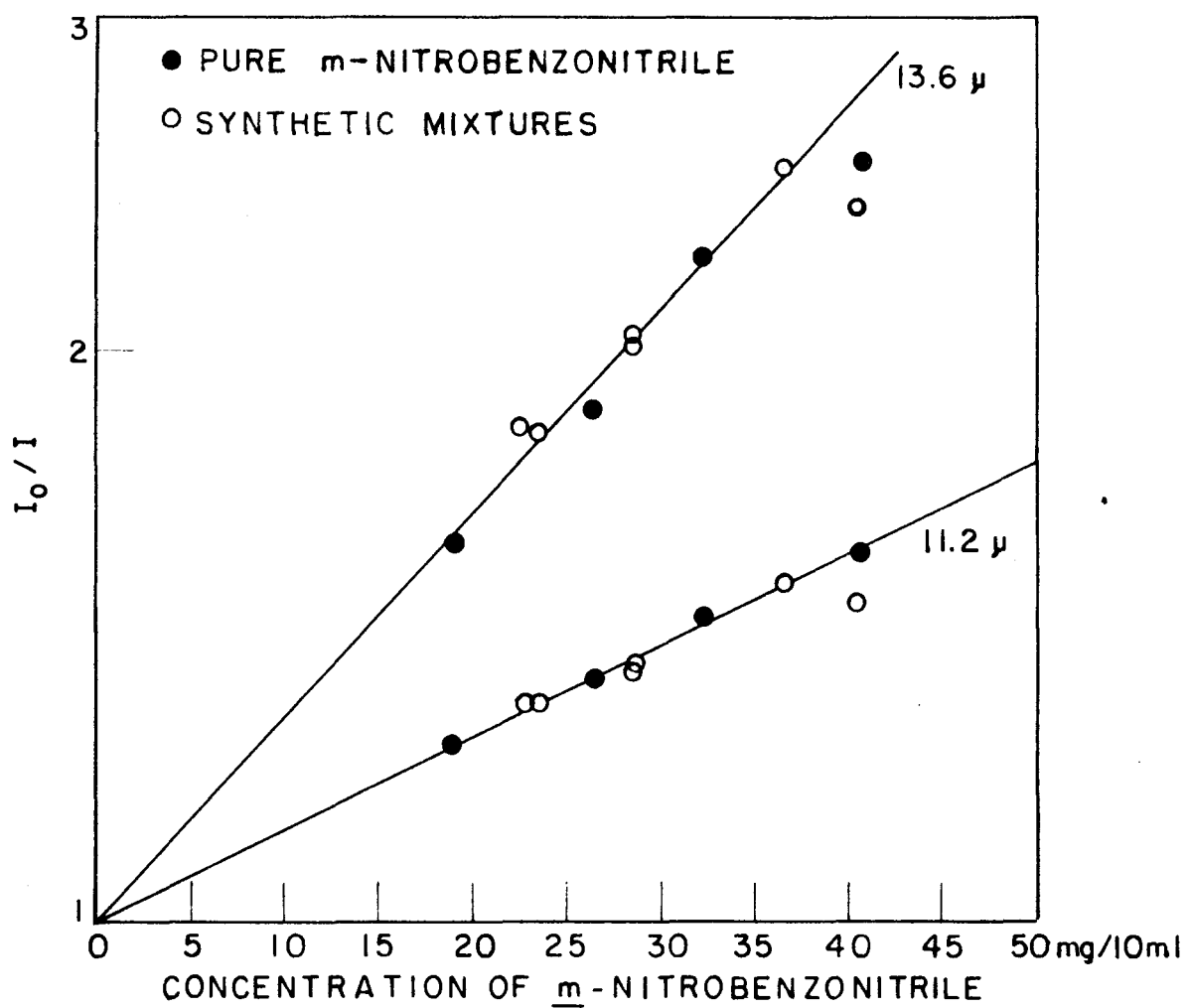


Figure 3. Calibration curves for *m*-nitrobenzonitrile

Table 6. Pure samples of m-nitrobenzonitrile

Sample	Concentration mg./10 ml.	D^a	
		11.2 μ	13.6 μ
1	26.4	1.34	1.86
2	40.8	1.56	2.52
3	19.0	1.24	1.58
4	32.1	1.45	2.24

$^aD = I_0/I$ at the wave length given.

averages are shown in Table 5. The close agreement of values estimated from the two calibration curves justifies the method employed for unifying the spectra.

Figure 4 gives the plot of the ortho to para ratio vs. $D_{13.4}/D_{11.7}$. On this graph are included the values obtained for the synthetic mixtures shown in Table 5 and the values estimated for the nitration products. The spread shown by the points from which this curve is drawn up gives a measure of the accuracy of the method. At higher values of the ortho to para ratio the points are more widespread but a change in the ortho to para ratio, here, of ± 0.18 units corresponds roughly to a change in $D_{13.4}/D_{11.7}$ of ± 0.017 units. The

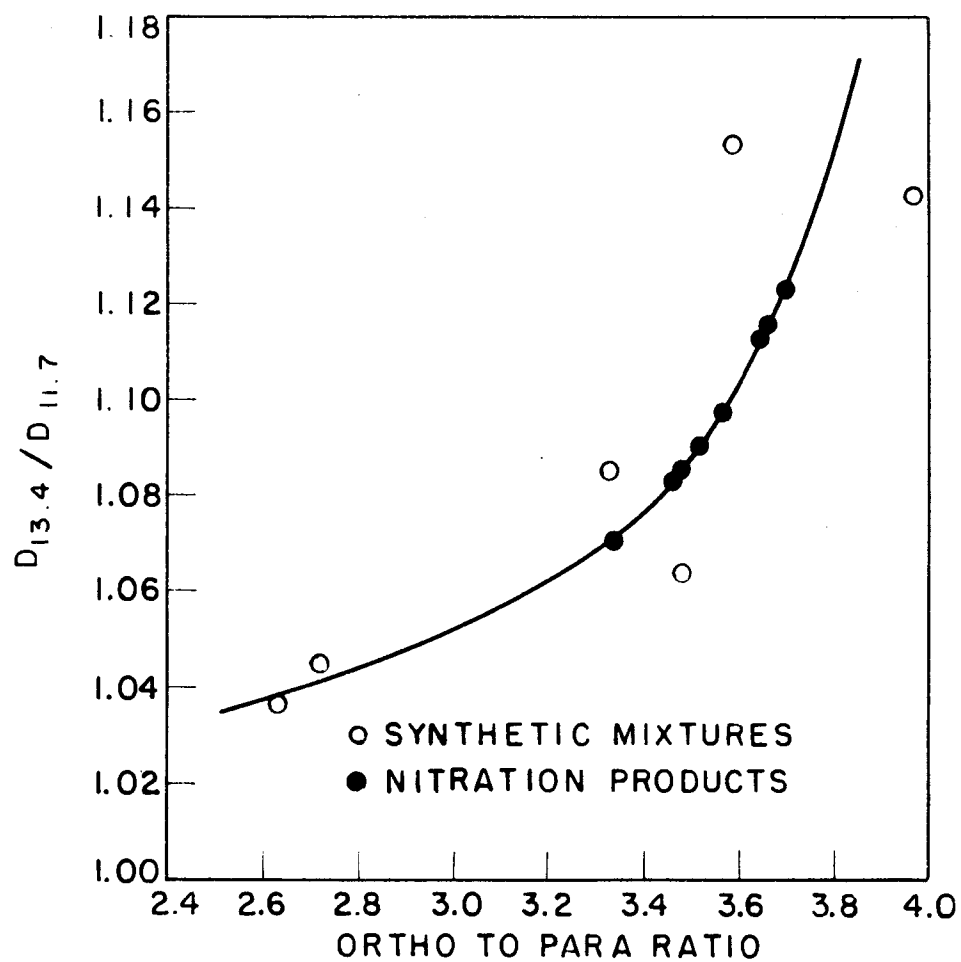


Figure 4. Calibration curve for estimating ortho to para ratio

accuracy with which the spectra can be read is about ± 0.01 units in the ratio. These estimates show that while the points appear widespread, the significance of the spread is small.

Table 7 gives the data obtained for the product mixtures from the quantitative nitration of benzonitrile. The estimated values of the percent m-nitrobenzonitrile and of the ratio of o-nitrobenzonitrile to p-nitrobenzonitrile are included.

The percent m-nitrobenzonitrile in all the samples lies between 72% and 82%. It is probable that the higher percentages are the more accurate and that lower percentages of m-nitrobenzonitrile obtained in some runs were caused by formation of side products. There is no significant change in the percent m-nitrobenzonitrile obtained with change in temperature. The lowest value obtained is that for the product of Run 7 which was kept at 35° for eight hours during the nitration. The low value obtained here may be due to further reaction of the m-nitrobenzonitrile during the longer reaction time. The low values obtained in Runs 5 and 6 may also be attributed to this cause except that Run 1, at 25°, was kept at this temperature for eight hours and still gives the largest value for the percent m-nitrobenzonitrile.

Table 7. Analysis of products of nitration of benzonitrile

Run	Sample Weight mg.	D^a				$\frac{D_{13.4}}{D_{11.7}}$	o/p	Estimate of meta Isomer			
		11.7 μ	13.4 μ	13.6 μ	11.2 μ			13.6 μ	11.2 μ	Av. mg.	%
1	43.9	1.16	1.29	2.45	1.50	1.112	3.65	36.0	36.1	36.0	82.0
2	47.5	1.22	1.36	2.58	1.53	1.115	3.66	38.2	38.0	38.1	80.2
3	47.2	1.26	1.35	2.55	1.52	1.071	3.32	37.7	37.7	37.7	79.9
4	39.1	1.19	1.29	2.20	1.43	1.084	3.48	31.8	32.0	31.9	81.6
5	47.7	1.22	1.33	2.40	1.48	1.090	3.52	35.2	35.0	35.1	73.6
6	47.5	1.24	1.36	2.47	1.50	1.097	3.56	36.5	36.3	36.4	76.6
7	46.4	1.20	1.30	2.25	1.46	1.083	3.46	32.7	34.0	33.4	72.0
8	47.5	1.22	1.37	2.53	1.52	1.123	3.70	37.4	37.5	37.4	78.7
9	48.0	1.22	1.37	2.48	1.51	1.123	3.70	36.8	37.0	36.9	76.9

$^aD = I_0/I$ at the wave length given.

Runs 5 and 6, and 8 and 9, were duplicating runs. A comparison of the results from them should give a measure of the precision of the method. For Runs 5 and 6 the average percent m-nitrobenzonitrile is 75.1%; the deviation from the average in these runs is 2.0%. In the case of Runs 8 and 9 the average percent m-nitrobenzonitrile is 77.8% and the deviation from this average is 1.2%. Since the deviation in the results is greater for the runs of longer reaction time, it is concluded that the low values obtained for the percent m-nitrobenzonitrile in these runs are due to side reactions and not to a variation in the activation energies for attack at the different nuclear positions.

From the data obtained it is not possible to calculate the percentage of o- and p-nitrobenzonitrile accurately. If it is assumed that nitration is complete, and, that no side products are obtained, then the sum of the o- and p-nitrobenzonitriles obtained must be the difference between the sample weight and the estimated amount of m-nitrobenzonitrile. This assumption seems justified in the cases where the percent m-nitrobenzonitrile is 78% to 82%. For Run 1, the sum of the o- and p-nitrobenzonitriles thus calculated is 7.9 mg. From this and the estimated ortho to para ratio of 3.65, the percent of o- and p-nitrobenzonitrile are calculated to be 14% and 4%, respectively. When a similar

calculation is made using the average value for the amount of m-nitrobenzonitrile estimated and the average value of the sample weights from Runs 8 and 9, 17.4% o-nitrobenzonitrile and 4.8% p-nitrobenzonitrile are estimated. Similar calculations for the other reaction products give values in the same range.

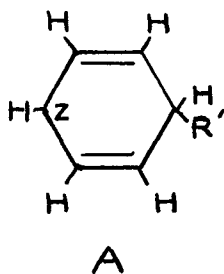
From the data obtained it is clear that the ortho to para ratios from all of the nitration experiments is greater than two. In no synthetic mixture in which the ortho to para ratio was less than two did the ratio of $D_{13.4}$ to $D_{11.7}$ rise above 1.04. The data from one such synthetic mixture are included in Table 5.

Since there are two ortho positions and only one para position available for substitution, the ortho to para ratio would be two if there were no directional influences present. It is certain therefore that there is present in benzonitrile some influence which enhances ortho substitution.

The suggested explanation of Hammond, Modic and Hedges³⁵ of the enhanced ortho substitution in compounds containing nonlinear unsaturated substituent group does not apply in this case. Since the nitrile group is linear, it could not exert an attraction for the ortho hydrogen or the entering electrophile in the same way proposed for the nitro group. The fact that the ortho to para ratio obtained for nitration

of benzonitrile is so high casts doubt on this explanation of the high ortho to para ratio obtained in nitration of the dichloronitrobenzene studied³⁵. These experiments show that the influence of the nitro and nitrile groups is substantially the same and that the ortho effect observed in both benzonitrile and nitrobenzene must be due more to electronic than to steric influences of the substituent groups.

In applying the molecular orbital method to the problem of aromatic substitution Wheland³⁶ has considered the structure of type A as contributing to the activated complex to a greater extent than other structures that can be written.



In this structure the attacking group R' is covalently bound to the ring carbon atom and z represents a positive charge and an associated open sextet of electrons if the attacking reagent, R' , is electrophilic or a negative charge and an associated unshared pair of electrons if the

reagent is nucleophilic. With this model for the activated complex the problem is essentially to determine the amount of energy that must be supplied in order to provide at the point of attack an unshared pair of electrons or an open sextet depending on whether the attacking reagent is electrophilic or nucleophilic. In setting up the problem for the case of a substituted benzene all the trigonal atoms are taken into account. In setting up the secular equation by which the energies of the molecular orbitals can be calculated, it is necessary to take into account the difference in electron affinities of the atoms when the substituent group contains a hetero atom, as in nitrobenzene, or when the ring is heterocyclic, as in the case of pyridine. A constant parameter, δ , is introduced to account for this difference in electronegativity. In the case of the substituent which contains hetero atoms with π -electrons to contribute to the whole, at least one of the resonance integrals and at least one of the overlap integrals must be considered to have values different from those in unsubstituted benzene. Wheland shows that these can be combined and introduces a parameter, ρ , to account for these differences. By proper assignment of values to the parameters δ and ρ he has been able to set up and solve secular equations for a number of substituted benzene

compounds in such a way as to account for the observed orientation as ortho and para or meta to the substituent group in the case of electrophilic or nucleophilic attack.

Dewar³⁷ has extended Wheland's method and, by adding another parameter to account for the change in electron affinity of the carbon atoms in the ring due to the inductive effect of the substituent group, has been able to account for observed ortho to para ratios obtained in substitution reactions for many substituted benzene compounds. He assumes that this change in electron affinity due to induction should die out along the chain and introduces a constant parameter ϵ to account for this effect. Thus the electron affinity of C_1 , the carbon atom in the ring to which the substituent group is attached, is $\epsilon\delta$, that of the ortho carbons, $\epsilon^2\delta$, etc. In his calculations he assigns ϵ the value one third and allows δ to vary from -1 to 3. He is thus able to calculate activation energies for substitution at the ortho, para, or meta positions as functions of δ . By taking appropriate values of δ his calculated results are brought into close agreement with experiment. According to these calculations for a -E (classical meta-directing) substituent the percent meta derivative should always be much larger than the percent ortho and para. The ortho to para ratio for

"normal" values of δ should be greater than two and that the ortho to para ratio should fall below two only for large values of δ . This means that para substitution is electronically enhanced only if the substituent group is very electronegative as compared to carbon. Dewar cites as examples results obtained on nitration of ethyl benzoate, benzoic acid, and nitrobenzene in which the observed ortho to para ratios are 2.0, 3.8, and 13.5, respectively when corrected for the statistical effect. Values of δ greater than two are considered improbable from dipole moment data and it is just at $\delta \geq 2$ that Dewar's calculations predict a possible low ortho to para ratio for the -E substituents. The data reported in this work on the ortho to para ratio obtained from the nitration of benzonitrile is similar to that cited by Dewar for benzoic acid. Since the steric requirements of these two groups are quite different it is difficult to understand how any steric influence can be devised to explain the effect of both groups. Whereas the nonlinear bulk of the carboxyl group might be considered to hinder approach of an attacking group and therefore, without consideration of the electronic effects decrease ortho substitution no similar argument could be applied to the linear nitrile group. On the other hand, if ortho substitution is considered to be enhanced by the nonlinear

carboxyl group due to its attraction for the hydrogen and the entering nitronium ion, this argument cannot be applied to the nitrile case in order to explain the high ortho to para ratio observed. It appears, then, that the influence is chiefly an electronic one and that Dewar's calculations are borne out by these experimental results.

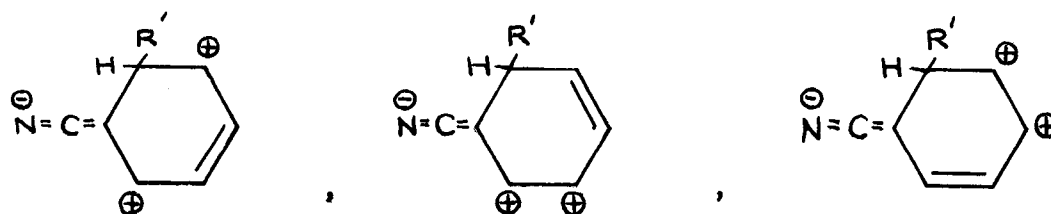
Brown³⁸ has calculated the atomic localization energies in substituted benzene compounds in which the substituent is a conjugated hydrocarbon system. Under these circumstances there is no difficulty in assigning values of 6 for differences in electron affinities but the π -electrons of the substituent group contribute to the electronic picture of the whole molecule. He has shown that in styrene and 1-phenyl butadiene as well as in biphenyl ortho substitution should be predominant over para. That this is not observed in the case of biphenyl has long been attributed to steric factors. Brown concluded that for any conjugated hydrocarbon system as substituent the molecular orbital approximation will ascribe a greater electronic reactivity to the ortho position than to the para position in the benzene ring.

These calculations and predictions seem to be borne out by the results of the present work. The difference in electronegativity of nitrogen and carbon is certainly less

than that of carbon and oxygen. In Dewar's calculations, then, the nitrile group would probably be assigned a smaller value of δ than is assigned to the nitro group and therefore the predicted ortho to para ratio for benzonitrile would be less than that predicted for nitrobenzene. The experimental results indicate that these predictions would be correct.

The crux of the simplified M O treatment is to indicate that the normal interaction of the unsaturated substituent with the ring is better preserved in the transition state for ortho attack than is the case in the transition state for para attack. It is furthermore pointed out that the consequent preference for ortho attack can be outweighed if the inductive effect of the substituent lowers the electron affinity of the ortho carbon atoms by a sufficiently large amount.

These results are in effect very much in agreement with Branch and Calvin's interpretation based on modified resonance theory⁶¹. From consideration of such structures as



⁶¹G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry", Prentice-Hall, Inc. New York, N. Y., 1941, p. 477.

for the transition state for ortho substitution of R' in benzonitrile and



for the transition state in para substitution the conclusion would be drawn that ortho substitution was favored due to the fact that three structures of this type can be drawn for the transition state and that one of these shows a greater separation of charge than either of the two structures drawn for para substitution. In spite of the weakness of this argument due to the neglect of interaction of the π - electrons, the conclusions are supported by the experimental results. The simplified molecular orbital approach is more sophisticated and does give numerical results which agree with experiment but the assignment of values of the necessary parameters must be carefully done in such a way that the mistakes of the earlier theories are not incorporated into the calculations. A neglect of electron interaction in the calculations involved in the M O treatment can be glossed over by proper assignment of parameters but a real understanding of the problem is not gained if this assignment

is done arbitrarily in such a way as to bring the results into agreement with experiment without due regard to the implications made.

SUMMARY

By means of an infrared method of analysis the ratio of ortho to para substitution occurring in the nitration of benzonitrile has been determined. The results show that the ortho to para ratio obtained is greater than two and for the cases studied the range is 3.3 to 3.7. No significant change in the ortho to para ratio due to change of reaction temperature was observed. It is concluded that the nitrile group like the nitro and carboxyl groups is meta-ortho directing and that the ortho direction is due to the electronic influences rather than to steric influences of the latter groups.

It was not possible to determine the isomer ratio obtained in the nitration of 2,5-dichlorobenzonitrile because no conditions in which hydrolysis of the nitrile group did not occur could be found. 2,5-Dichloro-4-nitrobenzonitrile and 2,5-dichloro-6-nitrobenzonitrile were prepared and their infrared spectra determined.

Unsuccessful methods of determining the amount of o-nitrobenzonitrile in the nitration product of benzonitrile led to a study of the catalytic hydrogenation of the three nitrobenzonitriles. It was shown that m- and p-nitrobenzonitrile were reduced to the corresponding m- and p-amino-

benzonitriles under these conditions but that o-nitrobenzonitrile was reduced and hydrolyzed in quantitative yields to o-aminobenzamide. A possible mechanism for this reaction is given.

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