Thesis for the Degree of Ph.D.

THE INFLUENCE OF THE NATURE AND POSITION OF ATOMS IN ORGANIC COMPOUNDS ON THE REACTIVITY OF OTHER ATOMS IN THE MOLECULE.

POLARITY EFFECTS IN SUBSTITUTED BENZYL BROMIDES.

by

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A subject of this type is one which must necessarily have a wide application, and the following researches have been undertaken with a view to obtaining some knowledge of the various influences exerted by the groups under investigation. During the work described several different series of compounds have been studied, by the application of suitable reactions, and this communication will therefore be divided into the following sections.

(1) A series of condensations was attempted with the three isomeric tolyl methyl ethers and amyl nitrite, in order to obtain some indication of the induced polar effect of the methoxy (OMe) group. The general polar effect of the methoxy group, and any steric effects apparent were also studied. The reaction involved was as shown below:

\[ \text{m-tolyl methyl ether} + \text{C}_5\text{H}_5\text{NO}_2 \rightarrow \text{oxime of m-methoxy benzaldehyde.} \]
(2) The hydrolyses of the three isomeric nitro benzyl bromides were carried out with a view to showing the induced polar effects due to the position of the NO$_2$ group, and some of the experiments in this section were devoted to showing the general polar effect of the NO$_2$ group.

\[
\begin{align*}
\text{CH}_2\text{Br} & \quad \text{CH}_2\text{Br} & \quad \text{CH}_2\text{Br} \\
\text{NO}_2 & \quad \text{NO}_2 & \quad \text{NO}_2 \\
\text{o-} & \quad \text{m-} & \quad \text{p-} \\
\text{nitr false benzyl bromide.} & \quad & \text{nitr false benzyl alcohol}
\end{align*}
\]

(3) The hydrolyses of the three isomeric &bromo toluic acids were also completed in an identical manner to show the induced polar effects due to the COOH group.

\[
\begin{align*}
\text{CH}_2\text{Br} & \quad \text{CH}_2\text{Br} & \quad \text{CH}_2\text{Br} \\
\text{COOH} & \quad \text{COOH} & \quad \text{COOH} \\
\text{o-} & \quad \text{m-} & \quad \text{p-} \\
\text{&bromo toluic acid} & \quad & \text{&bromo toluic acid}
\end{align*}
\]
(4) To emphasise the induced polar character of the bromine atom in the three dibromo toluic acids they were reduced with hydriodic acid, when the induced polar effect was reversed as anticipated.

$$\text{CH}_2\text{Br} - \text{CH}_2\text{Br} \rightarrow \text{CH}_3\cdot\text{C}_6\text{H}_4\cdot\text{COOH}$$

dibromo toluic acid

(5) To illustrate still further the general polar effect of the NO$_2$ group, a series of oxidations was attempted with various nitrated toluene derivatives. These were oxidised to the corresponding aldehydes, using chromyl chloride as an oxidising agent (Etard's reaction), and comparisons were made of the relative success of the reaction in each case. The compounds dealt with here were:

$$\text{CH}_3\cdot\text{NO}_2$$

o-nitro toluene

$$\text{CH}_3\cdot\text{NO}_2$$

2-4 di-nitro toluene

$$\text{CH}_3\cdot\text{NO}_2$$

o-nitro p-methoxy toluene.
As pointed out by Lapworth and Shoesmith (T. 1922 121, 1391), "The total influence which one atom or group exerts on the properties of another elsewhere in the same molecule is doubtless highly complex, and probably the resultant of several simultaneous effects". As they maintained the effect seems to be divided into three concurrent effects which may be classed as follows: (a) general polar or tone effects, (b) induced polar effects, and (c) steric effects.

This classification was recognised to a certain extent at an earlier date by Flürscheim (T. 1909, 95, 718), who divided the total effect into, (a) polar effects (b) quantitative effects (c) steric effects. The polar effects as described by Flürscheim are identical with the general polar or tone effects just mentioned, while the steric effects are similar in both cases. Flürscheim's quantitative effects however, while being position effects like the induced polar effects, do not vary in positive or negative character, and appear to become weaker as the distance between the group inducing the effect and the group whose reactivity is influenced, becomes increased.
In a theory advanced simultaneously by Lapworth (T. 1922. 121. 416), and Kermack and Robinson (T. 1922. 121. 428)*, this induced polar effect is attributed to the induction of alternatively positive and negative partial valencies along a chain of carbon atoms by a "key" atom.

This "key" atom is usually one of a strongly electro negative character, such as O, trivalent N, etc., but some positive atoms can also exhibit similar properties, though not usually in so marked a manner.

As might be expected an influence which tends to establish partial valencies of varying electrical character, is shown to best advantage in a conjugated system of the type originated by Thiele, where a subdivision of the affinity of each atom may be supposed to have occurred already. This is not however an assumption that induced alternate polarities can only be apparent in perfectly conjugated systems, but rather a supposition that such effects are brought into prominence through the existence of a favourable arrangement for their development.

A rather different theory to account for the polarity effects in conjugated systems, is brought forward by Lowry (T. 1923. 123. 822), who supposes a conjugated system to consist of a series of "mixed" double /

* See also Lapworth (Mem. Manchester Phil. Soc. 1920. 64. No.3) and Robinson (Mem. Manchester Phil. Soc. 1920. 64. No.4.)
double bonds all of identical character, instead of the usually accepted form of alternate double and single bonds. 

Lowry's notation $\begin{array}{c}
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\end{array}$

"mixed" double bonds.

Usual notation showing partial valencies.

$\begin{array}{c}
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\end{array}$

This mixed double bond is assumed to consist of an electro-valency and a co-valency, and this assumption results in all conjugated systems being of the alternate polar variety. This is a view which does not allow of any alternate polar effects outside a perfectly conjugated system and does not employ the notion of a "key" atom. It will be shown however that these induced alternate polar effects are very apparent in such compounds as substituted benzyl bromides where they act through a system which is not a perfectly conjugated one.

As the induced polar effects mentioned are likely to be more apparent in systems where there is a certain amount of conjugation, it is readily applicable to compounds in the aromatic series, and so all the substances dealt with in this investigation will be of this type. It is not intended however to confine this work to a study of induced polar effects, but an attempt will/
will be made to investigate the general polar and steric effects as well, and to show how all three are related in the various cases. The last mentioned steric effects will naturally in aromatic compounds, be confined to ortho substituents.

A striking example of induced polar effects of the type mentioned was shown by Lapworth and Shoesmith (T 1922. 121. 1391) in the case of the three isomeric methoxy benzyl bromides. From a consideration of the theory of induced polarity, and as will be seen from the formulae below, the methoxy group, when in the meta position, has a tendency to make the Br atom of the \( \text{CH}_2\text{Br} \) group more positive. Conversely when in the ortho and para positions, the tendency of the methoxy group is to make the Br atom more negative.

The oxygen atom of the methoxy group is taken as the "key" atom, and is denoted in the formulae as such by means of a dot attached to its polar sign.

![Chemical Structures](attachment:image)

Assuming/
Assuming that the negative character of the Br atom can be compared in the three isomers by the readiness with which the molecule is attacked by the negative hydroxyl ion in hydrolysis, one would expect the ortho and para compounds to be much more rapidly hydrolysed than the meta. This was found to be the case to a marked degree, and a reversal of these results was obtained when the positive character of the Br atom is compared by the reduction of the compound with hydriodic acid, a result which could only have been predicted by the theory in question.

Leading from these results an attempt was made to obtain some similar effects with other methoxy benzene derivatives, namely the three isomeric tolyl methyl ethers. It has been shown by Lapworth (T. 1901. 79. 1274) that o- and p- nitro toluene condense with amyl nitrite in the presence of dry sodium ethoxide to form the oximes of the corresponding aldehydes, and this reaction was applied to the tolyl methyl ethers mentioned.

Considering the alternate polar effect induced by the methoxy group, one would expect this reaction to take place more readily with the meta compound than with its isomers.
Unfortunately the anticipated results of these experiments were masked by the formation of a resin, probably of a nuclear variety, in all three cases. To ascertain if this resin was really due to nuclear disruption, a similar condensation was attempted with di-methyl resorcinol, and this was found to give identical results.

In order to discover the general polar effect of the $\text{NO}_2$ group on a reaction of this nature, a further condensation was carried out with o-nitro p-methoxy toluene ($\text{CH}_3 \cdot \text{C}_6\text{H}_3 \cdot \text{NO}_2 \cdot \text{OMe}$) and this time, while giving similar results, the condensation was noticeably less in intensity than any of the others. This last experiment gives an indication of the tendency of the $\text{NO}_2$ group to damp down the reaction.

As/
As the experiments just mentioned had not proved very successful, further attempts with methoxy benzene derivatives were abandoned, and a change made to other series of substituted benzyl bromides from those used by Lapworth and Shoesmith (loc. cit.)

The hydrolysis of the three isomeric nitro benzyl bromides was now attempted in order to ascertain the induced polar effect caused by the NO₂ group, the polar character of the Bromine atom being shown by the varying rate of the reaction in the three cases.

It may be noted here that shortly after this series was commenced, some researches were published by Oliver (Rec. trav. chim. 1922. 41. 301 and 646) on the hydrolysis of the nitro benzyl chlorides. The results shown by Oliver however were comparatively few in number, not being suitable for the production of the hydrolysis curves desired for comparison, and as the figures for the three isomers did not vary greatly, it was considered justifiable to proceed with the work in question. Also Oliver was conducting his investigations with a different object in view, his purpose being to show that the rate of hydrolysis of various isomeric substituted benzyl chlorides can be used to predict the directive influence of the substituant group. To quote an example of this, m-nitro benzyl chloride hydrolyses more rapidly than its ortho and para isomerides, consequently the nitro group/
group is one which directs another substituent into the meta position to itself. In a summary of his researches (Rec. trav. chim. 1923. 42. 775) Olivier says that he does not offer any explanation of this regularity, but as may be seen his results can be deduced from a consideration of the alternate polar effect caused by the NO₂ group.

As shown by the above diagram a nitro group tends to enhance the positive character of the H atoms in the meta position to itself, and so would tend to direct a substituent into the meta position (cf. Robinson Annual Reports 1922. p.99).

The hydrolysis of the three isomeric nitro benzyl bromides was carried out in alcohol and water at 78°C, and it was found that the meta compound hydrolysed more rapidly than the ortho and para compounds. This showed that the Br atom was, as expected, of a more negative character in the meta compound than in the ortho and para compounds. The difference observed is shown in the accompanying graph, where the percentage hydrolysis/
Hydrolysis of nitro benzyl bromides at 76°C.
hydrolysis is plotted against the time during which the hydrolysis was allowed to take place.

The difference between the three isomers was not so large as might have been expected, and there appeared to be absolutely no steric effects, both these effects apparently being overshadowed by the general polar effect. A comparison of the hydrolysis curves of these three isomers, with the hydrolysis curve of unsubstituted benzyl bromide, leads one to suspect that the general polar effect of the nitro groups is to slow down the intensity of the reaction in all cases. That the general polar effect of the NO₂ group is of this type, was shown by similar hydrolyses of m-nitro p-methoxy benzyl bromide, and m-nitro p-hydroxy benzyl bromide. Both these substances have the substituant groups/
groups so arranged that the induced effect would tend to cause extremely rapid hydrolysis of the Br atom. The rate of this hydrolysis however was not nearly so fast as would be expected owing to the general polar effect of the NO₂ group.

An attempt was made to reduce the nitro benzyl bromides with hydriodic acid, and so to show the positive nature of the Br atom in the para and ortho compounds, but owing to the fact that the NO₂ group was attacked, an estimation of the amount of reduction of the CH₂ Br group was impossible.

A similar investigation of a new series of substituted benzyl bromides, namely the ω-bromo toluic acids (CH₂ Br. C₆H₄. COOH), was now carried out, and in this case it was possible to obtain results from both the hydrolysis and the reduction of these compounds (a series of curves for comparison is shown).

The hydrolysis of the ω-bromo toluic acids was carried out in an identical manner to that of the nitro benzyl bromides, and here also the meta compound is the one which would be expected to hydrolyse most rapidly.

\[ \text{CH}_2\text{Br} \text{COOH} \]
\[ \text{CH}_2\text{Br} \text{COOH} \]
\[ \text{CH}_2\text{Br} \text{COOH} \]

\[ \text{o-} \]
\[ \text{m-} \]
\[ \text{p-} \]
Hydrolysis and Reduction of the α bromo toluic acids.

- Benzyl bromide (hydrolysis)
- Meta hydrolysis
- Para hydrolysis
- Ortho reduction
- Ortho hydrolysis

Time (hours): 0, 4, 8, 12, 16, 20
The hydropysis curves in this case show the meta compound to be much more rapidly hydrolysed than the para compound owing to the induced polar effect of the carboxyl group. The curve here obtained with the ortho compound appears to have taken an unexpected form, but this, as will be shown later, is due to the formation of phthalide. Using compounds of this type containing a carboxyl group one might perhaps expect the rate of the hydrolysis to be altered by the concentration of hydrion already present, but Olivier Rec. trav. chim. 1922. 41. 305) found that the addition of acid to the hydrolysis of the nitro benzyl chlorides did not appreciably alter the rate of the reaction.

Some figures for the hydrolysis of the ω chloro toluic acids have been published by Olivier (Rec. trav. chim. 1923. 42. 516) for the m- and p-compounds and also by Salkind and Ssemenow (J. Russ. Phys. Chem. Soc. 1914. 46. 512), but none of these were suitable for the comparative purposes required in this work.

These ω bromo toluic acids were now reduced with hydriodic acid, and as with the methoxy benzyl bromides (Lapworth and Shoesmith loc. cit.) this was found to proceed most rapidly when the Br atom possessed an induced positive character. The ω bromo p-toluic acid reduced very much faster than the meta compound as/

* Salkind and Ssemenow used the ω bromo toluic acids.
as anticipated, while the ortho compound appeared to be retarded by a considerable steric effect. To ensure the validity of these results the effect of hydriodic acid on the three isomeric toluic acids was investigated, but in no case did any appreciable reduction occur.

While engaged in some of the preparative work in connection with this research, it was noticed that the nitro group had a considerable effect on the oxidation of various toluene derivatives to the corresponding benzaldehyde by means of Étards reaction. This reaction involves the use of chromyl chloride \((\text{CrO}_3\text{Cl}_2)\) to convert the \(\text{CH}_3\) group to a \(\text{CHO}\) (aldehyde) group. To obtain results which might possess a comparative value, a series of oxidations under identical conditions were carried with various nitrated toluene derivatives. The compounds employed were o-nitro toluene, 2,4-di-nitro toluene, and o-nitro-p-methoxy toluene.

\[
\begin{align*}
\text{o-nitro toluene} & \quad \text{CH}_3 \quad \text{NO}_2 \\
\text{2,4-di-nitro toluene} & \quad \text{CH}_3 \quad \text{NO}_2 \\
\text{o-nitro p-methoxy toluene} & \quad \text{CH}_3 \quad \text{NO}_2 \quad \text{OMe}
\end{align*}
\]
When carrying out these experiments at a temperature of 46°C., a yield of 49-50% of aldehyde was obtained from the o-nitro p-methoxy toluene, while no aldehyde could be produced from either the o-nitro toluene or the 2-4 di-nitro toluene. The temperature of the reaction in the last two cases was then raised to 76°C. when 5% of aldehyde was obtained from the o-nitro toluene but none from the 2-4 di-nitro toluene. These results show that the general polar effect of the nitro group is of a greatly decelerating character, for the failure of the reaction with the o-nitro toluene and the 2-4 di-nitro toluene cannot be put down to steric causes, the possibility of this being the same in all three cases.
PREPARATIVE.

Preparation of the three isomeric tolyl methyl ethers.

These compounds were prepared from the corresponding cresols, by methylating with di-methyl sulphate in 10% sodium hydroxide solution.

\[
\text{CH}_3 \quad \text{CH}_3 \\
\text{OH} \quad \text{OH} \\
\text{NaOH} \quad \text{SO}_2(\text{OMe})_2 \\
\text{m-cresol} \quad \text{sodium tolyl oxide} \quad \text{m-tolyl methyl ether}
\]

The reaction was carried out at the boiling point of the solution, and was complete after a period of \(3\frac{1}{2}\) hours.

Yields obtained:
- o-tolyl methyl ether 72% of the theoretical B.P. 171°C.
- m-tolyl methyl ether 71% B.P. 175.3°C.
- p-tolyl methyl ether 79% B.P. 177°C.

Di-methyl resorcinol was obtained in a similar manner by the methylation of resorcinol. Yield: 75%. B.P. 215°C.
Preparation of anhydrous sodium ethoxide (NaO Et.).

This compound was first prepared as recommended by Lapworth (T. 1901, 12, 1274). A small quantity of metallic sodium was dissolved in twelve times its weight of absolute alcohol, and the excess alcohol removed in a stream of hydrogen at 180° C. This method however had the disadvantage that the product was obtained in a hard lump, difficult to pulverise, and so it was not likely to prove an efficient condensing agent. To obviate this difficulty a method similar to the one recommended by Brühl (Ber. 1902, 35, 3516; 1904, 37, 2066.) was adopted. In this method the major portion of the alcohol was first distilled off, a quantity of m-xylene introduced to the solution of sodium ethoxide in alcohol, and the whole evacuated at 100° C. The residual alcohol and then the m-xylene now distilled over leaving the sodium ethoxide as a fine white powder. To ensure the absolute dryness of the product, it was found advisable to repeat the treatment with m-xylene a second time.

It may be noted here that the sodium ethoxide prepared in this way was most reactive when perfectly fresh, and so it was prepared anew for each condensation using the flask in which the condensation was to be carried out.
Preparation of m-hydroxy benzaldehyde.

In order to be able to identify the expected product from the condensation with m-tolyl methyl ether and amyl nitrite (namely the oxime of m-methoxy benzaldehyde) it was necessary to prepare this product by other means, and this involved the preparation of m-hydroxy benzaldehyde. The first method attempted was by the reduction and diazotisation of m-nitro benzaldehyde, the nitro benzaldehyde being obtained by direct nitrination of benzaldehyde. (Tiemann and Ludwig Ber. 14, 2802; 15, 2045). The nitro benzaldehyde was reduced with stannous chloride and hydrochloric acid solution (15% cryst. SnCl₂ in conc. HCl), and the amino compound formed diazotised with sodium nitrite in the usual way. The diazo. salt was now hydrolysed by warming with water to 60°C, and the m-hydroxy benzaldehyde was obtained by extracting with ether. The yield obtained by this method was only 5% of the theoretical quantity, and so an attempt was made to improve it by using different proportions of stannous chloride and hydrochloric acid. In the second case the solution used consisted of 72% of anhydrous SnCl₂ in concentrated HCl., but here the yield was not improved beyond 10% of the theoretical quantity.
The mechanism of the above series of reactions is indicated below:

\[ \text{CHO} \xrightarrow{\text{HNO}_3} \text{CHO} \xrightarrow{\text{SnCl}_2 + \text{HCl}} \text{CHO} \xrightarrow{\text{NaNO}_2} \]

benzaldehyde \quad m\text{-nitro benzaldehyde} \quad m\text{-hydroxy benzaldehyde}

As the above mentioned method had not proved very successful, a new method was now adopted using m-cresol as a starting material (Shoemaker. T. 1923, 123, 2701). A solution of m-cresol in 10% aqueous sodium hydroxide was saturated with carbonyl chloride in the cold, when m-tolyl chloroformate separated out as a heavy oil. This chloroformate was further treated with an equimolecular solution of m-cresol in sodium hydroxide, and m-tolyl carbonate was formed as a white solid. The m-tolyl carbonate was washed, dried, and purified by recrystallisation from alcohol, and was found to be a glistening white crystalline solid, melting at 52°C.
52°C. The pure m-tolyl carbonate was now chlorinated with dry chlorine gas at a temperature of 160-170°C. in a flask fitted with a mechanical stirrer, and the chlorination was continued till the increase in weight corresponded to the introduction of four atoms of chlorine to each molecule of carbonate.

The tetra-chloro-m-tolyl-carbonate was now hydrolysed to the corresponding aldehyde carbonate with an alcoholic solution of sodium acetate, and 1 mol. of sodium acetate was used for each mol. of chlorine in the carbonate. The sodium acetate was used in the proportion of 40% anhydrous salt to 60% crystalline. The mixture was refluxed for three hours on a steam bath, and the excess alcohol was then distilled off. Excess of saturated sodium bisulphite solution was now added to complete the hydrolysis to the hydroxy benzaldehyde, and the whole boiled for one hour. After acidifying with hydrochloric acid, the solution was steam distilled until no sulphur dioxide was apparent in the distillate, and the m-hydroxy benzaldehyde obtained by extracting the non-volatile portion with ether.

\[
\begin{align*}
\text{CH}_3 & \quad \text{COCl}_2 \\
\text{Ona} & \\
\text{sodium tollyl oxide}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{m-cresol} \\
\text{in NaOH} & \\
m\text{-polyl carbonate}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{O-CO-O-} \\
\text{m\text{-polyl carbonate}
\end{align*}
\]
The m-hydroxy benzaldehyde was purified by recrystallisation from hot water, and melted at 104°C. The yield obtained by this method was nearly 40% of crude product, and 25% of pure substance, a figure which can be slightly improved by the use of formic acid instead of sodium acetate as a hydrolysing agent.

The m-hydroxy benzaldehyde was now converted to m-methoxy benzaldehyde by methylation with di-methyl sulphate, the methylated derivative being a colourless liquid boiling at 230°C. The oxime of this aldehyde was now prepared by warming it with hydroxylamine hydrochloride and sodium acetate in alcoholic solution, and was a viscous oily liquid which boiled at 163-164°C at 18 mm., and did not solidify at ordinary temperatures.
This oxime was extremely stable to hydrolysing agents, and did not hydrolyse on warming either with sodium hydroxide or dilute hydrochloric acid. When the oxime was warmed with a solution of p-nitro phenyl hydrazine in acetic acid a red crystalline solid was obtained, which was identical with the p-nitro phenyl hydrazone of m-methoxy benzaldehyde and melted at 168°C.

Preparation of o-nitro p-methoxy toluene.

This substance was prepared from p-cresol as a starting material. The p-cresol was first converted into p-tolyl carbonate by means of carbonyl chloride in a similar manner to the formation of the m-tolyl carbonate already mentioned, but in this case the carbonate was precipitated directly without passing through the stage of p-tolyl chloroformate. The product was purified by recrystallisation from alcohol and melted at 112°C.
The purified carbonate was now nitrated in 100% sulphuric acid solution, and the product separated by pouring on to ice. (Hollemann. Rec. trav. chim. 1917, 36, 271). The o-nitro p-tolyl carbonate which was formed by this nitration was purified by recrystallisation from alcohol and melted at 144°. This nitrated carbonate was then hydrolysed by boiling for one hour with excess of sodium hydroxide solution, and the mixture after acidifying was steam distilled to remove any trace of m-nitro p-cresol which might have been present. The o-nitro p-cresol was obtained by extracting the non-volatile portion with ether, and was a yellow crystalline solid melting at 77-77.5°.

The methylation of the nitrated cresol was then accomplished by using di-methyl sulphate in xylene solution. It was found that the best yield was obtained by dissolving the o-nitro p-cresol in m-xylene, and boiling this solution with anhydrous potassium carbonate and a slight excess of di-methyl sulphate. The mixture was refluxed for four hours and the o-nitro p-methoxy toluene was obtained by steam distillation. The product thus formed was purified by fractionation and boiled at 266-267°, the yield which was obtained being 39% of the theoretical quantity obtainable from the p-cresol used.
Preparation of the three isomeric nitro benzyl bromides.

Sufficient supplies of both the meta and the para nitro benzyl bromides were available in the laboratory and these were in a perfectly pure state. The melting point of the p-nitro benzyl bromide was found to be 97°C. and that of the meta compound 57°C.

Considerable difficulty was experienced in the preparation of the o-nitro benzyl bromide in a pure state, and various methods were tried in order to obtain/
obtain a sufficient quantity for experimental purposes.

The first scheme adopted was to prepare o-nitro benzaldehyde, and to convert it into the corresponding alcohol, which in its turn could be converted into the required o-nitro benzyl bromide. An attempt was made to prepare o-nitro benzaldehyde by oxidising o-nitro toluene to the corresponding aldehyde with chromyl chloride (Etards Reaction), but this, as will be described later, proved to be a complete failure, none of the required aldehyde being formed. Another method for obtaining o-nitro benzaldehyde was now evolved, using cinnammic acid as a starting material. The nitration of cinnammic acid (Beilstein and Kühberg, Annalen. 163, 126) yielded a mixture of ortho and para nitro cinnammic acids, which were then converted to the corresponding ethyl esters by boiling with alcohol in a stream of dry hydrochloric acid gas. According to Beilstein and Kühberg (loc. cit.) these two esters can be easily separated owing to their varying solubility in alcohol, but it was not found possible to isolate the o-nitro cinnammic ester in a pure state.

\[
\begin{align*}
\text{CH} \cdot \text{CH} \cdot \text{COOH} & \quad \xrightarrow{\text{HNO}_3} \quad \text{CH} \cdot \text{CH} \cdot \text{COOH} \\
\text{cinnammic acid} & \quad \text{and} \quad \text{CH} \cdot \text{CH} \cdot \text{COOH} \\
& \quad \text{NO}_2 \\
& \quad \text{and} \quad \text{NO}_2
\end{align*}
\]
Finally some pure o-nitro benzaldehyde was obtained from the British Drugs Houses Ltd. and attempts were made to convert it into the corresponding alcohol by means of a Cannizaro reaction (Friedlander Ber, 14, 2804; 18, 2403).

The product obtained from this reaction when separated from o-nitro benzoic acid was found to be chiefly unchanged o-nitro benzaldehyde, as only a small quantity of the alcohol was formed, and that in a very impure state.
The yield produced by this method was only about 5% of the theoretical quantity of crude product.

The method which was finally employed to prepare o-nitro benzyl alcohol consisted of chlorinating o-nitro toluene to o-nitro benzyl chloride, and converting the chloride into o-nitro benzyl alcohol. The o-nitro toluene was chlorinated at 120° - 130°C. with dry chlorine gas, and sulphur to the amount of half the weight of the nitro toluene was added as a catalyst. (Haussermann & Beck. Ber. 25, 2445).

The chlorination was continued till the evolution of HCl gas ceased, and was complete in about ten hours when using 100 gm. of o-nitro toluene. The product was now carefully washed to remove sulphur di-chloride and finally steam distilled, when first o-nitro toluene, and then o-nitro benzyl chloride, distilled over. The separation was finally completed by distilling the liquid portion of the distillate under reduced pressure, when o-nitro toluene was found to distill at 94-95°C. at 11 mm., and the o-nitro benzyl chloride at 135°C. at 11 mm.

The melting point of the pure o-nitro benzyl chloride was 48°C. and the yield amounted to 40% of the theoretical quantity.

The o-nitro benzyl chloride was then converted into the corresponding alcohol by boiling 1 part of o-nitro benzyl chloride with 2 parts of anhydrous sodium/
sodium acetate in concentrated aqueous solution, and
the acetate formed was hydrolysed to the o-nitro benzyl
alcohol with 50% sulphuric acid. Pure o-nitro benzyl
alcohol was obtained by recrystallisation from hot
water and melted at 72.5°C. An attempt was now made
to convert the o-nitro benzyl alcohol to the corres­
ponding bromide by dissolving it in benzene, and then
saturating the benzene solution with dry hydrobromic
acid gas, but this only converted about 2% of the
alcohol. In view of this fact phosphorus pentabromide was used for this purpose, and when the alcohol
was heated with the phosphorus pentabromide in the
dry state, o-nitro benzyl bromide was formed in
practically theoretical quantities.

\[
\text{CH}_3 \text{NO}_2 \xrightarrow{\text{O-nitroluene}} \text{CH}_3 \text{C} \xrightarrow{\text{O-nitro benzyl alcohol}} \text{CH}_2 \text{A}_c \xrightarrow{\text{O-nitro benzyl bromide}}
\]

O-nitro benzyl bromide has not been previously
described. The pure substance was a white solid
crystallising in fine needles which melted at 45.5°C.
This substance was found to be exceedingly volatile
in steam, and to possess highly lachrymatory properties.
The analysis of the o-nitro benzyl bromide was as follows: Found Br = 36.82%. Calculated from 
\[ \text{C}_7\text{H}_6\text{O}_2\text{NBr} \text{, Br} = 37.00\%. \]

Preparation of m-nitro p-methoxy benzyl bromide.

The first method used to produce this substance was through the preparation of the corresponding aldehyde, which could have been prepared by the application of Étard's reaction to m-nitro p-methoxy toluene. The m-nitro p-methoxy toluene was prepared by the nitration of p-cresol (Annalen 224, 138.), and the subsequent methylation of the m-nitro p-cresol, but the yields obtained were unsatisfactory owing to the presence of isomeric nitro compounds. Accordingly this method was abandoned in favour of a preparation of the aldehyde required directly, by the nitration of anisaldehyde (p-methoxy benzaldehyde). Anisaldehyde was nitrated according to the method of Einhorn and Grabfield (Annalen 243, 370), and the product separated by pouring on to ice. The m-nitro p-methoxy benzaldehyde was purified by recrystallisation from alcohol and melted at 73-74°C. The yield from this nitration was from 25-30% of the theoretical quantity.

An attempt was now made to prepare the m-nitro p-methoxy/
p-methoxy benzyl alcohol from the nitro anisaldehyde by Cannizaro's reaction as had been attempted in the case of the o-nitro benzaldehyde, but this also proved to be ineffective.

\[
\text{CHO} \quad \xrightarrow{\text{HNO}_3} \quad \text{CHO} \quad \xrightarrow{\text{conc NaOH}} \quad \text{CH}_2\text{OH} \quad + \quad \text{COOH}
\]

\text{anisaldehyde.} \quad \text{m-nitro p-methoxy benzaldehyde.} \quad \text{m-nitro p-methoxy benzyl alcohol}

It was now found possible to prepare m-nitro p-hydroxy benzyl alcohol by condensing o-nitro phenol with formaldehyde under the action of concentrated hydrochloric acid (Stoemer and Behre. *Ber.* 1901, 34, 2459.). 2 parts of o-nitro phenol, 5 parts formaldehyde solution, and 10 parts of concentrated hydrochloric acid were placed in a flask and refluxed for six hours. On cooling a heavy brown oil separated out. This oil was distilled in steam to remove any unchanged o-nitro phenol, when the non volatile portion was left as a crystalline mass, which was purified by recrystallisation from hot water. The pure m-nitro p-hydroxy benzyl alcohol was a yellow solid which crystallised in fine needles, and melted at 97°C.
It was found that considerable care had to be taken in the purification of this substance as the crude product was largely contaminated with a yellow solid which crystallised in plate form, and melted about 90°C.

This impurity was probably di-nitro di-hydroxy di-phenyl methane, with the formula

\[
\begin{array}{c}
\text{HO} \\
\text{NO}_2
\end{array}\quad
\begin{array}{c}
\text{CH}_2 \\
\text{NO}_2
\end{array}
\]

The m-nitro p-hydroxy benzyl alcohol was now methylated with methyl iodide and potassium hydroxide in methyl alcoholic solution, and the pure m-nitro p-methoxy benzyl alcohol was recrystallised from hot water as fine yellow needles melting at 69°C. The yield obtained in this preparation was 25-30% of the theoretical quantity, and the best results were obtained when an additional supply of formaldehyde was added to the mixture half way through the first part of the operation. The formaldehyde used in this synthesis was as strong a solution as could be prepared without causing appreciable polymerisation.

The m-nitro p-methoxy benzyl alcohol was dissolved in benzene and converted into the corresponding bromide by/
by saturating the benzene solution with dry hydrobromic acid gas. The yield was practically quantitative and the pure bromide when recrystallised from petroleum ether melted at 108°C. m-Nitro p-methoxy benzyl bromide, which has not been previously described, is a pale yellow solid crystallising in fine yellow needles.

The various steps involved in this preparation are shown below:
m-Nitro p-hydroxy benzyl bromide was prepared from the corresponding alcohol, mentioned above, in an identical manner to the m-nitro p-methoxy benzyl bromide, was purified by recrystallisation from petroleum ether and melted at 82°C. This substance, also a new compound, is a bright yellow solid crystallising in prismatic needles.

The analyses of these two bromides gave the following figures:

**m-Nitro p-methoxy benzyl bromide**

Bromine found = 32.94%

Bromine calculated from \( \text{C}_8\text{H}_8\text{O}_3\text{N Br} \) = 32.49%

**m-Nitro p-hydroxy benzyl bromide**

Bromine found = 34.46%

Bromine calculated from \( \text{C}_8\text{H}_4\text{O}_3\text{N Br} \) = 34.44%

---

**Preparation of the isomeric \( \omega \)-brom toluic acids.**

The first step in this synthesis was the preparation of the three isomeric toluic acids, which were all prepared in a similar manner from the corresponding toluidines. A suspension of toluidine hydrochloride in dilute hydrochloric acid was diazotised with concentrated sodium nitrite solution at 0°C., and the diazotisation was carried on in the usual way until/
until the presence of free nitrous acid could be detected in the solution. The solution of the diazo salt was then slowly poured into a hot solution of potassium cupro-cyanide, when tolyl cyanide was formed as a tarry oil. It was found an advantage to have the potassium cupro-cyanide solution at a temperature of 80-95°C, and to pour in the diazo solution through a condenser to avoid loss. After heating till the evolution of gas had ceased the mixture was steam distilled, and the tolyl cyanide separated from the aqueous distillate as a clear yellow oil. The p-tolyl cyanide solidified on cooling and had a melting point of 29°C, but the ortho and meta compounds remained liquid at ordinary temperatures.

The tolyl cyanides were converted into the corresponding toluic acids by boiling for 30 minutes with excess of 55% sulphuric acid, and were purified by recrystallisation from hot water.
The yields obtained from 60 gm. of toluidine in each case were:-

- **o toluic acid**: 25 gm. M.P. 104°C.
- **m toluic acid**: 32 gm. M.P. 110°C.
- **p toluic acid**: 50 gm. M.P. 179°C.

The toluic acids were next converted into the acid chlorides by heating with a slight excess of thionyl chloride, until no more hydrochloric acid gas was evolved. The **o-**, **m-**, and **p-toluoyl** chlorides were thus obtained and purified by distillation.

- **0-toluoyl chloride**: B.P. 212°C.
- **m-toluoyl chloride**: B.P. 220°C.
- **p-toluoyl chloride**: B.P. 100°C at 14 mm.

These acid chlorides were now brominated according to the method of Davies and Perkin (T. 1922, 121, 2202.), and the corresponding **o-bromo toluoyl** bromides thus formed, with the formula CH₂Br. C₆H₄. COBr.

The bromination was carried out at 185-195°C., and bromine to the amount of 2 mols. was added through a dropping funnel whose stem was below the surface of the liquid in the flask. The **o-bromo toluoyl** bromides were purified by distillation under reduced pressure, and were all colourless liquids which fumed on exposure to the atmosphere and decomposed rapidly with the evolution of hydrobromic acid.

**ω-bromo**/
ω-bromo o-toluoyl bromide B.P. 158-161°C at 13 mm.
M.P. 33°C.

ω-bromo m-toluoyl bromide B.P. 160-165°C at 14 mm.
M.P. 23-25°C.

ω-bromo p-toluoyl bromide B.P. 165-170°C at 12 mm.
M.P. 39-40°C.

(cf. Davies & Perkin loc. cit).

Davies and Perkin did not prepare the ω-bromo p-toluoyl bromide by this means, but only the ortho and meta compounds, and they did not quite any melting point for the meta derivative.

Analysis of ω-bromo p-toluoyl bromide.

Bromine found = 54.54%
Bromine calculated from C₉H₆O Br₂ = 57.55%.

(This figure is rather low, and is accounted for by the fact that a certain amount of decomposition was almost unavoidable while preparing the bromide for analysis)

The ω-bromo toluoyl bromides were finally converted into the corresponding ω-bromo toluic acids by hydrolysis with formic acid solution. The acid bromide was placed in a flask with twelve times its weight of formic acid (1.2 s.g. 80%), and warmed gently to a temperature of 30-35°C. The hydrolysis was complete after one hour, and the product was obtained by pouring into excess of cold water and filtering. The three isomeric ω-bromo toluic acids were purified by recrystallisation from benzene, a process which had to be/
be repeated several times to remove traces of dibromide which apparently were present. The melting points of the three isomers were: \( \omega \)-bromo o-toluic acid M.P. 146°C, \( \omega \)-bromo m-toluic acid M.P. 150°C, \( \omega \)-bromo p-toluic acid M.P. 223°C.

The various steps in the process from toluic acid are as shown:

\[
\begin{align*}
\text{CH}_3 & \quad \overset{\text{SOCl}_2}{\longrightarrow} \quad \text{CH}_3 \\
\text{COOH} & \quad \text{COCl} \\
\text{CH}_3 & \quad \overset{\text{Br}}{\longrightarrow} \quad \text{CH}_2\text{Br} \\
\text{COCl} & \quad \text{COBr} \\
\text{CH}_2\text{Br} & \quad \overset{\text{HCOOH}}{\longrightarrow} \quad \text{CH}_2\text{Br} \\
\text{COOH} & \quad \text{COOH}
\end{align*}
\]

\( \beta \)-toluic acid \( \beta \)-toluoyl chloride \( \omega \)-bromo \( \beta \)-toluoyl bromide \( \omega \)-bromo \( \beta \)-toluic acid

The yield in these preparations was 50-55% in each case but considerable care had to be taken to ensure the absence of moisture during the process. The analyses of the three compounds were as follows:

\( \omega \)-bromo o-toluic acid

Bromine found = 37.51%

Bromine calculated from \( \text{C}_8\text{H}_7\text{O}_2\text{Br} \) = 37.20%
39.

ω-bromo m-toluic acid.
Bromine found = 37.53%
Bromide calculated = 37.20%

ω-bromo p-toluic acid.
Bromine found = 37.62%
Bromine calculated = 37.20%

A study of the literature revealed the fact that these compounds had already been prepared by Salkind and Ssemenow (J. Russ. Phys. Chem. Soc. 1914, 46, 508.), but in a totally different manner, which was not applicable to all three isomers. The meta and para derivatives were prepared by brominating the corresponding toluic acids in boiling bromoform solution, while the ortho compound was made by heating phthalide with hydrobromic acid to 100°C in a sealed tube. The method here employed seems to be more convenient, and in the case of the ortho compound at least considerably less expensive.
Series of condensations with amyl nitrite and the three isomeric tolyl methyl ethers.

The most favourable conditions for these condensations were found by means of several preliminary experiments with ortho and para nitro toluene and from these the best results were obtained when using freshly prepared sodium ethoxide, and absolutely anhydrous ether. The procedure which was adopted for this reaction was as follows:— A flask containing 6-7 gm. of freshly prepared sodium ethoxide and 200 cc. of anhydrous ether was connected with a reflux condenser, and a mixture of 10 gm. tolyl methyl ether and 11 gm. amyl nitrite was poured in through the condenser. The contents of the flask were kept thoroughly mixed by intermittent shaking for a period of four hours, after which the condenser was removed, the flask carefully sealed up, and left to stand for three days. On opening the flask the contents were poured into 300 cc. of water, the two layers resulting were then separated, and examined for their contents.

When a condensation was attempted with m-tolyl methyl ether, the colour of the reacting substances became rapidly darker, and a slight evolution of heat was apparent. After some time the colour reached a deep/
deep red shade, and at the conclusion of the experiment this colour was retained by the aqueous alkaline layer. The two layers were then carefully separated, the ethereal layer dried over anhydrous sodium sulphate, when its contents were obtained by fractional distillation.

The products of this ethereal layer, as separated by fractionation, proved to be chiefly amyl nitrite, and unchanged m-tolyl methyl ether, together with a small quantity of amyl alcohol.

The aqueous layer was now acidified, extracted with ether and the ether removed, a process which would have resulted in the isolation of the oxime of m-methoxy benzaldehyde had this substance been formed. The product thus obtained was of a resinous nature and soluble in alkali but unfortunately it was not possible to purify it or obtain it in a crystalline form. Attempts were made to hydrolyse this product and so obtain some indication of its composition, but these were not successful, and a treatment with a solution of p-nitro phenyl hydrazine failed to show the presence of any m-methoxy benzaldehyde. This should be compared with the fact that when a specimen of the oxime of m-methoxy benzaldehyde was heated with the p-nitro phenyl hydrazine solution, it was converted into the p-nitro phenyl hydrazone of the aldehyde.

Comparative/
Comparative condensations were attempted with the ortho and para tolyl methyl ethers, and the treatment in each case was identical. A very similar result was obtained, except for the fact that the colour in these two latter cases was developed much more slowly, and did not become so pronounced. It is of interest to note that in the case of the ortho compound the bulk of resinous product obtained was much smaller than with the other two isomers, and this may offer some indication of the presence of a steric effect.

Two further condensations were attempted in this series, namely one with di-methyl resorcinol, and one with o-nitro p-methoxy toluene. In the first case the deepening of the colour was very rapid and much more pronounced than with any of the others, while the product obtained was exceedingly tarry. The condensation with o-nitro p-methoxy toluene gave results similar to the rest, but to judge from the depth of colour produced and the small quantity of product, the reaction had been exceedingly slight.

The details of the products which were obtained from the original ethereal layer in these experiments are given as follows:

(1) m tolyl methyl ether/
<table>
<thead>
<tr>
<th>Fraction</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composé</td>
<td>m tolyl methyl ether</td>
<td>p tolyl methyl ether</td>
<td>o tolyl methyl ether</td>
</tr>
<tr>
<td>Zone</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>Rôle</td>
<td>(4)</td>
<td>(5)</td>
<td>(6)</td>
</tr>
<tr>
<td>Temp.</td>
<td>95-100°C</td>
<td>95-101°C</td>
<td>96-101°C</td>
</tr>
<tr>
<td></td>
<td>135-140°C</td>
<td>136-140°C</td>
<td>135-140°C</td>
</tr>
<tr>
<td></td>
<td>172-175°C</td>
<td>172-175°C</td>
<td>171-177°C</td>
</tr>
<tr>
<td></td>
<td>94-99°C</td>
<td>94-99°C</td>
<td>94-99°C</td>
</tr>
<tr>
<td></td>
<td>135-139°C</td>
<td>135-139°C</td>
<td>135-139°C</td>
</tr>
</tbody>
</table>
An interesting point which was noted during these experiments is the fact that a mixture of amyl nitrite and m-tolyl methyl ether became rapidly darker in colour on standing, and after some days deposited a small quantity of crystals. A similar effect was noticed with the ortho and para compounds and also with di-methyl resorcinol, the last mentioned substance producing the effect very rapidly. These crystals in every case were found to be soluble in sodium hydroxide, but owing to the small quantity formed, it was not found possible to obtain a pure specimen, or to identify the substance of which they were composed.

**Hydrolysis of the nitro benzyl bromides.**

The hydrolysis of these compounds was first attempted using N/10 sodium hydroxide in 95% alcohol (cf. Lapworth and Shoesmith loc. cit.), but it was found that the nitro benzyl alcohol formed was decomposed by the alkali, and other methods had to be adopted. From an investigation of the product obtained by the action of sodium hydroxide on p-nitro benzyl alcohol, the decomposition was suspected to be due to the formation of p-azoxy benzoic acid, but definite proof of this fact could not be obtained.

The hydrolysis of m-nitro p-methoxy benzyl bromide was/
was also attempted in this way, and some figures were obtained. The reaction was carried out at a temperature of 25°C, and about 1 gram of the substance was accurately weighed and dissolved in 100 cc. of the alcoholic sodium hydroxide solution. At stated intervals of time 10 cc. of this solution was extracted with a pipette, run into cold water, and neutralised with 10 cc. of N/10 hydrochloric acid. The excess acid was now titrated with standard sodium hydroxide, and so a measure of the amount of bromide hydrolysed was obtained:

\[ t = \text{time during which hydrolysis was allowed to proceed.} \]
\[ x = \text{per cent of m-nitro p-methoxy benzyl bromide hydrolysed.} \]

<table>
<thead>
<tr>
<th>t</th>
<th>x</th>
<th>t</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 min.</td>
<td>69.7%</td>
<td>150 min.</td>
<td>132.2%</td>
</tr>
<tr>
<td>30 min.</td>
<td>97.1%</td>
<td>210 min.</td>
<td>134.5%</td>
</tr>
<tr>
<td>60 min.</td>
<td>116.2%</td>
<td>330 min.</td>
<td>135.0%</td>
</tr>
<tr>
<td>120 min.</td>
<td>131.3%</td>
<td>1050 min.</td>
<td>135.3%</td>
</tr>
</tbody>
</table>

As will be seen from the figures obtained, the reaction reached an equilibrium state at a point considerably in excess of that required for the total hydrolysis of the bromine atom, and this is probably due to a partial demethylation of the methoxy group corresponding to 48.8% hydrolysis to the m-nitro p-hydroxy/
p-hydroxy benzyl alcohol. That this excess figure was due to partial de-methylation is argued by analogy with the demethylation of the o-nitrated phenyl methyl ether when treated with sodium hydroxide.

\[
\begin{align*}
\text{Owing to the unsuitability of strong alkali, the hydrolysis was finally effected in alcohol and water solution, and a temperature of } 76^\circ \text{C. was employed to give good comparative figures with all the compounds investigated.}
\end{align*}
\]

The method employed in these hydrolysis was as follows:-

About .10 gm. of the bromide to be hydrolysed was accurately weighed into a 25 cc. standard flask.

20 cc./
20 cc. of absolute alcohol were now measured into the flask, the bromide dissolved by shaking, and 5 cc. of distilled water added.

The diminution in volume, due to the admixture of alcohol and water, was made up by adding absolute alcohol until the flask was filled to the graduation mark, and the flask was then maintained at a temperature of 76° C. for a stated time.

The hydrolysis was stopped by washing the contents of the flask into cold water, and a measure of the amount of hydrolysis which had occurred was obtained by direct titration of the free hydrobromic acid liberated with standard sodium hydroxide, using methyl red as an indicator.

The process was repeated for varying periods of time and a series of determinations after hydrolysis for 1/2, 1, 2, 4, 8, 16, and 32 hours was made with each of the nitro benzyl bromides under investigation.
t = time during which hydrolysis was allowed to take place.

w = weight of substance used.

x = per cent of substance hydrolysed.

### o-nitro benzyl bromide.

<table>
<thead>
<tr>
<th>t (hours)</th>
<th>w (g)</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>½</td>
<td>0.1267 g</td>
<td>10.8%</td>
</tr>
<tr>
<td>1</td>
<td>0.1190 g</td>
<td>19.2%</td>
</tr>
<tr>
<td>2</td>
<td>0.1022 g</td>
<td>32.4%</td>
</tr>
<tr>
<td>4</td>
<td>0.1010 g</td>
<td>54.7%</td>
</tr>
<tr>
<td>8</td>
<td>0.1081 g</td>
<td>78.9%</td>
</tr>
<tr>
<td>16</td>
<td>0.1040 g</td>
<td>93.9%</td>
</tr>
<tr>
<td>32</td>
<td>0.0998 g</td>
<td>99.1%</td>
</tr>
</tbody>
</table>

### m-nitro benzyl bromide.

<table>
<thead>
<tr>
<th>t (hours)</th>
<th>w (g)</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>½</td>
<td>0.1228 g</td>
<td>12.0%</td>
</tr>
<tr>
<td>1</td>
<td>0.1037 g</td>
<td>23.0%</td>
</tr>
<tr>
<td>2</td>
<td>0.1083 g</td>
<td>38.5%</td>
</tr>
<tr>
<td>4</td>
<td>0.1171 g</td>
<td>59.3%</td>
</tr>
<tr>
<td>8</td>
<td>0.1196 g</td>
<td>85.1%</td>
</tr>
<tr>
<td>16</td>
<td>0.1194 g</td>
<td>96.2%</td>
</tr>
<tr>
<td>32</td>
<td>0.1176 g</td>
<td>99.8%</td>
</tr>
<tr>
<td>t</td>
<td>w</td>
<td>x</td>
</tr>
<tr>
<td>---</td>
<td>-----</td>
<td>----</td>
</tr>
<tr>
<td>$\frac{1}{2}$ hours</td>
<td>0.1168 g.</td>
<td>11.0%</td>
</tr>
<tr>
<td>1 &quot;</td>
<td>0.1045 g.</td>
<td>19.5%</td>
</tr>
<tr>
<td>2 &quot;</td>
<td>0.1147 g.</td>
<td>32.8%</td>
</tr>
<tr>
<td>4 &quot;</td>
<td>0.1015 g.</td>
<td>54.6%</td>
</tr>
<tr>
<td>8 &quot;</td>
<td>0.1146 g.</td>
<td>78.9%</td>
</tr>
<tr>
<td>16 &quot;</td>
<td>0.1068 g.</td>
<td>95.3%</td>
</tr>
<tr>
<td>32 &quot;</td>
<td>0.1041 g.</td>
<td>99.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>t</th>
<th>w</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\frac{1}{2}$ hours</td>
<td>0.1067 g.</td>
<td>73.2%</td>
</tr>
<tr>
<td>1 &quot;</td>
<td>0.1008 g.</td>
<td>90.2%</td>
</tr>
<tr>
<td>2 &quot;</td>
<td>0.1023 g.</td>
<td>95.5%</td>
</tr>
<tr>
<td>4 &quot;</td>
<td>0.1116 g.</td>
<td>97.1%</td>
</tr>
<tr>
<td>8 &quot;</td>
<td>0.1057 g.</td>
<td>96.7%</td>
</tr>
<tr>
<td>16 &quot;</td>
<td>0.1039 g.</td>
<td>99.3%</td>
</tr>
<tr>
<td>32 &quot;</td>
<td>0.1039 g.</td>
<td>99.8%</td>
</tr>
</tbody>
</table>

p-nitro benzyl bromide.

m-nitro p-methoxy benzyl bromide.
### m-nitro p-hydroxy benzyl bromide

<table>
<thead>
<tr>
<th>t</th>
<th>w</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2 hours</td>
<td>0.1009 g</td>
<td>85.1%</td>
</tr>
<tr>
<td>1/2 &quot;</td>
<td>0.1024 g</td>
<td>96.4%</td>
</tr>
<tr>
<td>1 &quot;</td>
<td>0.1031 g</td>
<td>99.2%</td>
</tr>
<tr>
<td>2 &quot;</td>
<td>0.1028 g</td>
<td>99.7%</td>
</tr>
<tr>
<td>4 &quot;</td>
<td>0.1030 g</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

### Benzyl Bromide (Unsubstituted)

<table>
<thead>
<tr>
<th>t</th>
<th>w</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2 hours</td>
<td>0.1639 g</td>
<td>59.7%</td>
</tr>
<tr>
<td>1 &quot;</td>
<td>0.1247 g</td>
<td>84.9%</td>
</tr>
<tr>
<td>2 &quot;</td>
<td>0.1026 g</td>
<td>93.7%</td>
</tr>
<tr>
<td>4 &quot;</td>
<td>0.1219 g</td>
<td>97.2%</td>
</tr>
<tr>
<td>8 &quot;</td>
<td>0.0814 g</td>
<td>99.5%</td>
</tr>
<tr>
<td>16 &quot;</td>
<td>0.0975 g</td>
<td>99.6%</td>
</tr>
<tr>
<td>32 &quot;</td>
<td>0.1066 g</td>
<td>99.8%</td>
</tr>
</tbody>
</table>
Thermostat used for Hydrolyses and Reductions.
In the case of the m-nitro p-hydroxy benzyl bromide it was found impossible to use sodium hydroxide for the estimation of the liberated H Br, and so N/20 N H₄OH was used, as this did not hydrolyse the unchanged bromide sufficiently rapidly to alter the end point of the titration.

The apparatus used for these experiments consisted of a wide necked flask fitted with a reflux condenser, and the 25 cc. flask containing the solution for hydrolysis was fitted through a second hole in the stopper of the large flask. A quantity of carbon tetra chloride was placed in the large flask, and on heating this the interior of the apparatus was maintained at the boiling point of carbon tetra chloride (76°C.) for an indefinite period. The temperature error of this apparatus did not exceed 0.25°C. for lengthy periods. A sketch of the apparatus is shown.

(For hydrolysis curves see p. 11.)

An attempt was made to reduce the nitro benzyl bromides with hydriodic acid but an estimation of the amount of reduction occurring with the CH₂Br group was rendered impossible owing to the nitro group being reduced.

Hydrolysis/
Hydrolysis of the α-bromo toluic acids.

The hydrolysis of the α-bromo toluic acids was carried out in an identical manner to that of the nitro benzyl bromides and at the same temperature. When titrating the liberated hydrobromic acid with sodium hydroxide, an allowance had to be made for the quantity of sodium hydroxide sufficient to neutralise the carboxyl group in these compounds. A preliminary titration to ascertain the amount of this allowance was made and this was found in each case to be in agreement with the amount required by theory. A similar series of time intervals was employed as with the previous series and the proportions of alcohol and water were as before.

<table>
<thead>
<tr>
<th>t</th>
<th>w</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>½ hours</td>
<td>0.1068 g.</td>
<td>5.43%</td>
</tr>
<tr>
<td>1 &quot;</td>
<td>0.1158 g.</td>
<td>7.32%</td>
</tr>
<tr>
<td>2 &quot;</td>
<td>0.1031 g.</td>
<td>4.90%</td>
</tr>
<tr>
<td>4 &quot;</td>
<td>0.1089 g.</td>
<td>4.72%</td>
</tr>
<tr>
<td>8 &quot;</td>
<td>0.1126 g.</td>
<td>4.80%</td>
</tr>
<tr>
<td>16 &quot;</td>
<td>0.1152 g.</td>
<td>4.78%</td>
</tr>
<tr>
<td>32 &quot;</td>
<td>0.1025 g.</td>
<td>4.81%</td>
</tr>
</tbody>
</table>
It will be seen from a study of these results that the \( \omega \)-bromo o-toluic acid did not behave as one would expect, and this, as is explained elsewhere, was due to the formation of phthalide.

(For hydrolysis curves see p. 13.)
Reduction of \( \omega \)bromo toluic acids.

The \( \omega \)bromo toluic acids are substances which are not very soluble in acetic acid in the cold, and so the reduction was carried out in an apparatus similar to that used for the hydrolysis, and maintained at a temperature of 110°C by the vapour of boiling toluene. About 0.1 gm. of the substance was accurately weighed into a 25 cc. flask, 15 cc. of glacial acetic acid added, and the \( \omega \)bromo toluic acid dissolved by warming the flask. 10 cc. of constant boiling hydriodic acid solution were now run into the flask and after shaking to mix the contents the flask was placed in the thermostat described and kept at 110°C for the required period. The reduction was stopped by washing the contents of the flask into cold water, and the liberated iodine was then titrated with standard sodium thiosulphate solution, using starch as an indicator.

The amount of reduction which had occurred after stated periods was calculated from a consideration of the equations

\[
\begin{align*}
\omega & \rightarrow H + 1 - Br \\
\text{and } Br & \rightarrow H \ Br + l_2
\end{align*}
\]

\( t \) = time during which reduction was allowed to proceed.
\( w \) = weight of substance used.
\( x \) = per cent of \( \omega \)bromo toluic acid reduced.

Note: A blank experiment was conducted in each case to ascertain the amount of air oxidation occurring.
55.

$\omega$-bromo o-toluic acid.

<table>
<thead>
<tr>
<th>t</th>
<th>w</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>1½ hours</td>
<td>0.1026 g.</td>
<td>10.9%</td>
</tr>
<tr>
<td>3 &quot;</td>
<td>0.1223 g.</td>
<td>24.1%</td>
</tr>
<tr>
<td>6 &quot;</td>
<td>0.1161 g.</td>
<td>41.6%</td>
</tr>
<tr>
<td>12 &quot;</td>
<td>0.0931 g.</td>
<td>51.1%</td>
</tr>
</tbody>
</table>

$\omega$-bromo m-toluic acid.

<table>
<thead>
<tr>
<th>t</th>
<th>w</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>1½ hours</td>
<td>0.1010 g.</td>
<td>24.4%</td>
</tr>
<tr>
<td>3 &quot;</td>
<td>0.1003 g.</td>
<td>43.1%</td>
</tr>
<tr>
<td>6 &quot;</td>
<td>0.1001 g.</td>
<td>68.2%</td>
</tr>
<tr>
<td>12 &quot;</td>
<td>0.1060 g.</td>
<td>86.2%</td>
</tr>
</tbody>
</table>

$\omega$-bromo p-toluic acid.

<table>
<thead>
<tr>
<th>t</th>
<th>w</th>
<th>x</th>
</tr>
</thead>
<tbody>
<tr>
<td>1½ hours</td>
<td>0.1044 g.</td>
<td>49.3%</td>
</tr>
<tr>
<td>3 &quot;</td>
<td>0.1033 g.</td>
<td>73.0%</td>
</tr>
<tr>
<td>6 &quot;</td>
<td>0.1001 g.</td>
<td>90.8%</td>
</tr>
<tr>
<td>12 &quot;</td>
<td>0.0901 g.</td>
<td>99.3%</td>
</tr>
</tbody>
</table>

For comparative purposes a similar series was completed with unsubstituted benzyl bromide as follows:-
Benzyl Bromide (Unsubstituted).

<table>
<thead>
<tr>
<th>t, hours</th>
<th>w, g.</th>
<th>x, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1½</td>
<td>0.1518</td>
<td>33.9</td>
</tr>
<tr>
<td>3</td>
<td>0.1549</td>
<td>55.4</td>
</tr>
<tr>
<td>6</td>
<td>0.1426</td>
<td>78.0</td>
</tr>
<tr>
<td>12</td>
<td>0.1231</td>
<td>91.6</td>
</tr>
</tbody>
</table>

(For Reduction curves see p. 13.)

In order to be quite sure that the reduction taking place was not due to reduction of the carboxyl group, attempts were made to reduce the three toluic acids under identical conditions. After six hours the amount of reduction in each case was as follows:

- o toluic acid 0.16%
- m toluic acid 0.49%
- p toluic acid 0.43%

As any reduction of the carboxyl group occurring was extremely small no corrections have been made to the figures obtained.
As has already been mentioned a series of oxidations of various nitro toluene derivatives to the corresponding aldehydes was carried out, using chromyl chloride as an oxidising agent. The method first employed in these reductions was as recommended by Weyl. (Methode der Organischen Chemie 1911. Vol. II, Part 1, p. 6).

The first of these oxidations was carried out with o-nitro p-methoxy toluene and 10 gm. of this substance were dissolved in 100 gm. of carbon disulphide. To this solution 19 gm. (2 mol.) of chromyl chloride were slowly added through a dropping funnel, and a slight evolution of heat was noticeable. After all the chromyl chloride had been added, the solution was refluxed on a steam bath for 30 mins., and the bulky brown precipitate which had been formed during the reaction was filtered off. This intermediate compound was carefully washed with fresh carbon disulphide and then hydrolysed by warming with water to 50°C., when the solution was cooled, acidified with dilute sulphuric acid, and the product obtained by extraction with ether.

When this product was purified and examined, it proved/
proved to be o-nitro p-methoxy benzaldehyde as expected, and was recrystallised from ligroin in pale yellow needles melting at 96°C. It forms the following derivatives:

- a p-nitro phenyl hydrazone M.P. 246°C.
- a semi-oxamazone M.P. 242°C.
- a semi-carbazone M.P. 262°C.

On heating with acetone and dilute sodium hydr-oxide it formed the 6-6\textsuperscript{a} di-methoxy indigo with the formula.

\[\text{(cf. Annalen.588.45)}\]

The yield of o-nitro p-methoxy benzaldehyde which was obtained was approximately 50\% of the theoretical quantity.

A similar oxidation was now attempted under identical conditions with o-nitro toluene, but although a certain amount of intermediate compound was formed no o-nitro toluene could be obtained. In order to see if the reaction would proceed more favourably at a/
a higher temperature, carbon tetrachloride was substituted for carbon disulphide as a solvent, and the reaction carried out at the boiling point of the new solvent for the same period as before. With this alteration in the method it was possible to obtain about half a gram of o-nitro benzaldehyde from 10 grams of o-nitro toluene.

An attempt was now made to oxidise 2-4 di-nitro toluene to 2-4 di-nitro benzaldehyde in the same way but no trace of the expected product could be detected, using in one case carbon disulphide, and in the other carbon tetrachloride, as the solvent.

The results obtained from this series of oxidations were as follows:

10 gm. o-nitro p-methoxy toluene  Temp. 46°C gives 5.5 gm. aldehyde.

10 gm. o-nitro toluene  Temp. 46°C gives no aldehyde.
                  Temp. 76°C gives 0.5 gm.

10 gm. 2-4 di-nitro toluene
                  Temp. 46°C gives no aldehyde.
                  Temp. 76°C gives no aldehyde.

A curious fact noted during these experiments was that in every case a quantity of the dark brown intermediate compound was formed, and when this was hydrolysed it produced in some cases the original toluene, instead of the corresponding aldehyde. In one case however a small quantity of o-nitro benzoic acid/
acid was identified but this might have been due to the presence of a little moisture during the experiment.

According to Weyl (loc. cit.) and as is apparently generally accepted the mechanism of this reaction is as follows.

\[
\text{\( R \cdot CH_3 + 2 CrO_3Cl_2 \rightarrow R \cdot CH + OCrCl_2(OH) \)}
\]

\[
\text{\( R \cdot CHO + CrO_3 + Cr_2O_3 + HCl \)}
\]

Now if the formula here shown for the intermediate compound is correct, it is difficult to see how the hydrolysis of this intermediate compound could result in anything but an aldehyde. From this one is led to suspect that this reaction is rather more complex than is represented, and it is possible that this point might repay further investigation.
It is now of interest to study the results of these experiments, in so far as they provide information as to the various effects produced. An endeavour will be made to show in part the relation existing between the three types of effect, namely (a) the general polar or tone effect, (b) the induced polar effect, and (c) the steric effect.

A large number of results drawn from the dissociation constants of substituted aromatic acids and bases have been compiled by Flurscheim (T. 1909. 95. 718). From these he deduced a series of groups in descending order of their general polar effect, namely \( \text{NH}_2^- \), \( \text{OH}^- \), \( \text{OMe}^- \), \( \text{Cl}^- \), \( \text{Br}^- \), \( \text{I}^- \), \( \text{Me}^- \), \( \text{H}^- \), \( \text{CHO}^- \), \( \text{CN}^- \), \( \text{NO}_2^- \), \( \text{SMe}^- \). Those groups which are placed before \( \text{H}^- \) tend to increase the reactivity of the molecule while those coming after \( \text{H}^- \) have a decreasing influence on the reactivity. Olivier (Rec. trav. chim. 1923. 42. 775) deduced a similar series \( \text{Me}^- \), \( \text{H}^- \), \( \text{Cl}^- \), \( \text{NO}_2^- \), from the rate of hydrolysis of various substituted benzyl chlorides, and it will be seen that these agree except for the position of the halogens. In both these series the \( \text{NO}_2^- \) group is one which would be expected to have a large depressive effect on the reactivity of/
of the molecule.

Robinson (Ann. Reports 1922, p.98) advances a theory that the reaction in the case of the hydrolysis of the benzyl chlorides, is fundamentally an attack on the molecule as a whole by the hydroxyl ion, and that the rate of the hydrolysis tends to increase as the electro positive nature of the atoms in the substituant group increases. This series of Olivier's

Me - H - Cl - NO₂ represents a descending order with regard to the electronegative nature of the constituent atoms and the NO₂ group is seen to be at the lower end of the series. If this hypothesis explaining the nature of the general polar effect is accepted it will be seen that such groups as OH and OMe are out of the position which they might be expected to occupy in the series. This enhanced general polar effect exhibited by these two groups is accounted for on the basis that they may be partially conjugated with the nucleus. (Robinson. Ann. Reports. loc. cit.)

Considering the results obtained from the series of condensations with the three tolyl methyl ethers and amyl nitrite, it is obvious that any induced polar or steric effects are overshadowed by the general tendency of the reaction to produce nuclear resins, as was shown by the experiment with di-methyl resorcinol. This tendency of hydroxy and methoxy groups to promote/
promote tarring in the presence of strong acid or alkali, is often met with during preparative work, and was very noticeable in connection with the preparation of m-hydroxy benzaldehyde. The assumption that these two groups may be conjugated with the nucleus, would help to explain the tendency to promote resinification of a nuclear variety.

Apart from a tendency to tar, an explanation of the failure of the condensation with m-tolyl methyl ether might be suggested by the fact that it possesses absolutely concordant polarities, and this according to Lowry (loc. cit.) would tend to be a stabilising factor and prevent any reaction from taking place.

When the two induced polar effects, due to different "key" atoms at the opposite ends of a chain of carbon atoms, are superimposed and agree in character throughout, the polarities in such a system are called concordant. This is the case with the m-tolyl methyl ether.

\[
\begin{align*}
\text{m-Tolyl methyl ether} & \quad \text{m-Methoxy benzyl bromide}
\end{align*}
\]
In the m-methoxy benzyl bromide as shown above the polarities are not concordant but crossed, and so according to Lowry's views, this substance should be less stable than an isomer with concordant polarities, such as the p-methoxy benzyl bromide. The hydrolysis of the methoxy benzyl bromides however (Lapworth and Shoesmith. loc. cit.), shows that this is not the case, so it is doubtful if Lowry's is an adequate explanation of the behaviour of the condensations mentioned.

The last of this series of condensations, carried out with o-nitro p-methoxy toluene, shows to some extent the general polar effect of the NO₂ group, for this experiment did not proceed with the vigour exhibited by the other ones. This tone effect of the nitro group is well shown by a comparison of the hydrolysis of the three nitro benzyl bromides with that of the unsubstituted benzyl bromide. There is some doubt however as to the validity of a comparison with an unsubstituted compound, so the rate of hydrolysis of the m-nitro p-methoxy benzyl bromide was measured, in order to compare it with the results obtained by Lapworth and Shoesmith for the p-methoxy benzyl bromide. This gives a definite confirmation of the general polar effect due to the NO₂ group in this reaction, and is further borne out by the possibility of preparing m-nitro p-hydroxy benzyl bromide as/
65.

as a stable substance, and by its hydrolysis at a measurable rate.

The general polar effect of the NO$_2$ group on another type of reaction is found to be of a similar nature, as shown by the difference of reactivity of various nitrated toluenes when oxidised by chromyl chloride. Apparently this effect tends also to increase with the number of nitro groups present, as seen by the difference between the o-nitro toluene and the 2,4-di-nitro toluene during this reaction.

In spite of the large general effect of the NO$_2$ group it is still capable of showing alternate induced effects when the hydrolyses of the three isomeric nitrobenzyl bromides are compared. The direction of this effect is in complete agreement with the theory of alternate polarities as advanced by Lapworth, the isomer containing a negatively induced Br. atom hydrolysing more rapidly than the others. An attempt to indicate the positively induced character of the Br. atom in the ortho and para compounds by means of reduction with hydriodic acid was unfortunately impossible owing to reduction of the NO$_2$ group.

An even better confirmation of the value of this theory of induced polarities, is shown with the series of o-bromo toluic acids. The hydrolysis of these compounds shows a considerable diversion with the different/
different isomers and the order of reactivity \( m > p > o \) is quite apparent. This shows that the Br atom in the \( m \) compound has a negatively induced character as compared with the \( p \)- and \( o \)-compounds, whilst the reduction with hydriodic acid shows the order \( p > m > o \), demonstrating the positively induced character of the Br atom in the \( p \)-compound as compared with the meta.

These results offer a striking illustration of the theory of induced alternate polarities and appear to show without doubt the transmission of an alternate electrical character along a chain of carbon atoms by a suitable "key" atom.

The \( \omega \)-bromo o-toluic acid exhibits what would appear to be a very large steric effect, especially in the hydrolysis, and this as shown by Salkind and Saemenow (J. Russ. Phys. Chem. Soc. loc. cit.) is due to the formation of phthalide.

\[
\text{Phthalide} + \text{HBr} \rightarrow \text{\( \omega \)-bromo o-toluic acid}
\]

\[
\text{\( \omega \)-hydroxy o-toluic acid} + \text{HBr}
\]
An equilibrium of the three phases shown above is probably established, and when the equilibrium point is finally reached, as shown by the hydrolysis curve, one would expect phase 1 to be totally decomposed. This would result in the figure obtained being a measure of the amount of phase 3 left in the solution. Owing to this complication the figures obtained would not really be a representation of the percentage hydrolysis of the ß-bromotoluic acid, but instead a measure of the excess of total acidity beyond the amount equivalent to the COOH group in the original acid. Now as the Br would all be present as H Br when an equilibrium was reached, this figure will be a representation of the percentage of ß-hydroxytoluic acid left unconverted to phthalide. The rapid rise at the commencement of the hydrolysis curve drawn from these figures is probably due to the fact that the conversion of phase 1 to phase 3 is more rapid than the production of phthalide (phase 2).

There is also a very large steric effect apparent in the reduction of the ß-bromotoluic acid which may be due partly to the formation of phthalide. In this connection it is of interest to note that the ß-hydroxy o-toluic acid may be reduced to o-toluic acid with hydriodic/
hydriodic acid and yellow phosphorus (Hessert Ber. 1878. II. 238).

Any steric effects present either in the series of condensations with the tolyl methyl ethers, or in the hydrolysis of the nitro benzyl bromides are completely masked by the considerable general polar effects present in both cases.

When the hydrolysis and reduction curves of the unsubstituted benzyl bromide are compared with the similar curves obtained from the α bromo toluic acids it appears to be the case that the general polar effect of the carboxyl group is not very pronounced especially in the reductions. The direction of this slight general polar effect appears to be of a depressive character but not sufficiently so to interfere with the other effects present.

The deductions which might be made from a consideration of these results are:—

(1) The methoxy group shows a distinct tendency to promote tarring probably of a nuclear variety.

(2) In all cases considered the nitro group appears to have a strongly depressive influence on the reactivity of the molecule as a whole.

(3) The theory of induced alternate polarities is strongly upheld by the effects observed in two different/
different series of substituted benzyl bromides namely: (a) the nitro benzyl bromides and (b) the \textit{\textalpha}bromo toluic acids.

(4) The general polar effect of the carboxyl group appears to be slightly depressive in character.

(5) In cases where the general polar effect is large, both the induced polar effects and the steric effects tend to become less apparent.

9th November, 1923.