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Thesis for the Degree of D.Sc.

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

by

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The influence which an atom or group of atoms exerts on the other atoms in the same organic molecule has long been recognised. The rules propounded by Hubner (Ber., 1875, 8, 875.), Noelting (Ber., 1876, 9, 1797) and Crum Brown and Gibson (J.C.S., 1892, 61, 367) with respect to the manner in which various atoms and groups present in a benzene nucleus direct the entrance of other substituents into the nucleus, and the well known rule of Markownikoff (Annalen, 1870, 153, 256) concerning the addition of halogen acids to ethenoid compounds were the earliest attempts to systematise the accumulated data on the subject. The rules proved to be of inestimable value but were limited in their application until extended with a view to discovering the true nature and hence the cause of the observed differences of reactivity, and Holleman (Die direkte Einführung von Substituenten in den Benzolkern 1910, pp. 466-70) Michael (J. prakt. Chem., 1892, 46, 205) Vorlander (Annalen, 1902, 320, 99. Ber., 1919, 52, 263) Flurscheim (J. prakt. Chem., 1902, 66, 321; 1905, 71, 597, J.C.S. 1909, 95, 718; 1910, 97, 84 and onwards), and many others have been in a large measure successful in extending the above rules/

rules with such an object in view.

Some chemists are of the opinion that the differences are due to influences essentially steric or spatial in origin,but it is now generally recognised that an explanation is to be sought in the influence which one atom exerts on another atom in the same molecule, not merely in virtue of the influencing atom's position in the molecule but also in virtue of an intrinsic property of the influencing atom itself. This property may broadly be postulated as due in some measure to the electro-chemical nature of the influencing atom or group.

However wide in its postulates a theory may be, it is in general discovered that some of the important observations made both previous to and after the appearance of the theory are incapable of being explained by its aid and the present researches were undertaken with a view to discovering any regularities which might exist in the reactivity of the halogen atoms present in various types of aromatic halogen compounds. The whole research was suggested by the views enunciated by Lapworth (Mem. Manchester Phil. Soc. 1920, 64, No.3) and which are grouped together as the Principle of Induced Alternate Polarities.

This principle was recognised mainly as a result of many observations on the manner in which the atoms in/

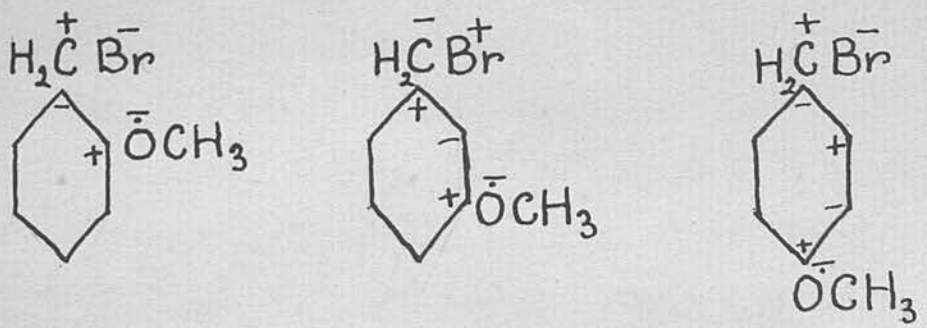
in the molecule of an organic compound are affected by the presence of an atom such as oxygen. The direct result of the influence exerted by this atom is the alternate enhancing and repressing of the reactivity of the hydrogen atoms attached to alternate carbon atoms in a hydrocarbon chain attached to a divalent oxygen atom. Hydrogen which is so situated in the molecule that its activity is increased possesses induced positive polar characteristics since its reactivity approaches that of a hydrogen ion, whilst hydrogen, the activity of which is decreased, possesses induced negative polar characteristics since the ordinary electro-positive nature of the atom is diminished. The prinicple does not assume the appearance of a positive or negative change in the molecule. It is at once important to note that the alternating influence is most readily transmitted along a carbon chain in which the carbon atoms are connected together by alternate double and single linkages.

The preparation of compounds which contain halogen atoms attached to carbon atoms connected together in the above manner is a matter of great difficulty, hence investigations of the reactivity of the halogen atom in such compounds have not been carried out.

Suitable compounds are readily obtainable in the aromatic/

aromatic series, since the alternation of the properties of the carbon atom in a substituted benzene nucleus, demonstrated so clearly in the similarity of the behaviour of the hydrogen in ortho and para positions, suggests that the benzene nucleus should be a very efficient transmitter of the induced effects outlined above, provided that the similarity is not merely spatial or structural in origin.

If now the three isomeric methoxybenzyl bromides be considered and the alternation of the influence (which is transmitted through the carbon atoms) be represented by alternate + and - signs on alternate atoms, commencing with the negative oxygen atom (the "key-atom" denoted by $\dot{-}$) then the bromine atom should possess induced negative polar characteristics in the o and p isomerides and induced positive polar characteristics in the m-isomeride



Hence/

Hence the o and p isomerides should lose their bromide as bromidion more rapidly than the meta compound, whilst when subjected to the attack of a reagent which would remove the bromine as a result of its combining with the negative ion of the reagent, these isomerides should be the most stable.

In order to prove that this is actually the case two reactions were employed, namely, hydrolysis and reduction.

$$(1)\quad X - \overset{-}{Hal} + \overset{+}{H}\overset{-}{OH} \longrightarrow X\text{-}OH + HHal$$

$$(II)\quad X - \overset{+}{Hal} + \overset{+}{H}\overset{-}{I} \longrightarrow X\text{-}H + Hal\text{-}I$$

Reaction (1) should take place most readily with the o and p isomerides and reaction (11) should take place most readily with the m-isomeride.

The order in which these compounds lost their bromine as bromidion when emulsified with dilute aqueous sodium hydroxide was found to fulfil this expectation and was p>o>m. In order to eliminate any effects which may be considered to be due to differences in solubility of the isomerides in the alkali, the hydrolyses were repeated in solution in aqueous alcohol and also in aqueous alcoholic sodium hydroxide. The order remained unchanged and in solution the hydrolysis of the para isomeride was found to be instantaneous at any temperature, and

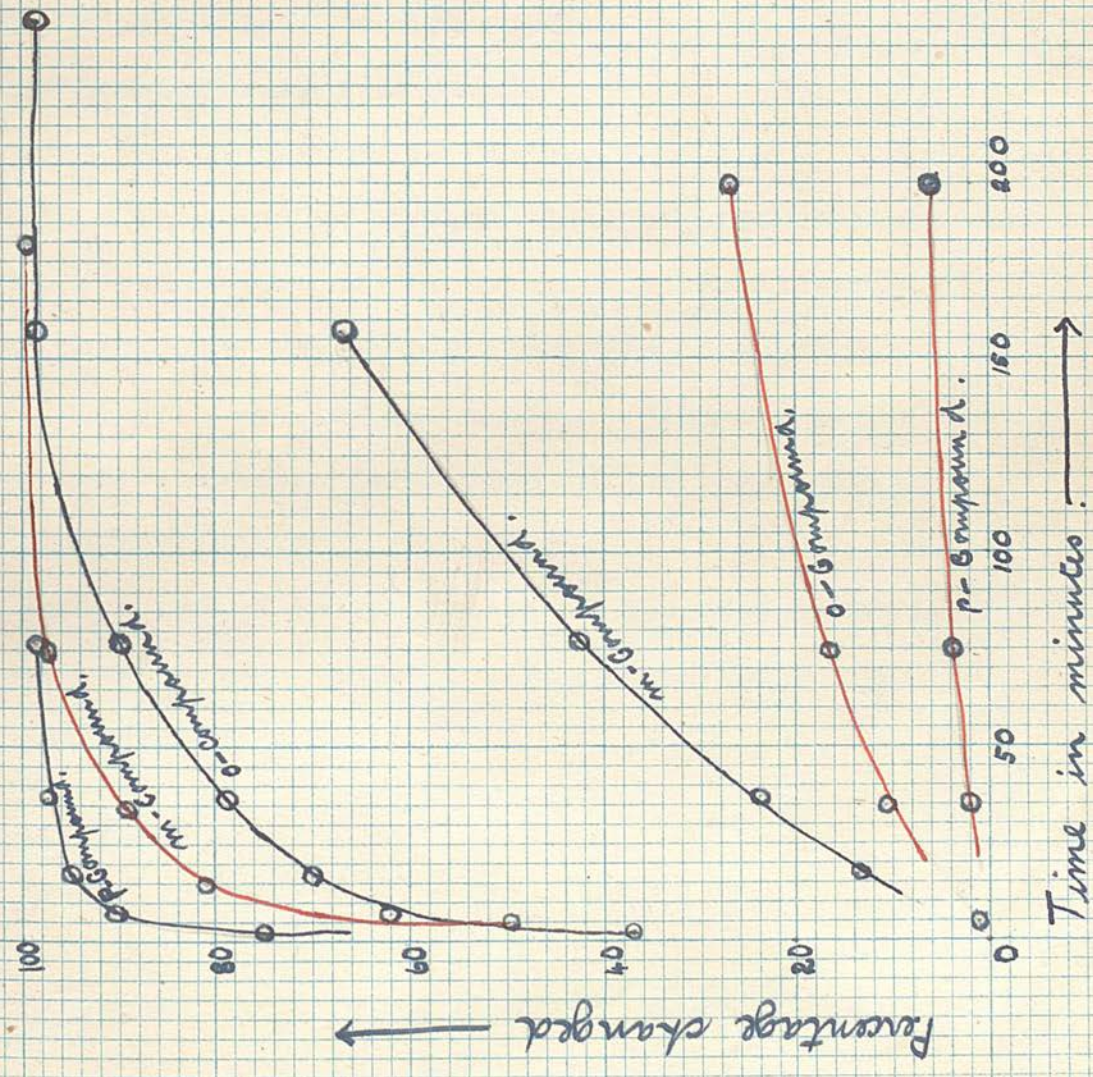
whilst/

FIGURE I.

Hydrolysis and reduction curves of the isomeric methoxybenzyl bromides

—— represents hydrolysis at 55°.

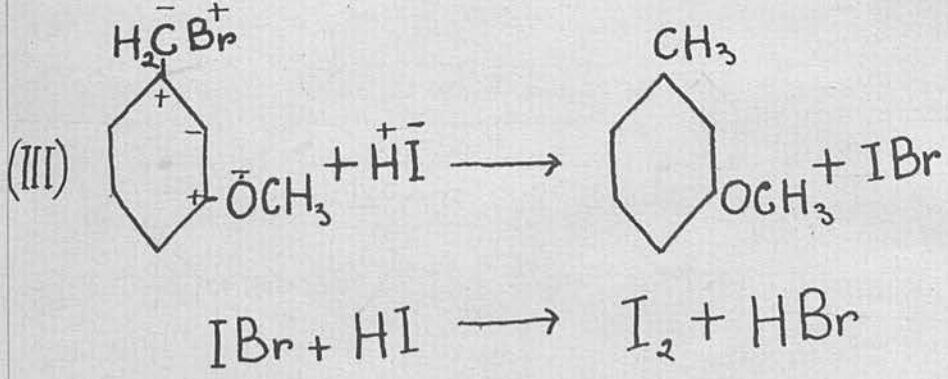
—— " reduction " 25°.



whilst the ortho was also almost completely hydrolysed under the same conditions, the meta isomeride was comparatively stable.

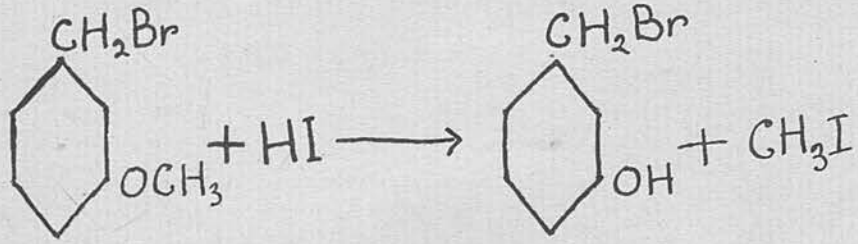
The isomerides were then subjected to the action of dry hydrogen iodide in glacial acetic acid. This reagent was chosen because the ortho and para hydroxybenzyl alcohols readily resinify in presence of aqueous acid, and preliminary experiments showed that after a time resin actually appeared in a reduction mixture consisting of acetic acid as solvent and aqueous hydriodic acid as reducing agent. The anhydrous reagent proved to be very useful and rendered possible a long series of reductions at a temperature of 25°. Under the conditions given in the experimental portion of the thesis the order in which the isomerides were reduced was m>o>p. Figure I illustrates the remarkable difference in the reactivities (see also publication I, pp. 1395).

The course of the reduction of the meta isomeride however may be open to doubt since it may not be as has been assumed, namely:-



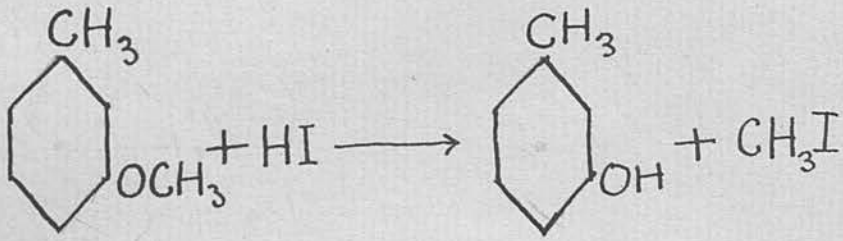
$$IBr + HI \longrightarrow I_2 + HBr$$

but

(IV) 

$$CH_3I + HI \longrightarrow CH_4 + I_2.$$

That the reaction does take place in the normal manner was proved by the isolation of m-tolylmethyl ether from the reduction mixture. Demethylation also takes place during this reduction but the methyl iodide produced does not liberate iodine from hydrogen iodide and the reactions taking place are therefore III and V

(V) 

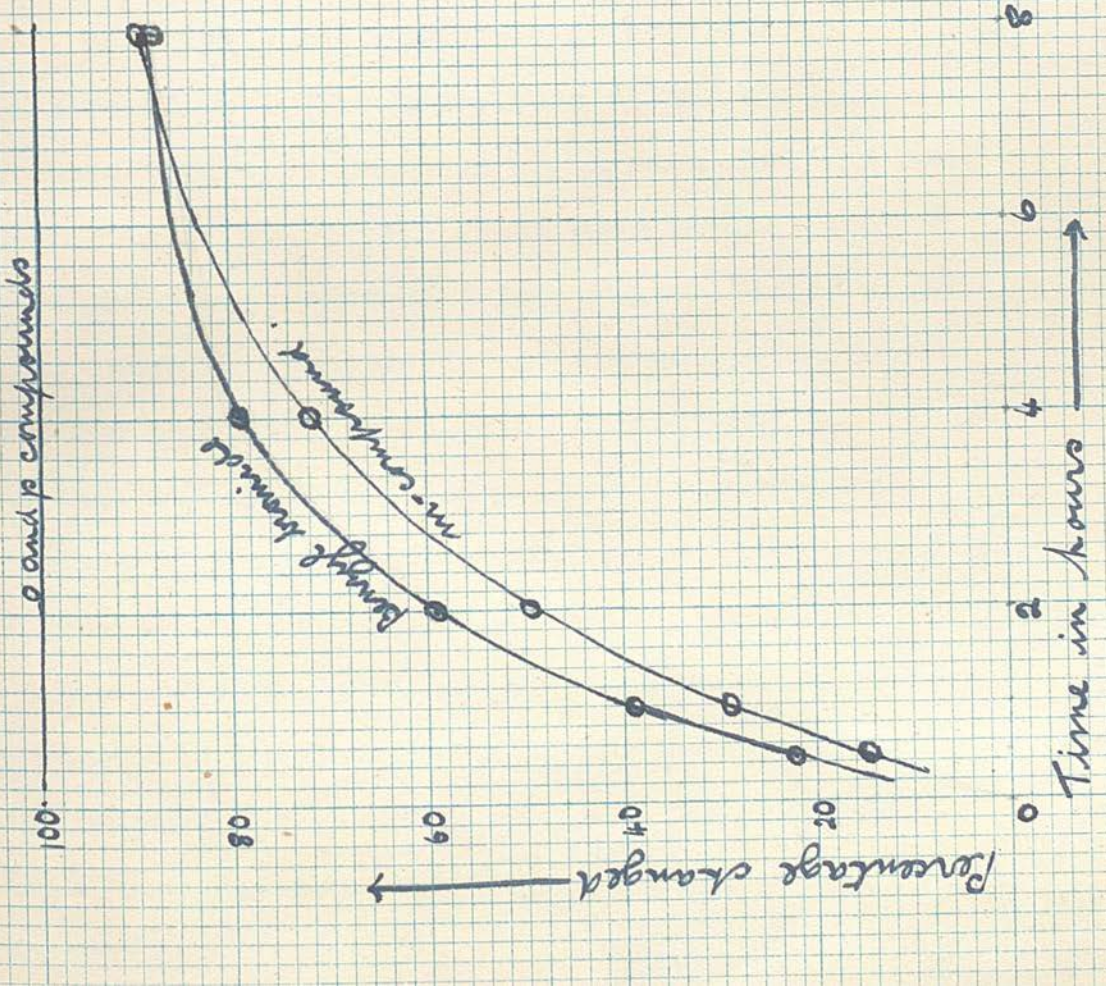
(see publication II).

This reversal of the order of the reactivity of the bromine atom in the three isomerides when the reagent is changed from a hydrolysing to a reducing agent provides a striking example of the usefulness of the principle of induced alternate polarities and also of the truth of the views contained therein.

In/

FIGURE II

Hydrolysis of the isomeric methoxybenzyl bromides and benzyl bromide at 60°



In addition to purely induced polar effects demonstrated in the methoxybenzyl bromides, the effect of the methoxyl group on the molecule as a whole must be considered, since it is well known that some groups such as the nitro and carboxyl groups stabilise the hydrogen atoms of a benzene nucleus although further substitution products show that these groups exert a directive influence which results in the production of meta disubstituted derivatives. This "general" influence may be large or small or may be masked by the strong inducing influence of the "key-atom" of the group. To discover the potency of this influence which of course is purely a matter for experimental proof, hydrolysis and reduction of benzyl bromide were carried out. The hydrolyses at 60° are illustrated in figure II in which it is seen that the complete order of hydrolysis reads p>o > unsubs > m. Benzyl bromide is converted into benzyl iodide at 25° by the reducing agent used, and the complete order of reduction therefore reads m>o > unsubs and p. From this it may be concluded that the directing influence of the methoxyl group is great compared with the general influence exerted by this group.

The inducing influence would be expected to decrease with the increasing of the number of carbon atoms between the inducing atom and the reacting halogen and therefore the ortho isomeride would be expected/

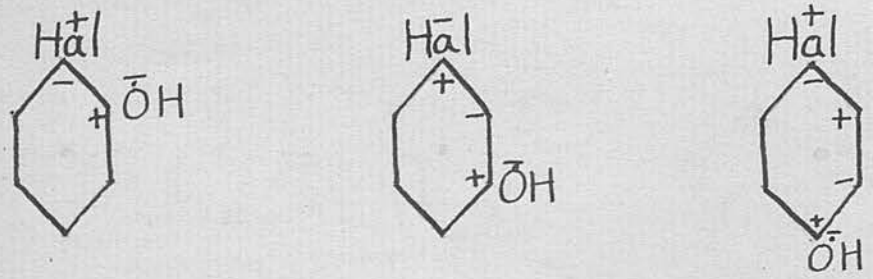
expected to be more reactive than the para towards hydrolysing agents. This however is not the case.

The proximity of the methoxyl group to the $-CH_2Br$ group may be thought to be responsible for the slower rate of hydrolysis of the ortho isomeride as compared with that of the para isomeride and [redacted] steric effects of this nature should not be disregarded. On the other hand the ortho isomeride also approximates to the meta in the manner in which it is reduced, and hence purely steric effects cannot be responsible for this abnormality which is discussed further on pp. 82.

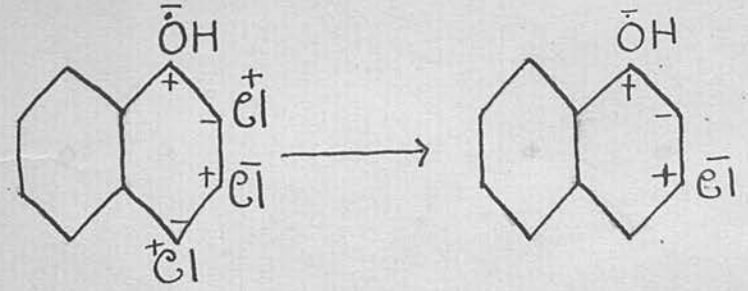
A long series of investigations were then undertaken in order to show how the oxygen atom influences the reactivity of halogen atoms in various halogenated benzenoid derivatives, and to see to what extent it is possible to trace effects due to the three influences already enumerated, namely, induced polar influences, general polar influences and steric influences.

Reduction of the halogenated phenols.

The halogen atoms in the halogenated phenols are to be regarded as one place nearer the "key-atom", that is the oxygen atom, than is the bromine in the methoxybenzyl bromides. Thus the halogen atoms which have acquired an induced positive polar character should be those present in the o and p isomerides.



The order of ease of reduction should therefore be o and p > m. Investigation proved that this is so. The substituted phenols investigated were iodo, bromo and chlorophenols and 4-iodo-resorcinol. The order in which the halogen atoms are removed from these compounds is, p-iodo > o-iodo > p-bromo > o-bromo > p-chloro. The meta isomerides show no tendency to be reduced. 4-Iodoresorcinol looses its halogen with extraordinary ease. It is of interest to note that Franzen and Stauble (J. prakt. Chem. 1921, (11), 103, 3-chloro-1-naphthol 352-390) prepared by the reduction of 2 : 3 : 4-trichloro-α-naphthol with hydriodic acid. The resulting monochloro compound is quite stable to the reducing agent.



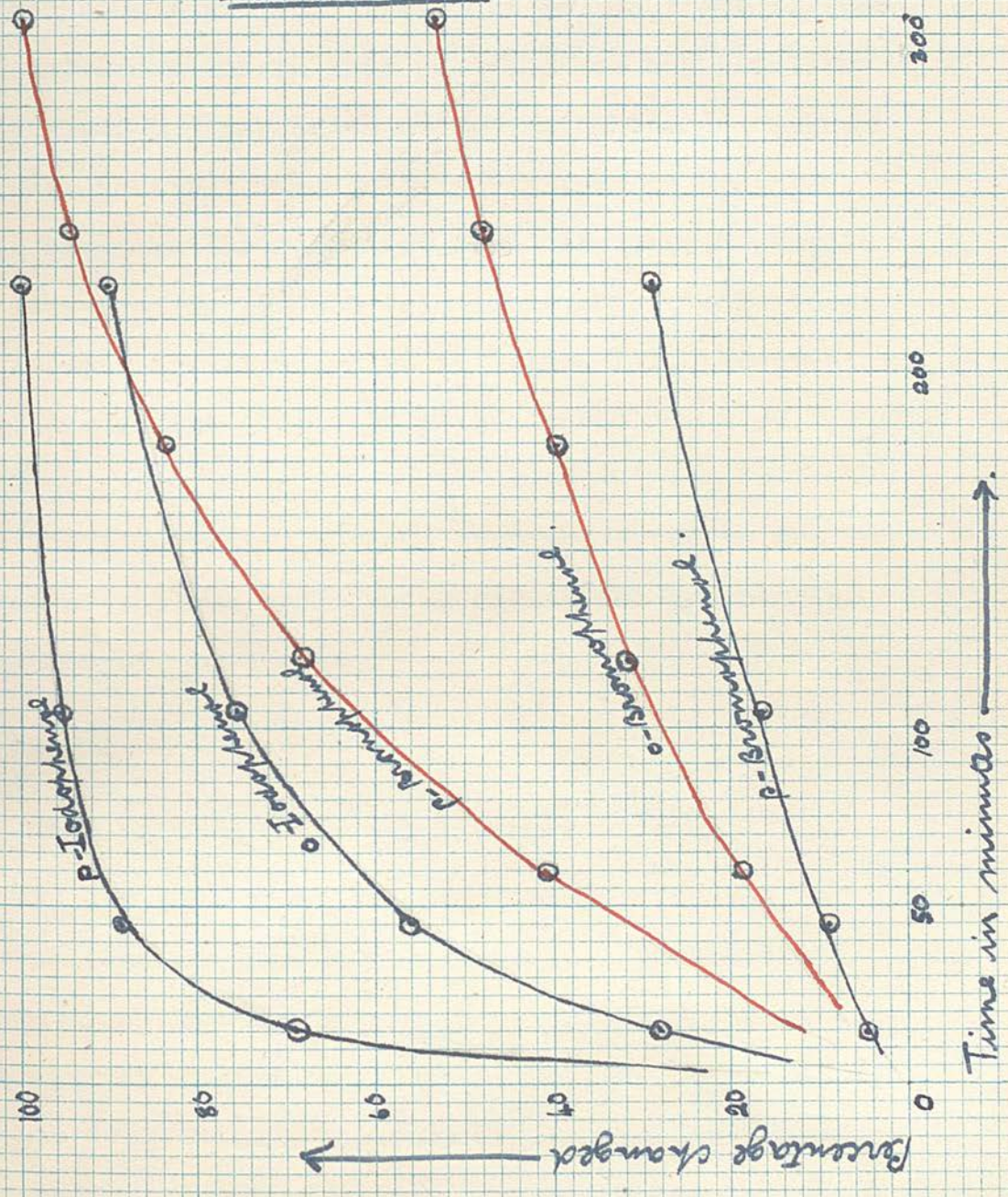
In this connection Nicholet (J. Amer. Chem. Soc., 1921, 43, 2081) has shown that halogen atoms in ortho and/

FIGURE III

Reduction of the halogenated phenols.

——— represents reductions at 25°

" " " 78°.



and para substituted iodoanilines and bromoanilines and also in 3-iodo-4-hydroxybenzoic acid are removed by boiling the compounds with hydrochloric acid and attributes this to the presence of "positive" halogen. He does not state that iodine in compounds in which the halogen is in meta position to hydroxyl is not removed by the reducing agent and it is just as important to show that halogen atoms in this position are non reactive to hydrogen iodide, as to prove that those in ortho and para positions are readily replaced by hydrogen. It is important to note that para halogenated phenols are more readily reduced than their ortho isomerides. The results are illustrated in figure III, the great lability of the iodine in p-iodo-phenol is very striking.

The halogenated phenols were subjected to the action of various hydrolysing agents but apparently no hydrolysis took place.

The isomeric ω-bromotoluic acids.

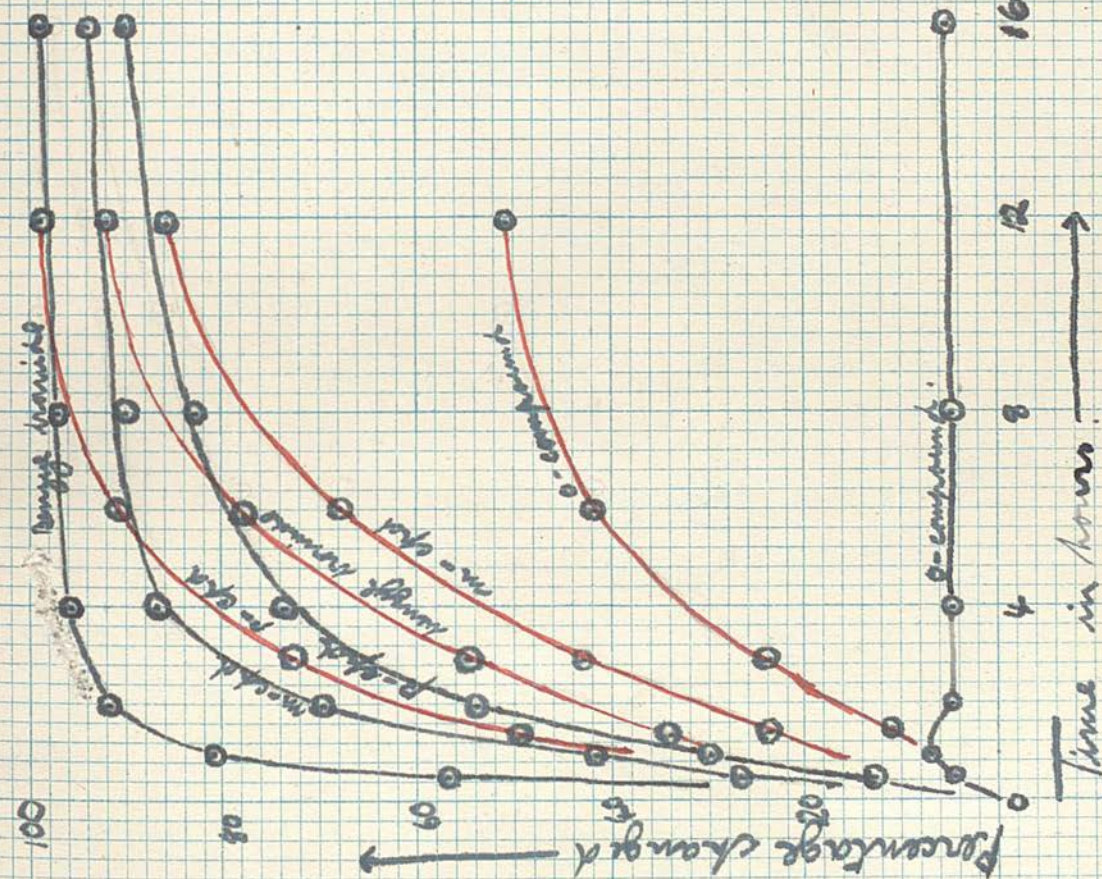
An application of the principle of induced alternate polarities to the isomeric ω-bromotoluic acids shows that the bromine atoms are induced in a manner which may be regarded as the reverse of that already described in the case of the methoxy-benzyl bromides.

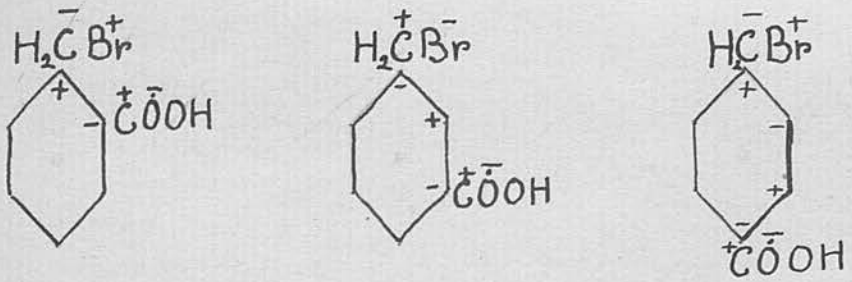
FIGURE IV

Hydrolysis and reduction of the isomeric ω-bromotoluic acids

——— represents hydrolysis at 76°.

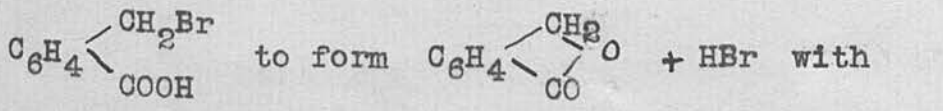
——— " reduction at 110°





Here the bromine atom which has acquired an induced negative character is present in the meta isomeride. Thus the order of ease of hydrolysis of these compounds should be m>p and o , the reverse of the order which was found in the methoxybenzyl bromides. Experiment proved this to be the case. The ortho isomeride behaved in an abnormal manner. The rate of hydrolysis of this compound appeared to rise to a maximum and then fall to a constant value which actually represents an equilibrium as regards the several reactions which are taking place during the hydrolysis of ω-bromo-o-toluic acid. This effect is illustrated in Figure IV and is due to spatial influences.

Whilst the order of ease of hydrolysis should be m > o and p the order of ease of reduction of these compounds should be p and o > m. The para isomeride was found to be reduced more rapidly than the meta isomeride, but the ortho compound only liberated iodine in the quantities representing about one half of that expected. This is due to the tendency of

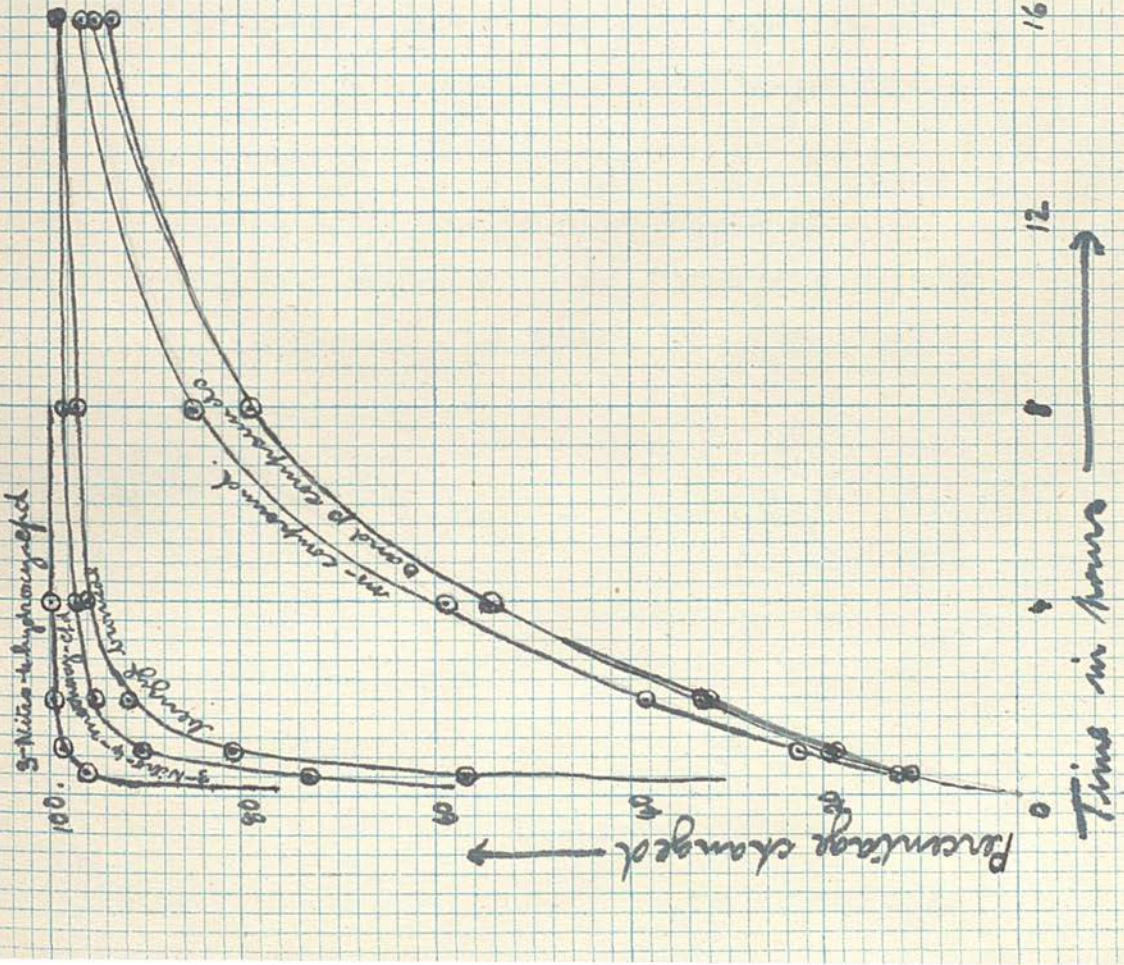


to form

+ HBr with

FIGURE V.

Hydrolysis of the nitrobenzyl bromides, 3-nitro-4-methoxy, and 3-nitro-4-hydroxybenzyl bromides

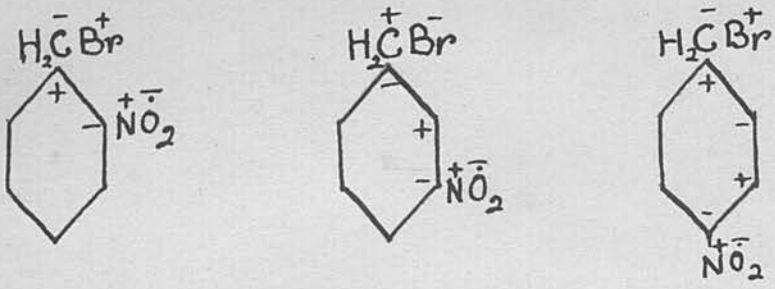


withconcomitant loss of reducing power. Reduction of the carboxyl group in such media as were used in these investigations takes place to a very small extent and may be ignored for such comparisons.

As is apparent from figure IV, all the isomeric ω-bromotoluic acids are more difficult to hydrolyse than benzyl bromide. The general polar influence of the carboxyl group therefore is quite marked, and has resulted in the stabilising of the molecule of the substituted benzyl bromide towards hydrolysing agents.

The influence of the nitro group.

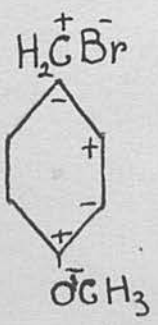
The nitro group would be expected to influence the $-CH_2Br$ group in a manner similar to that exerted by the carboxyl group. This is so, and of the isomeric nitrobenzyl bromides the meta is the most readily hydrolysed isomeride. The difference of ease of hydrolysis is not very great but it is that which would have been anticipated

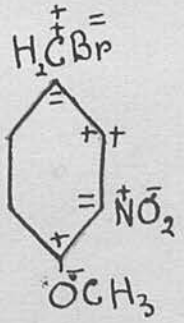


All the bromides however are far more difficult to hydrolyse than the unsubstituted bromide as shown in figure V.

The/

The stabilising influence of the nitro group is further illustrated by the manner in which the reactivity of p-methoxybenzyl bromide is diminished on the introduction of a nitro group into the meta position to the $-CH_2Br$ group. The nitro group was introduced into the molecule in this position in order to eliminate any spatial or steric effects which might influence the reactivity of the molecule when the nitro group is in ortho position to the reacting group. 3-Nitro-4-methoxybenzyl bromide is hydrolysed by aqueous alcohol at approximately the same rate as benzyl bromide is hydrolysed. Thus it is not possible to predict differences of reactivity unless the compounds considered are isomeric with one another. If this fact were overlooked then 3-nitro-4-methoxybenzyl bromide would be expected to be more reactive than the very reactive p-methoxybenzyl bromide, in virtue of the enhanced negative character of the bromine atom, induced by the nitro group, an effect more than balanced by the strong general inhibiting influence of the nitro group.





As a result of this observation signs such as + + and - - which are often met with in the literature lose one of the interpretations commonly assigned to them.

The inhibiting influence of the nitro group has made possible a comparison of the hydrolysis of a p-hydroxybenzyl bromide and a p-methoxybenzyl bromide. 3-Nitro-4-hydroxybenzyl bromide is more readily hydrolysed by aqueous alcohol than 3-nitro-4-methoxybenzyl bromide (see figure V).

Hydriodic acid was found to reduce the nitro group. Hence the investigation of the change of the order of reactivity with change of reagent was not possible.

This concluded the investigations on the influence exerted by the oxygen atom.

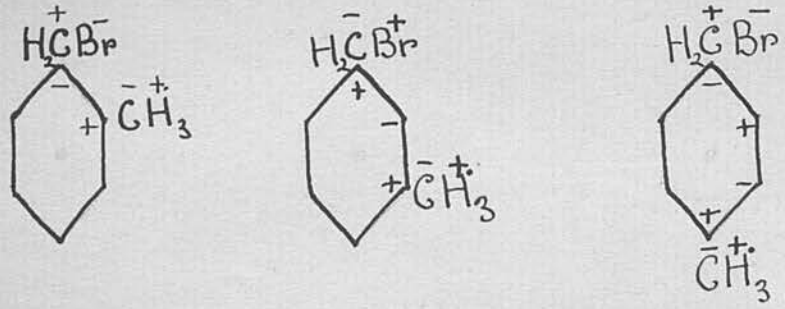
Atoms other than oxygen may influence the reactivity of other atoms in the same molecule and in this respect nitrogen behaves analogously to oxygen. Additional data on this point could not be obtained in these investigations since aminobenzyl bromides cannot be prepared.

Hydrogen acting as a positive "key-atom" in groups such as the methyl group may induce differences in reactivity. An example of the inducing influence of hydrogen has recently been quoted by Lapworth (Mem.,/

(Mem., Manchester Phil. Soc., 1920, 64, III 10.) who showed how differences in the acidity of the three isomeric cresols are in perfect agreement with those which would be expected from a consideration of polarities induced on the hydrogen atoms of the hydroxyl groups by the hydrogen of the methyl group. An attempt was therefore made to extend our knowledge on the rôle played by hydrogen in inducing differences of reactivity in substituted benzyl bromides and iodo toluenes.

The isomeric ω-bromoxylenes.

The ω-bromoxylenes should behave in a manner absolutely analogous to that already discovered in the case of the isomeric methoxybenzyl bromides since the hydrogen atoms of the methyl group act as positive "key-atoms" denoted by $-H^{+\cdot}$ and hence the induced polar character of the bromine atom in the ortho and para isomerides is negative and that of the bromine atom in the meta isomeride is positive.



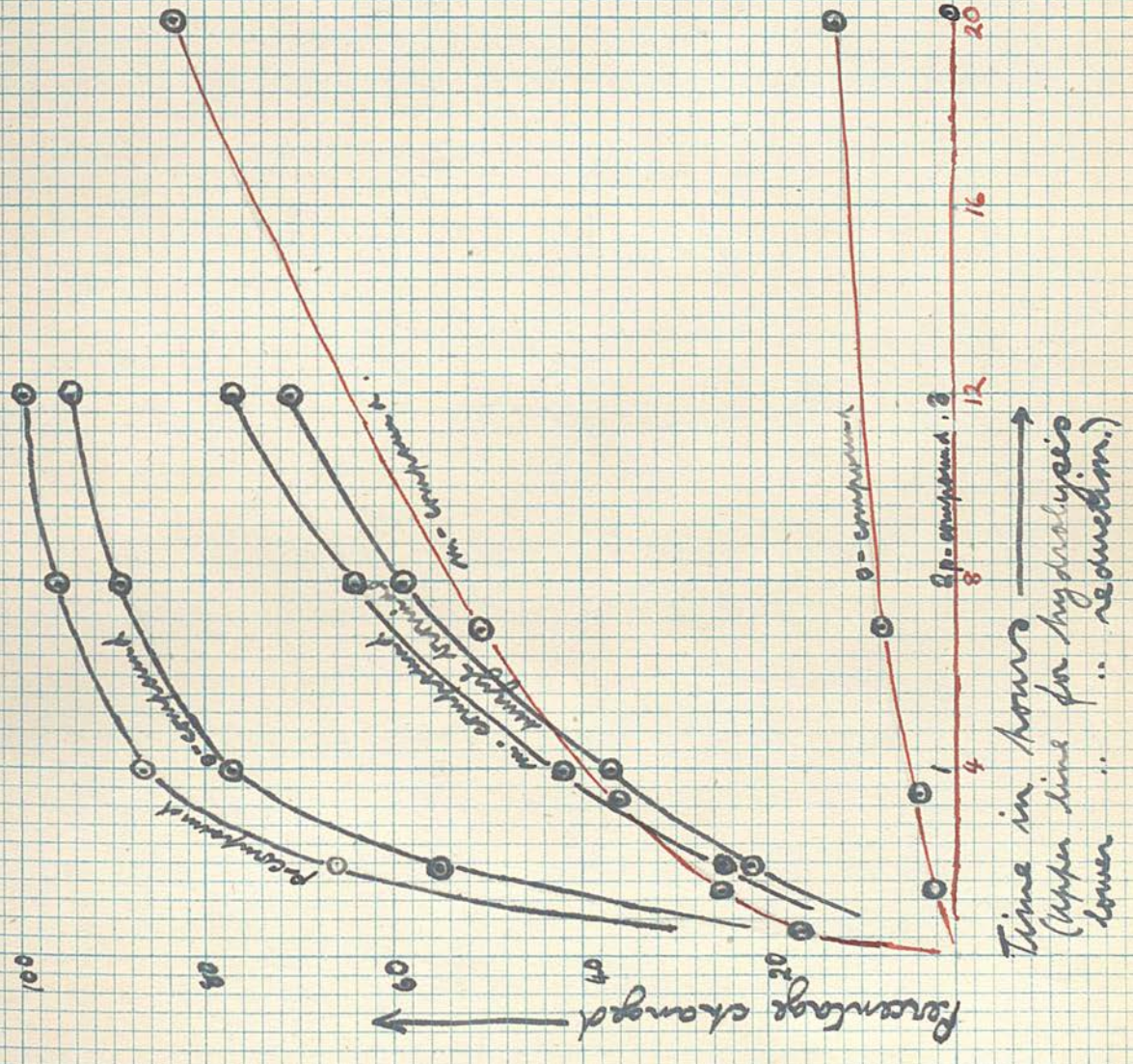
Thus/

FIGURE VI

Reduction and Hydrolysis of the isomeric ω-bromocymenes

—— represents hydrolysis at 60°

—— " reduction " 25°.



Thus the order of ease of hydrolysis should be o and p > m and of reduction m > o and p. This was exactly what was discovered by experiment and it was possible to show that under conditions by which ω-bromo-m-xylene is almost quantitatively reduced by hydrogen iodide to m-xylene the isomeric ω-bromo-p-xylene is converted to ω-iodo-p-xylene. Thus one isomeride exchanges its bromine atom for the positive ion of the hydrogen iodide whilst the other exchanges it for the negative ion. The action of hydrogen iodide on the two isomerides is therefore represented as follows:-

$$C_6H_4\begin{cases}CH_2\,\overset{+}{Br} & 1)\\ CH_3 & 3)\end{cases} + \overset{+-}{2HI} \longrightarrow C_6H_4(CH_3)_2 + I_2 + HBr$$

$$C_6H_4\begin{cases}CH_2\,\overset{-}{Br} & 1)\\ CH_3 & 4)\end{cases} + \overset{+\ -}{H\ I} \longrightarrow C_6H_4\begin{cases}CH_2I & 1)\\ CH_3 & 4)\end{cases} + HBr.$$

The manner in which the ortho isomeride reacts both to hydrolysing and reducing agent is exactly analogous to that observed in the case of o-methoxy-benzyl bromide and the complete order of hydrolysis is p > o > m and of reduction m > o > p (see Fig. VI).

The general influence exerted by the methyl group is quite marked and all the ω-bromoxylenes are more easily hydrolysed than the unsubstituted benzyl bromide and this series differs from the nitrobenzyl bromides and the ω-bromotoluic acids all of which

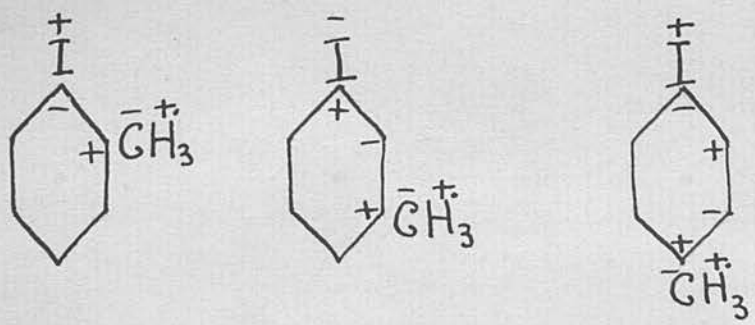
are more difficult to hydrolyse than benzyl bromide itself.

A comparison of the reduction of benzyl bromide and these isomerides showed that under conditions by which the o and m compounds are reduced the unsubstituted compound is merely converted to the corresponding iodide.

Iodine is a more electro positive element than bromine and hence a benzyl iodide should be more slowly hydrolysed than the corresponding benzyl bromide. In accordance with this expectation it was found that ω-iodo-p-xylene is more slowly hydrolysed than the corresponding ω-bromo-p-xylene.

The isomeric iodotoluenes.

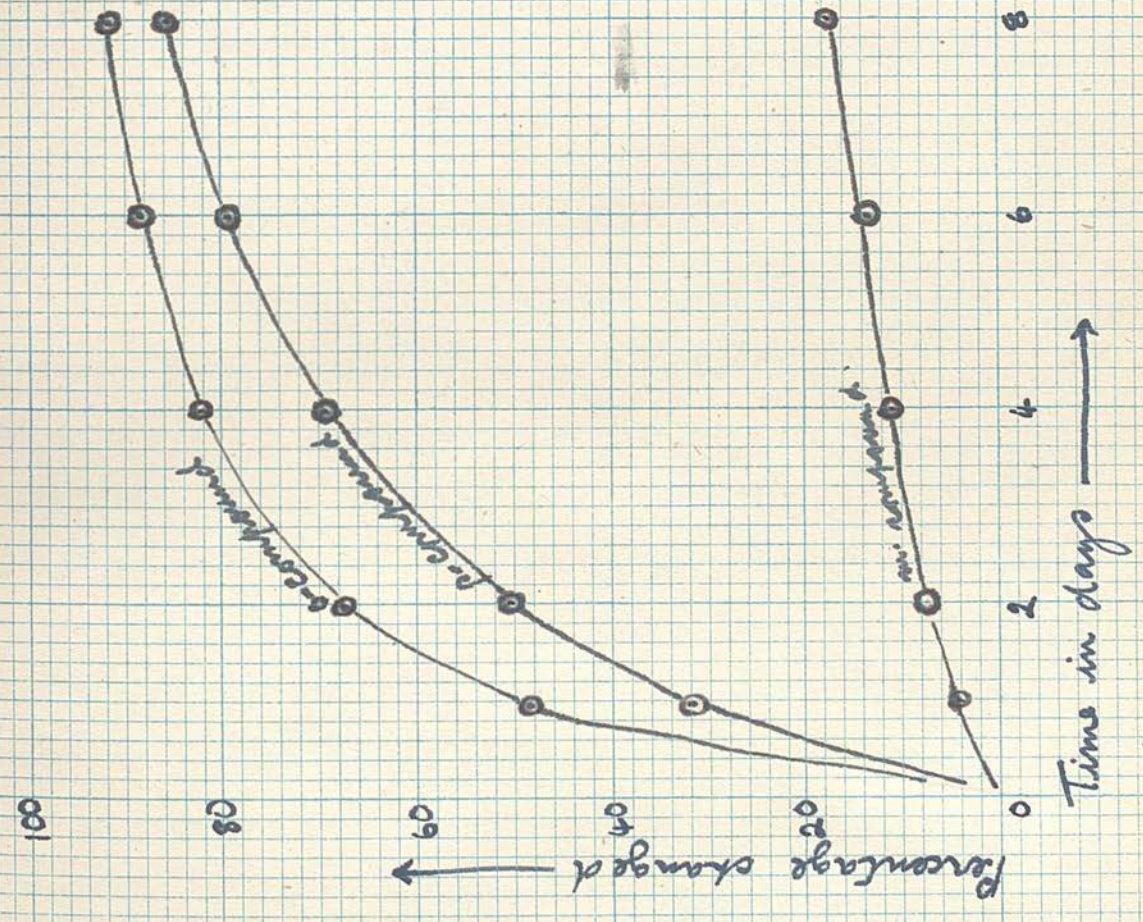
In the three isomeric iodotoluenes the iodine atoms which have acquired an induced positive polarity are those present in the o and p isomerides (cf. the iodophenols).



Hence/

FIGURE VII

Reduction of the isomeric iodotoluenes at 25°



Hence a comparison of the orders of the differences of the reactivity of the halogen atoms in the ω-bromoxylenes and iodotoluenes should lead to results analogous to those obtained in the comparison of the methoxybenzyl bromides and the iodophenols. This was found to be the case excepting that o-iodotoluene is more rapidly reduced to toluene than is p-iodotoluene, and in addition the meta isomeride is slowly but definitely reduced by hydrogen iodide at 25° (see figure VII). This latter observation shows that the reactivity of the iodine in m-iodotoluene approximates more nearly to that of the iodine in the other isomerides, than was found to be the case in the corresponding iodophenols.

The halogenated benzyl bromides.

The directive influence exerted by halogen atoms is apparent from the manner in which substituents enter into o and p positions in monohalogenated benzene derivatives, and also from the various additive reactions summarised in the Markownikoff rule. If therefore the principle of induced alternate polarities be applied in this case the o and p isomerides are seen to contain in the side chain a bromine atom which has acquired an induced negative polarity, and hence should be more readily removed by hydrolysing agents,/

FIGURE VIII

Hydrolysis of the isomeric chlorobenzyl bromides and isomeric bromobenzyl bromides at 76°.

——— represents hydrolysis of chloro compounds

———— " " " bromo "

------ " " " benzyl bromide

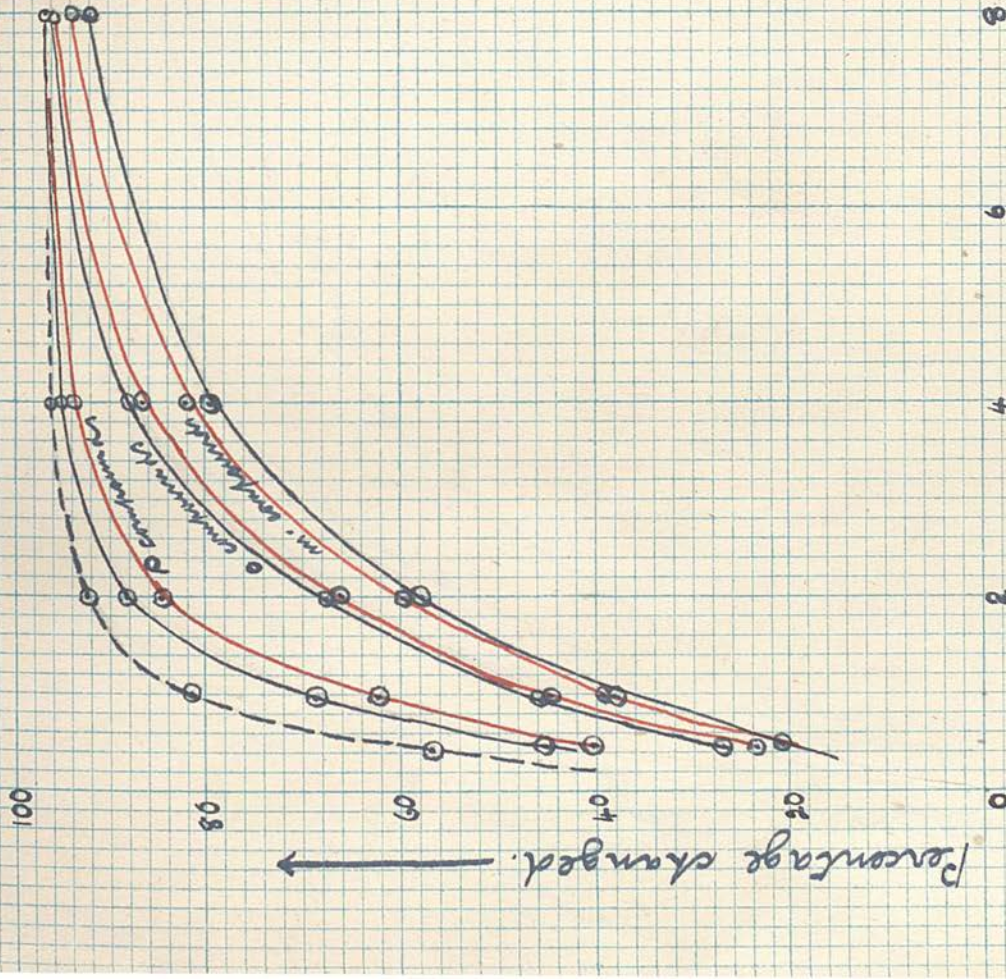
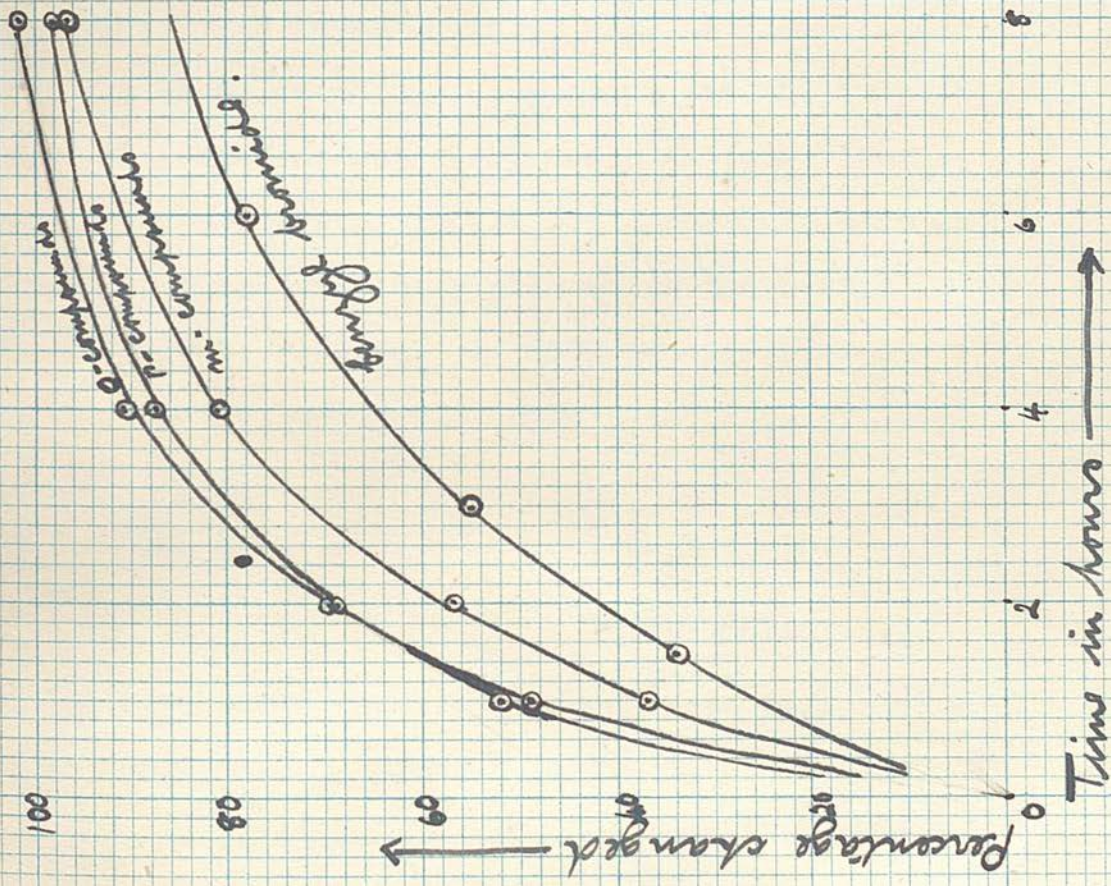
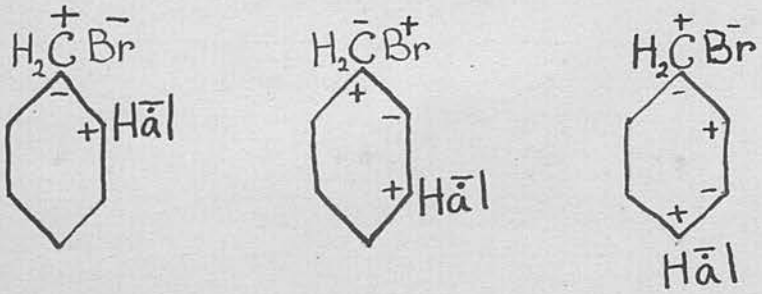


FIGURE IX

Reduction of the chloro and bromobenzyl bromides at 110°.



agents, but less readily removed by a reducing agent than that in the meta isomeride which has acquired an induced positive polarity.



The chlorobenzyl bromides and bromobenzyl bromides were first investigated, and whilst the order of ease of hydrolysis was found to be as expected (see figure VIII) the order of ease of reduction was the reverse of that anticipated, and was o and p > m (see figure IX). This surprising result could possibly have an explanation in the rapidity with which the benzyl iodides would be reduced. If the reduction was a reduction of the iodide and hence summarised by the reaction

(1) $R.CH_2Br + H\text{-}I \longrightarrow R.CH_2I + H\text{-}Br$

(2) $R.CH_2I + H\text{-}I \longrightarrow R.CH_3 + I_2$

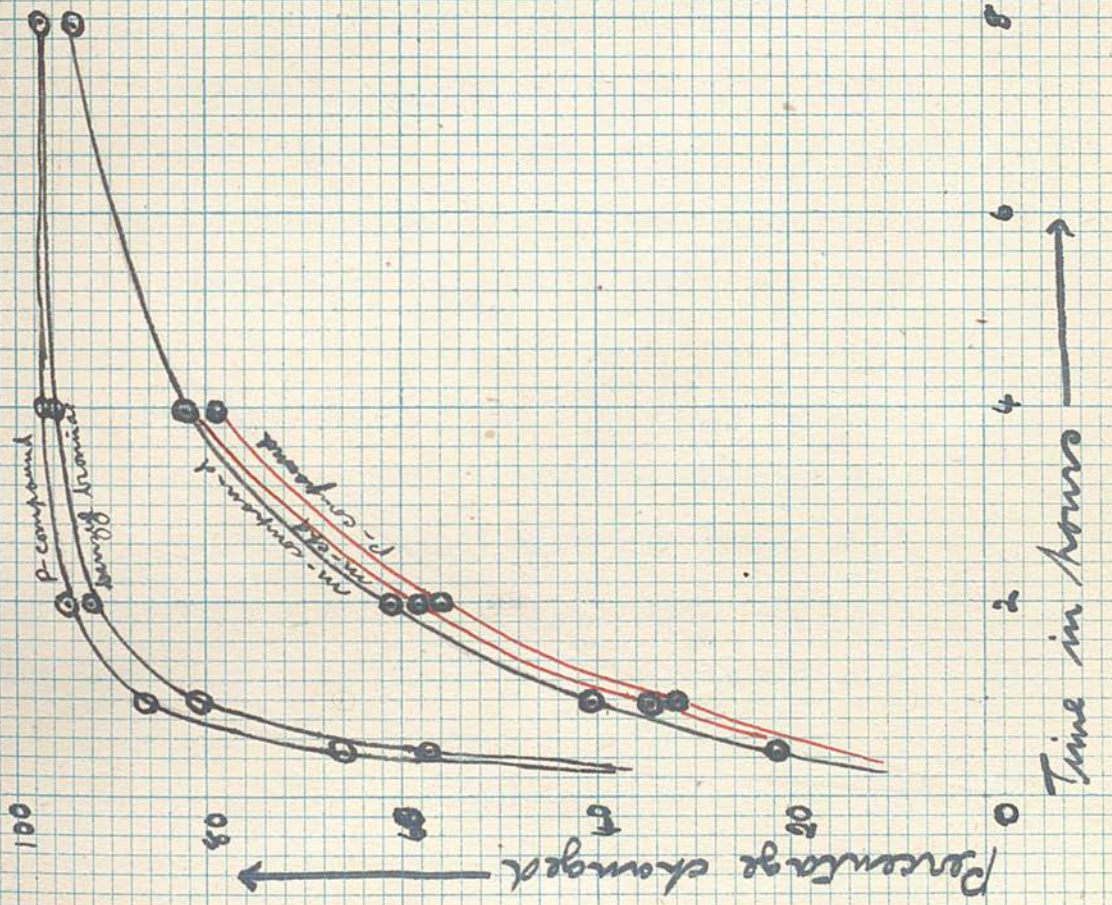
then the more rapid formation of the para halogenated benzyl iodides owing to the negative nature of the bromine atoms in these compounds would be responsible for this abnormality. In order to see whether this is the reason, the isomeric bromobenzyl iodides were prepared and their reduction proved to take place at/

FIGURE X

Hydrolysis and reduction of the isomeric fluorobenzyl bromides

——— represents hydrolysis at 76°

——— " reduction - 110°



at exactly the same rate as the corresponding bromides. Thus it appears as if the majority of the reduction curves at first considered to be those of substituted benzyl bromides are in reality those of substituted benzyl iodides, a fact which rather adds to than detracts from the remarkable nature of the previous observations. Reaction I is therefore rapid since it is a purely mass action effect whilst II depends on induced polarity effects.

The last series of substituted benzyl bromides to be examined were the fluorobenzyl bromides and in this case the order of ease of hydrolysis was found to be p>m and that of reduction m>p (see figure X). The difference in the ease of reduction was very slight but the order was quite definite. This observation, namely that fluorine is a more strongly directing atom than chlorine or bromine is important in that the suggestion put forward by Robinson and Kermack (J. 1922., 121, 428.) as to the cause of induced alternating polarity effects receives a certain amount of confirmation. This point is discussed in detail on pp. 108 et seq.

Since o and p iodotoluenes lose their nuclear iodine in presence of hydrogen iodide the isomeric iodobenzyl bromides were not investigated. It is perhaps noteworthy that a little of the nuclear halogen of the o and p chloro and bromobenzyl bromides/

bromides is removed by the prolonged action of hydrogen iodide but not in sufficient quantity to affect the order of ease of reduction.

All the chloro and bromobenzyl bromides were more difficult to hydrolyse than the unsubstituted benzyl bromide but were more readily reduced. The order of ease of hydrolysis of the fluoro compounds compared with the unsubstituted compound was p > unsubst. > m whilst the order of reduction was m > p and unsubst.

A complete summary of the results obtained in these investigations reads as follows, the fulfilment or nonfulfilment of the expectation refers only to the order of reactivity of the meta and para isomerides.

Methoxybenzyl bromides.

Hydrolysis p > o > unsubs > m (as expected)

Reduction m > o > unsubs > p (" ")

Halogenated phenols.

Reduction p-I > o-I > p-Br > o-Br > p-Cl > m isomerides (as expected). No hydrolysis detected.

ω-Bromotoluic acids.

Hydrolysis m > p > o < unsubs (as expected)

Reduction p > unsubs > m > o (" ")

Nitrobenzyl bromides.

Hydrolysis m>p and o<unsubs. (as expected)

ω-Bromoxylenes.

Hydrolysis p>o>m>unsubs (as expected).

Reduction m>o>p>unsubs.(" ").

Iodotoluenes.

Reduction o>p>m>unsubs. (as expected)

Fluorobenzyl bromides.

Hydrolysis p> unsubs>m (as expected)

Reduction m> p unsubs. " "

Chlorobenzyl bromides.

Hydrolysis p>o>m<unsubs. (as expected)

Reduction p and o> m >unsubs. (not expected).

Bromobenzyl bromides.

Hydrolysis p>o>m< unsubs. (as expected)

Reduction p and o>m>unsubs. (not expected).

Bromobenzyl iodides.

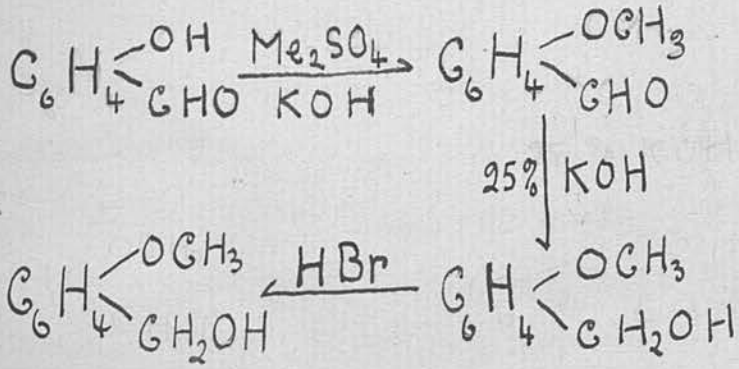
Reduction p>m>unsubs. (not expected).

EXPERIMENTAL.

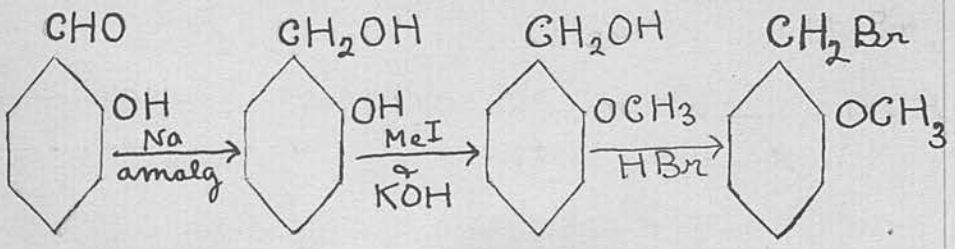
PREPARATIVE.

The Isomeric Methoxybenzyl Bromides.

The isomeric methoxybenzyl bromides were prepared by Späth (Monatsch., 1913, 34, 1995) through the series of reactions summarised by the following:-



Modifications in the preparation of the intermediate compounds in these reactions were introduced and details of these have been published (see publications I and II). In general it may be said that the above series of reactions was found to be the best possible for the preparation of the meta and para isomerides, whilst the ortho compound was obtained most conveniently by the series of reactions



General remarks on the improved methods.

o-Methoxybenzyl Bromide. o-Hydroxybenzyl alcohol (saligenin) was obtained by shaking redistilled salicylaldehyde in aqueous emulsion with sodium amalgam. Small quantities of sodium bicarbonate were added to the reduction mixture from time to time. When the reduction was finished the saligenin was extracted from the solution at once, and purified by means of animal charcoal. Before the introduction of this method many attempts to prepare saligenin were a complete failure owing to the tendency of saligenin to form saliretin resin in presence of even a trace of any acid used to neutralise the alkali before extraction with ether (cf. Publ. I. pp. 1396, Publ. II, pp. 2701.).

The methylation of this alcohol to o-methoxy benzyl alcohol must be carried out with methyl iodide (Pschorr, Wolfe and Buckow, Ber., 1900, 33, 165); methyl sulphate proved to be unsuitable for this purpose. Molecular quantities of methyl iodide and saligenin were dissolved in alcoholic potash (10%) and/

and left to stand for three days. The alcohol and unchanged methyl iodide were distilled away, the residue diluted with water, the product extracted away with ether, purified by washing with dilute alkali and distilled. It had b.p. 246°.

o-Methoxybenzyl bromide was then prepared by saturating a benzene solution of o-methoxybenzyl alcohol with hydrogen bromide. The bromide distilled at 118° at 18 mm. pressure and solifidied almost immediately at ordinary temperatures. It crystallised from light petroleum in colourless six-sided plates m.p. 46°.

m-Methoxybenzyl bromide. No essential modifications were introduced into this preparation except in the preparation of m-hydroxybenzaldehyde (which however can now be obtained in quantity from several well known firms) and also the preparation of m-methoxybenzaldehyde in which it was found that boiling the methylation mixture of m-hydroxybenzaldehyde, methyl sulphate and aqueous sodium hydroxide results in a better yield of the methylated aldehyde than that obtained when the reaction mixture is maintained at a lower temperature. After a long series of experiments, reduction of this aldehyde by means of 25 per cent alcoholic potassium hydroxide was found to be the best method for obtaining m-methoxybenzyl alcohol. m-Methoxybenzaldehyde has b.p. 231° and m-methoxy-benzyl/

m-methoxybenzyl alcohol has b.p. 250°. It is very essential to note that the ethereal extracts containing these compounds must be extracted several times with alkali before drying for the final distillation.

m-Methoxybenzyl bromide was prepared by saturating a benzene solution of m-methoxybenzyl alcohol with dry hydrogen bromide. The pure bromide has b.p. 127° at 16 mm.

p-Methoxybenzyl bromide. The preparation of this compound was troublesome since the tendency of the bromide to resinify is very marked unless the following conditions are observed. The reduction of anisaldehyde (prepared from anethole by the method given in detail in publication II, pp. 2702) to anisalcohol must be repeated twice. Contrary to the statement of Späth (loc. cit.) the presence of aldehyde increases the risk of tarring in the final distillation. The bromide must be dried very carefully and distilled below a pressure of 16 mm., that is, a temperature of 129°.

Anisalcohol was prepared from anisaldehyde by adding the aldehyde to three times its bulk of 25 per cent alcoholic potassium hydroxide and allowing the reaction mixture to stand for 24 hours. The alcohol was distilled away from this mixture in steam, the anisalcohol/

anisalcohol extracted from the residue with ether and then after this ethereal solution had in turn been extracted with alkali and dried, the alcohol distilled. It had b.p. 255-7° and was again subjected to the action of 25 per cent alcoholic potassium hydroxide and the whole process repeated. The anisalcohol had then b.p. 256-8° and solidified at ordinary temperatures.

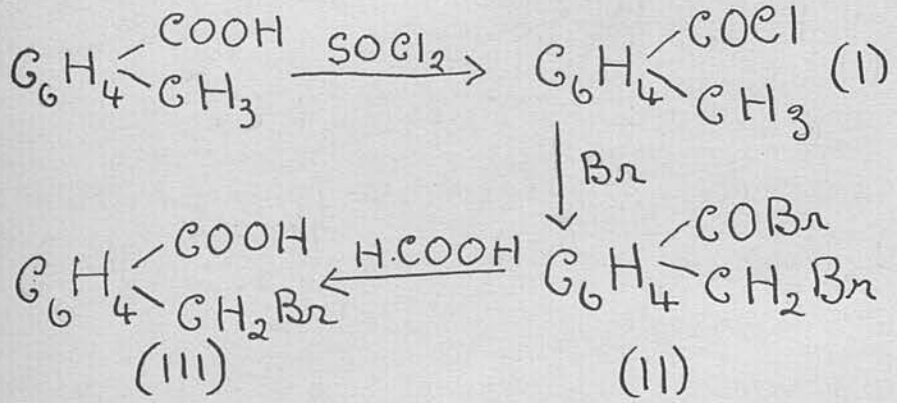
p-Methoxybenzyl Bromide was obtained from the alcohol in the usual manner and had b.p. 128-9° at 16 mm. Long fine white needles appeared in the liquid but when these came into contact with the moist air they at once melted probably owing to the slight hydrolysis which took place.

The Isomeric ω-Bromotoluic Acids.

The isomeric ω-bromotoluic acids have been prepared by Salkind (J. Russ., Phys., Chem., Soc., 1914, 46, 508) and Salkind and Ssemenow (ibid 512). In order to obtain the meta and para isomerides these investigators brominated the corresponding toluic acids in bromoform solution. The ortho compound they obtained from phthalide which was heated in a sealed tube with hydrobromic acid at 100°. For the purposes of the experiments recorded here they were all prepared by the general method adopted by Perkin and

Davies/

Davies (T., 1922, 121, 2202) to prepare ω-bromo-o-and-m-toluic ethyl esters. The reactions are summarised as follows:-



General method of preparation of the isomeric ω-bromo-toluic acids.

ω-Bromotoluoyl bromides (II).

25 grams (1 mol) of the toluoyl chloride was maintained at a temperature of 185°-195° during the gradual addition of 25 grams (2 mols) of bromine. The crude ω-bromotoluoyl bromides obtained in this way were purified by distillation under reduced pressure.

ω-Bromo-o-toluoyl bromide boils at 158-161° under a pressure of 13 mm. and has m.p. 33° (cf. Davies and Perkin loc. cit.)

ω-Bromo-m-toluoyl bromide has b.p. 160-165° / 14 mm. and m.p. 23-25°.

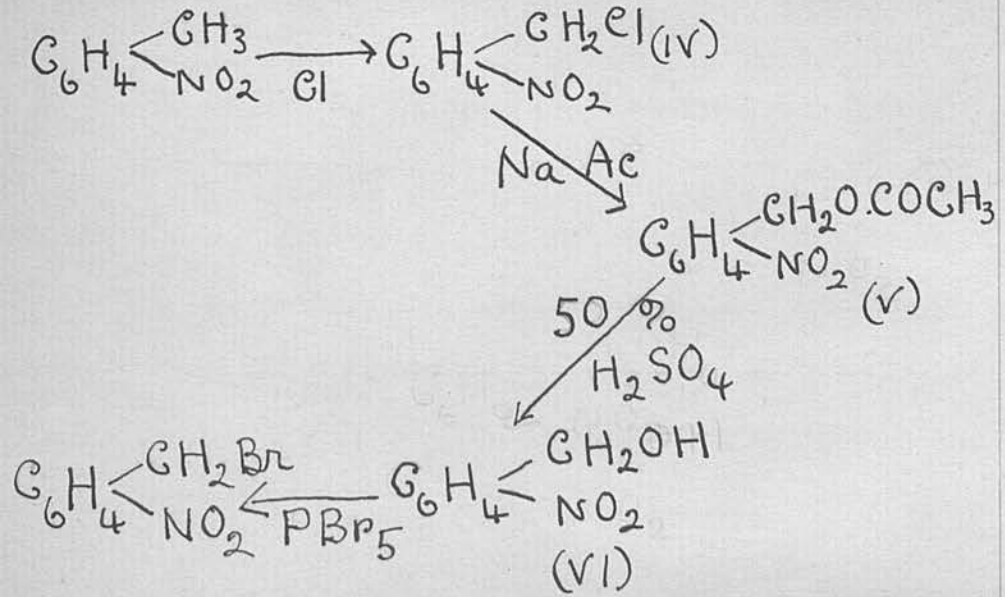
ω-Bromo-p-toluoyl bromide has b.p. 165-170°/ 12 mm. and m.p. 39-40° (Br found = 54.5 per cent; $C_8H_6Br_2$ requires Br = 57.5 per cent, the low analysis figure is due to hydrolysis by atmospheric moisture).

ω-Bromotoluic acids (III).

25 grams of the ω-bromotoluoyl bromide and 300 grams of 80 per cent formic acid were maintained at a temperature of 30-35° for one hour. The hydrolysis mixture was then poured into a large excess of water and the precipitated acid filtered off and dried. Each of them was purified by crystallisation from benzene. The m.p. of the ortho compounds was 146°, of the meta 150° and of the para 223°. Salkind and Ssemenow give 147°, 151-2° and 223° respectively for these constants. An estimation of the bromine hydrolysed by alcoholic potash showed that the compounds were quite pure.

The Isomeric Nitrobenzyl Bromides.

o-Nitrobenzyl bromide. The scheme adopted for the preparation of this compound is summarised by the following:-



o-Nitrobenzyl chloride (IV), prepared by direct chlorination of o-nitrotoluene in presence of sulphur at 120-130° as recommended by Haeusermann and Beck (Ber., 1892, 25, 2445.), was boiled with sodium acetate in concentrated aqueous solution. The o-nitrobenzyl acetate (V) so obtained was then converted into o-nitrobenzyl alcohol (VI) by boiling 50 per cent sulphuric acid. This alcohol was crystallised from hot water and readily gave o-nitrobenzyl bromide when mixed with the calculated quantity of phosphorus pentabromide. The new bromide crystallised from light petroleum in light yellow plates, m.p. 45.5°. (Found Br = 36.8. $C_7H_6O_2N$ Br requires Br = 37.0 per cent).

m-Nitrobenzyl bromide m-Nitrobenzaldehyde was prepared by the nitration of benzaldehyde by means of potassium nitrate and concentrated sulphuric acid (Friedländer and Henriques Ber., 1881, 14, 2802; Tiemann and Ludwig, ibid, 1882, 15, 2045) and then reduced to m-nitrobenzyl alcohol by aqueous potassium hydroxide (Becher, Ber., 1882, 15, 2090).
The crude alcohol was then dissolved in twice its own volume of dry benzene and the solution saturated with dry hydrogen bromide. Two layers were formed during this operation and continued agitation was necessary to ensure complete conversion to bromide. Crystals separated from the lower layer on standing.

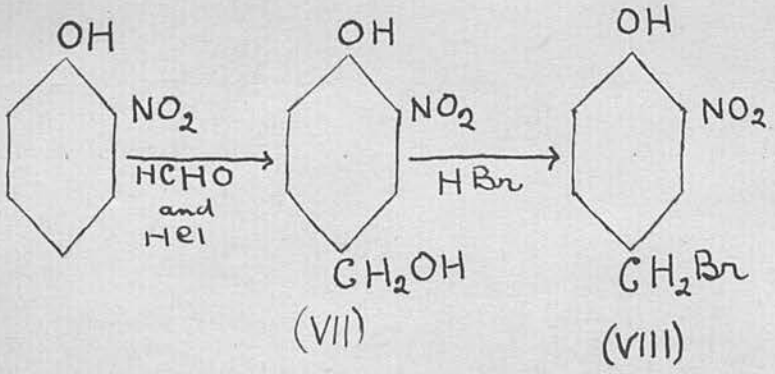
A/

A further quantity of these were obtained after the benzene had been evaporated away from the upper layer. The crude bromide was recrystallised from light petroleum when it melted at 57° and was found to be quite pure.

p-Nitrobenzyl bromide. This was prepared by direct bromination of p-nitrotoluene in a sealed tube for 2 hours at 120° as recommended by Lyons and Reid (J. Amer. Chem. Soc., 1917, 39, 1729). The crude bromide so obtained had to be recrystallised several times from light petroleum before the estimation of the hydrolysable bromine showed that the compound was quite free from benzal bromide. It then melted at 98.5°.

3 - Nitro -4- hydroxybenzyl bromide.

This compound was prepared by the following series of reactions



o-Nitrophenol (2 parts), concentrated hydrochloric acid (10 parts) and concentrated aqueous formaldehyde/

formaldehyde solution (5 parts) were boiled together under a reflux condenser for 6 hours. The formaldehyde solution was as concentrated as could be obtained without the separation of polymer. The supply of formaldehyde was renewed after three hours. At the end of six hours the solution was cooled when a heavy brown oil was deposited. This was separated from the aqueous layer and unchanged o-nitrophenol distilled away in steam from the oil. The non-volatile 3-nitro-4-hydroxybenzyl alcohol (VII) separated from the cold solution as a crystalline mass and was purified by crystallisation from hot water. It crystallised as bright yellow needles, m.p. 97° (cf. Stoermer and Behn, Ber., 1901, 34, 2459). These were dissolved in the minimum quantity of dry benzene and the solution was then saturated with dry hydrogen bromide from which the new 3-nitro-4-hydroxybenzyl bromide (VIII) was obtained after the benzene had been evaporated away. It crystallised from light petroleum in yellow prismatic needles of m.p. 82°. (Found Br = 34.46; $C_7H_6O_3$ N Br requires Br = 34.44 per cent.)

3-Nitro-4-methoxybenzyl bromide.

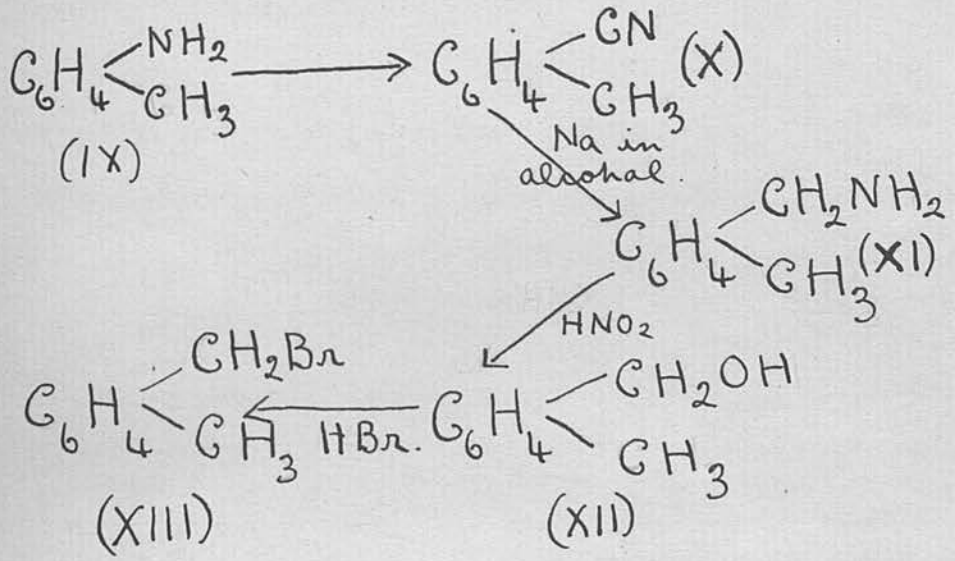
3-Nitro-4-methoxybenzyl alcohol was prepared by methylating 3-nitro-4-hydroxybenzyl alcohol by methyl iodide and potassium hydroxide in methyl alcoholic solution in the usual manner. It was recrystallised from/

from hot water when it melted at 69° and was then converted into the corresponding bromide in benzene solution by means of dry hydrogen bromide as before.

3-Nitro-4-methoxybenzyl bromide crystallised from light petroleum in pale yellow needles of m.p. 108° (Found Br = 32.84; $C_8H_8O_3$ N Br requires Br = 32.49 per cent.).

The ω-Bromoxylenes.

These were all obtained by a general method summarised in the scheme



The electrolytic reduction of the toluic acids was attempted but found to be very unsatisfactory. Hence the toluidines (IX) were converted into the corresponding nitriles (X) in the usual manner by means of the action of potassium cuprocyanide on the diazonium salt.

The/

The nitriles were then purified by distillation in steam. They had b.p.s. o- 202-4°; m- 210-12° and p- 215-17° respectively.

The nitriles were reduced to the tolylmethylamines (XI) by means of sodium and alcohol. (cf. Kröber Ber., 1890, 23, 1026 and Sommer. ibid., 1900, 33, 1073.) Thirty grams of the nitrile were dissolved in one litre of perfectly dry alcohol. Sodium (100 grams) was added to the boiling solution through an upright condenser. When all the sodium had dissolved the reduction mixture was diluted with water, acidified with hydrochloric acid and the alcohol distilled away in a current of steam. The residual acid solution was made alkaline with sodium hydroxide and the liberated tolylmethylamine distilled over in steam. It was extracted from the distillate with ether, dried over sodium sulphate and purified by distillation.

The yields of the o-, m-, and p- tolylmethylamines obtained by this general method were, o- fifty per cent, m- thirty per cent and p- sixty per cent of the expected quantity. They distilled at 200-202°, 198-200° and 194-6° respectively.

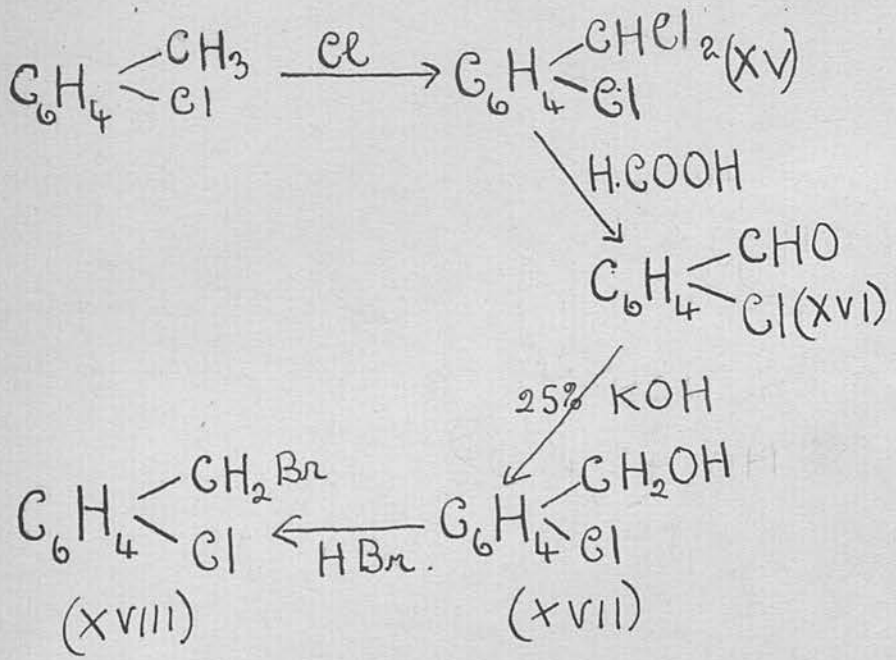
The corresponding tolylcarbinols (XII) were obtained from the amines by the addition of twice the necessary quantity of sodium nitrite to a solution of the base in an excess of dilute hydrochloric acid. Nitrogen was evolved at once. The mixture was allowed to/

to stand overnight and the reaction then carried to completion on the water bath. The carbinol was extracted from the reaction mixture with ether and after the ether had been evaporated away the residue purified by distillation in steam. From the ethereal extract of the distillate the carbinol was obtained pure. The yields of the respective isomerides were o- fifty per cent, m- seventy per cent and p- forty per cent of the expected. o-Tolylcarbinol melted at 33° and distilled at 112-114° at 9 mm., m-tolylcarbinol distilled at 108-111° at 10 mm., and p-tolylcarbinol melted at 60°. The poor yields of the ortho and para isomerides are due to the fact that appreciable resinification took place during steam distillation of the tolylcarbinols.

The isomeric ω -bromoxylenes (XIII) were obtained from the corresponding tolylcarbinols by the usual method of saturating the dry benzene solution of the latter with dry hydrogen bromide. The ortho isomeride distilled at 102° at 11 mm., and melted at 20°; the meta isomeride distilled at 97-99° at 8 mm., and the para isomeride at 100° at 9 mm., and melted at 35.5°.

Preparation of the Halogenated Benzyl Bromides.

The isomeric ortho and para chlorobenzyl bromides were prepared by the method summarised in the following scheme.



Ortho and para chlorotoluene were prepared from the corresponding toluidines in the usual manner. These compounds were then maintained at a temperature of 160° and chlorine passed into them until an increase of weight corresponding to the formation of p-chlorobenzal chloride (XV) had taken place (PCl_5 was added to the chlorotoluene before chlorination, 5 per cent of the weight of the original oil being used.) The chlorobenzaldehydes were then prepared in the following manner.

The chlorinated oil (50 grms) was boiled with

100/

100 cc. of 98 per cent formic acid (Sp. gr. 1.20) for half an hour. At the end of this time the evolution of HCl had ceased and the whole was therefore poured into an excess of cold water. The cooled solution was neutralised with concentrated sodium hydroxide solution and the neutralised solution then extracted with ether. The ether was evaporated away from the ethereal extract and the residue thoroughly agitated with freshly prepared sodium bisulphite solution. The solid sodium bisulphite compound which was formed in this way was filtered off, thoroughly washed with alcohol and ether, dried and decomposed in aqueous solution by concentrated aqueous sodium carbonate. The liberated aldehyde (XVI) was extracted with ether and after the ether had been distilled away the aldehyde remained behind. The ortho compound had b.p. 210° and the para compound had m.p. 48°. The yield was approximately 50 per cent of that expected in each case.

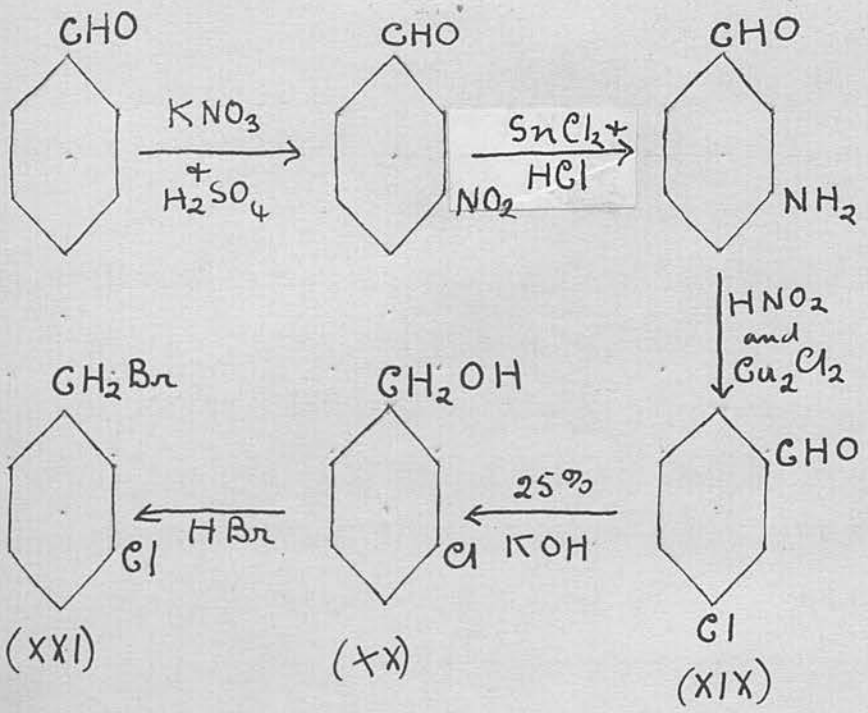
o-Chlorobenzyl alcohol was prepared from o-chlorobenzaldehyde by the usual Cannizzaro method, i.e., 15 grams of the aldehyde were poured into 45 cc. of 25 per cent alcoholic caustic potash and the reaction completed by allowing the mixture to stand at ordinary temperatures for 48 hours. The ethyl alcohol was then distilled away from the reaction mixture in steam and the residue extracted with ether. From this extract/

extract o-chlorobenzyl alcohol was obtained as a white solid of m.p. 70°. It was purified by crystallisation from light petroleum.

o-Chlorobenzyl bromide was obtained from the white needle-shaped crystals of o-chlorobenzyl alcohol which were dissolved in dry benzene. Dry hydrogen bromide was passed into this solution until it was saturated. The aqueous layer was separated from the upper benzene layer which was dried over $CaCl_2$. The benzene was evaporated from this under reduced pressure and o-chlorobenzyl bromide obtained as a colourless liquid of b.p. 101-2°/ 9 mm. (Found Br = 39.05; C_7H_6 Cl Br requires Br = 38.9 per cent.)

p-Chlorobenzyl bromide was prepared from p-chlorobenzaldehyde in the same way. The aldehyde 15 grams was dissolved in about 10 cc. of hot absolute alcohol and added to a mixture of 12 grams KOH, 8 cc. of water and 20 cc. of absolute alcohol. The reaction mixture was thoroughly agitated for about a quarter of an hour in order to ensure complete mixing. After this the mode of procedure was exactly as described in the case of the ortho isomeride. p-Chlorobenzyl bromide thus obtained is a solid m.p. 51°. (Found Br = 38.7; C_7H_6Cl. Br requires Br = 38.9 per cent.).

m-Chlorobenzyl bromide was obtained by the following series of reactions



m-Nitrobenzaldehyde prepared by nitration of benzaldehyde with potassium nitrate and concentrated sulphuric acid was carefully recrystallised from light petroleum. It then melted at 59-60°. This was undertaken in order to ensure freedom from o-isomeride. It was then converted to m-chlorobenzaldehyde by the method of Ardmann and Schwechten (Annalen, 1890, 260, 59.)

m-Nitrobenzaldehyde (100 grams) was slowly added to a mixture of 450 grams stannous chloride and 600 cc. of concentrated HCl. External cooling was necessary during this operation. When the mixture was quite cold and reduction complete the flask was immersed in a freezing mixture. The amino aldehyde was then at once diazotised by a solution of 50 grams of sodium nitrite in 180 cc. of water. The diazotised base was then added to a solution of cuprous chloride prepared by/

by boiling together 30 grams of cupric chloride, 15 grams of copper wire, 130 cc. of concentrated hydrochloric acid and 30 cc. of water. The whole was then carefully heated on the water bath and the m-chlorobenzaldehyde distilled over in a current of steam. The aldehyde was extracted from the distillate with ether and the ethereal extract in turn extracted four times with small quantities of 10 per cent aqueous sodium hydroxide. The aldehyde was obtained from the dried ethereal extract by distillation. It had b.p. 213-4° and weighed 42 gms.

m-Chlorobenzyl alcohol was then prepared from the aldehyde in the usual manner and had b.p. 242-3° and not 234° as given by Mettler (Ber., 1905, 38, 1749.)

m-Chlorobenzyl bromide was prepared by saturating a dry benzene solution of the alcohol in the usual way. It had b.p. 109-10° at 10 mm. (Found Br = 38.64; C_7H_6 Cl. Br requires Br = 38.9 per cent.).

The Preparation of the Isomeric Bromobenzyl Bromides.

The bromobenzyl bromides cannot be obtained by a series of reactions corresponding with those already seen to be successful in the previous cases. Chlorination of the bromotoluenes led to the production of very impure products and it was discovered that/

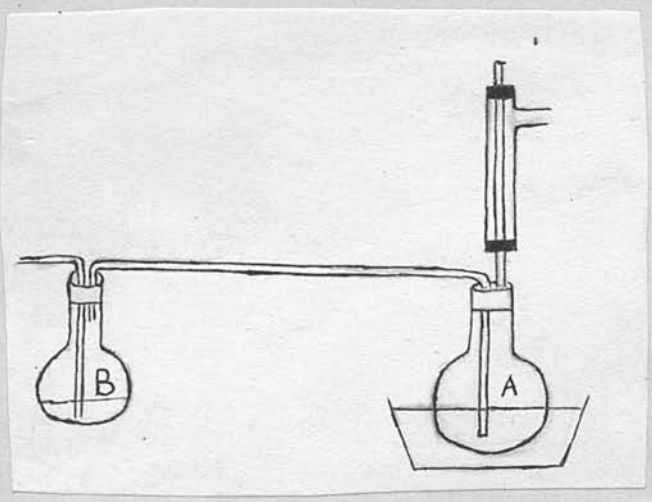
that chlorine displaces bromine from the nucleus to an extend representing at least 50 per cent of that which is possible. The isomeric bromobenzyl bromides however are all solids and can be obtained in a state of great purity by recrystallising the crude bromination products of the bromotoluenes.

Preparation of the bromotoluenes. (Acrée Ber., 1904, 37, 994.).

The toluidine (50 grams) was dissolved in 250 grams of hydrobromic acid (sp. gr. 1.375). The toluidine hydrobromide was diazotised at -10° and then added to a hot solution of cuprous bromide which was prepared by boiling together 80 grams copper sulphate, 60 grams of sulphuric acid and 320 cc. of water. The bromotoluenes were obtained by steam distillation of the reaction mixture in the usual way. The yield in each case was about 32 grams. The above procedure is quite satisfactory for the preparation of the ortho and meta isomerides but p-toluidine is not completely soluble in the quantity of hydrobromic acid stated, and 50 cc. of water must therefore be added in order to complete the solution.

The isomeric bromobenzyl bromides were obtained by direct bromination of the bromotoluenes in the following way. A weighed quantity (1 mol) of the bromotoluene/

bromotoluene was placed in flask A and a quantity of bromine corresponding to one and a half molecules placed in B. A current of dry air was passed into the bromine and this in turn directed into the bromotoluene which was placed in an oil bath maintained at a temperature of 180-200°.



When all the bromine had been passed into the bromotoluene the brominated oil was distilled under reduced pressure and in all cases the portion distilling at 120-140° at 17 mm. was collected and cooled to -15° and the crystals at once spread on a porous tile. These were twice recrystallised from a small quantity of alcohol when they were found to be excellent samples of the bromobenzyl bromides. The ortho compound had m.p. 31-2° and contained bromine hydrolysed by alcoholic potassium hydroxide = 32.1%; m- compound had/

had m.p. 39-40° found hydrolysable Br = 31.8% and p-compound had m.p. 62-3° found hydrolysable Br = 31.8%. $C_7H_6Br_2$ should contain hydrolysable Br = 32.0%. (cf. Jackson, Ber. 1876, 9, 932.)

The isomeric bromobenzyl iodides were all prepared from the corresponding benzyl bromides by the following general method. A solution of 10 grams of potassium iodide in 7 cc. of water and 30 cc. of acetone was added to a solution of 5 grams of the bromide in 20 cc. of acetone. The whole was then boiled for one hour and then poured into water. The solid which separated out after this treatment was collected, pressed on a porous tile and recrystallised from light petroleum.

o-Bromobenzyl iodide crystallises in shining white needles of m.p. 47°. Found I = 42.75; $C_7 H_6 Br I$ requires I = 42.7 per cent.

m-Bromobenzyl iodide crystallises in white six sided prisms of m.p. 42°. Found I = 42.8 per cent.

p-Bromobenzyl iodide crystallises in shining white needles of m.p. 73°. Found I = 43.0 per cent.

m- and p- Fluorotoluenes.

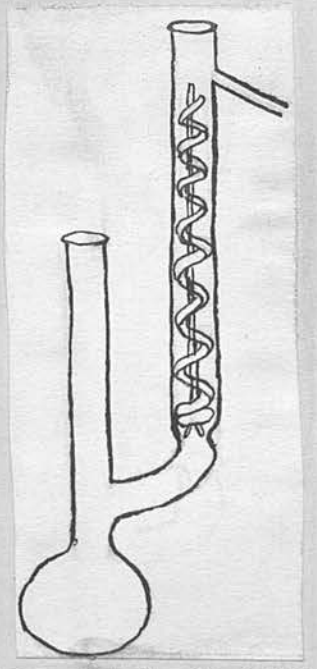
The toluidine (25 gms.) was brought into solution in a mixture of 30 cc. of concentrated sulphuric acid and 80 cc. of water. The solution was cooled to -5° and/

and the toluidine diazotised by the gradual addition of a solution of 20 gms. of sodium nitrite in 50 cc. of water. The temperature of the solution during diazotisation was not allowed to rise above 5°. The diazotised base was then added to about 400 cc. of commercial hydrofluoric acid (50-60%) contained in a 1,500 cc. copper flask. Considerable evolution of heat took place but the reaction was efficiently controlled by keeping the copper flask surrounded by ice. The flask was then fitted with a copper reflux condenser and carefully and slowly warmed on a water bath for one hour. The m-fluorotoluene was then distilled from this copper flask directly into 200 cc. of 30% caustic soda contained in a copper beaker which was surrounded by a good freezing mixture. The distillation was continued until a distinct rise in temperature was noted in the caustic soda solution and then stopped. The liquid in the beaker which was still markedly alkaline was extracted thrice with ether, the combined ethereal extracts rendered free from emulsion by means of a saturated solution of ammonium sulphate and then dried over anhydrous sodium sulphate. The fluorotoluene was obtained from this in the usual manner and had b.p. 116-7°. (The fraction 110-120° was collected; yield about 15 gms.)

m-/

m- and p-Fluorobenzyl bromides.

The fluorotoluene (100 grams) was brominated in the apparatus described on pp. 43, one molecule of bromine (total weight 150 grams) being used. In order to avoid nuclear substitution of the halogen the brominations were carried out with small quantities (20 grams) of the fluorotoluene. The brominated oil was then hydrolysed with approximately twice its volume of boiling formic acid (98% Sp. Gr. 1.20) for two hours. The solution was diluted with water neutralised with aqueous potassium hydroxide, and the mixture of aldehyde, bromide, alcohol and unchanged m-fluorotoluene extracted away with ether. The aldehyde was precipitated from the ethereal solution as the sodium bisulphite compound. This was then filtered off and thoroughly washed with ether. The combined ethereal extract and washings were dried over sodium sulphate, the ether then evaporated away, the residual oil dissolved in benzene, and the benzene solution saturated with dry hydrogen bromide. This solution was allowed to stand over calcium chloride for some time and then fractionated under diminished pressure by means of the apparatus shown, which it was later discovered had already been described by Widmer(Helv., chim. acta. 1924, VII, 59.)



The fraction which distilled between 72-80° at 12 mm. was refractionated at 8 mm. and the sample then discovered to be impure was extracted again with sodium bisulphite solution and the residual oil saturated in benzene solution with dry hydrogen bromide as before. The bromide was obtained pure from this solution by distillation.

m-Fluorobenzyl bromide had a b.p. 76-8°/15 mm. and p-fluorobenzyl bromide had b.p. 82-3°/12 mm. Found Br = 42.0 (for meta isomeride), 42.0 (for para isomeride). C_7H_6FBr requires Br = 42.3 per cent.

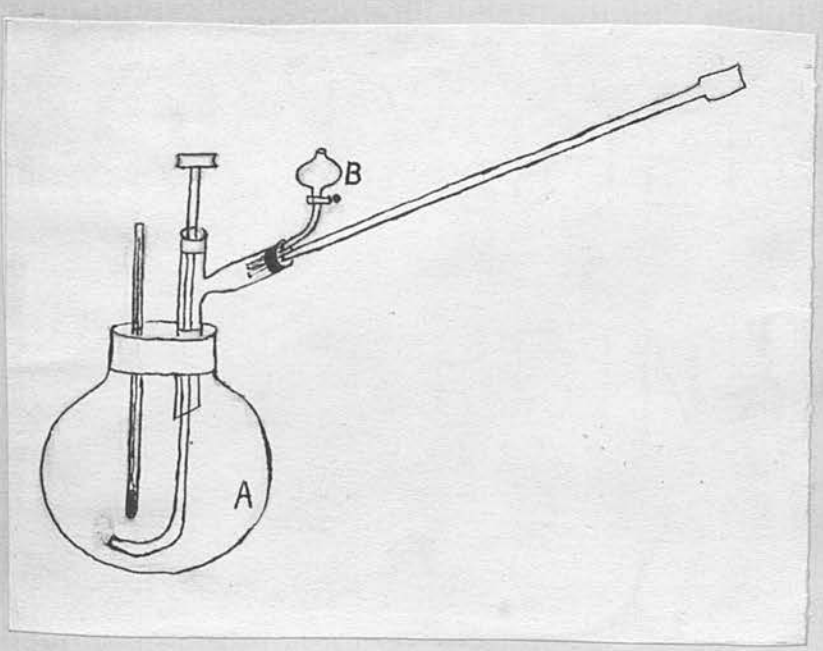
The preparation of the meta isomeride was a very difficult problem on account of (a) the lachrimatory nature of the compound, (b) the formation of a constant boiling point mixture of m-fluorobenzyl bromide, m-fluorobenzyl alcohol and m-fluorobenzaldehyde and (c) the difficulty encountered in freeing the bromide from the last traces of impurity.

Preparation/

Preparation of the halogenated phenols.

The ortho and para halogenated phenols were prepared from the corresponding amino phenols by the usual methods.

m-Chlorophenol was most conveniently obtained from m-nitraniline which was first converted into m-chloronitrobenzene and then reduced to m-chloroaniline by means of iron filings and hydrochloric acid (cf. Morgan, J., 1900, 77, 1204.) in the apparatus shown here:-



m-Chloronitrobenzene (100 grams), at a temperature of 50° was allowed to flow drop by drop from the funnel B into a mechanically stirred mixture 200 grams iron filings, 400 cc. of water and 15 cc. of conc. hydrochloric acid in the flask A. After a slight preliminary warming the heat of the reduction was sufficient to maintain the temperature of the reaction/

reaction at 95°. When all the chloronitrobenzene had been added, an hour's heating at 90° completed the reduction. The reaction mixture was then cooled and neutralised by the addition of 30 grams of sodium bicarbonate and the chloroaniline distilled over in steam. The distillate was extracted with ether and the ethereal solution dried over sodium sulphate. The yield of chloroaniline was 50 per cent of the expected.

m-Chloroaniline was then diazotised as described by Varnhold (J. pr. Chem. 1887, 36, 27.) and the solution of the diazotised base heated on the water bath until evolution of nitrogen had ceased. It was then filtered and the chlorophenol extracted from the solution with ether and purified by distillation.

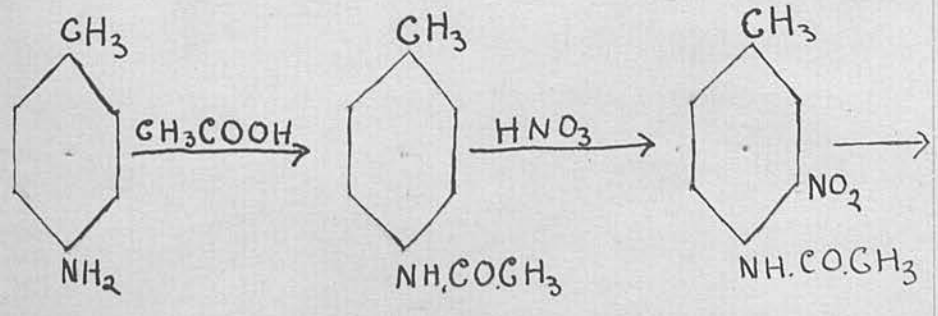
m-Bromophenol was prepared in a similar manner. It was found however that bromination of nitrobenzene (Wheeler and McFarland: Amer. Chem. J., 1897, 19, 366) is much more satisfactory than chlorination. m-Bromonitrobenzene was then reduced by iron and hydrochloric acid and the m-bromoaniline diazotised and converted to m-bromophenol (Diels and Bunzl Ber., 1905, 38, 1495.) The phenol distilled under 12 mm. pressure at 125-7° and not at 135-40° as stated by Diels and Bunzl.

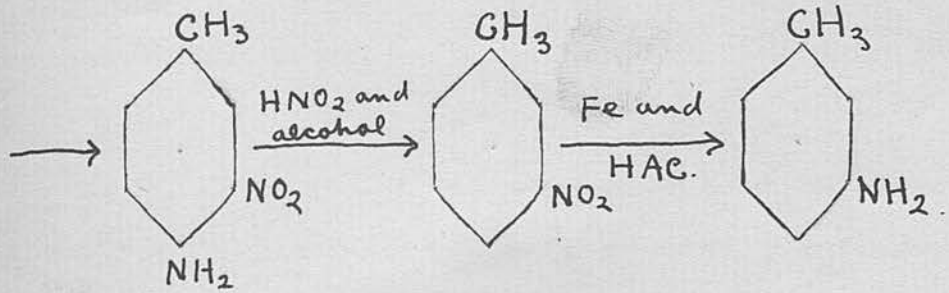
m-Iodophenol was obtained from m-nitraniline according/

according to the methods of Nölting and Stricker (Ber. 1887, 20, 3020.) The intermediate m-iodonitrobenzene was reduced by means of iron and hydrochloric acid.

4-Iodoresorcinol. The method used was that described by Stenhouse (Annalen, 1874, 171, 311.) In order to iodinate 20 grams of resorcinol it is necessary to use 220 grams of litharge. This obviously prevents the reduction of the iodoresorcinol by the hydriodic acid produced in the reaction.

The isomeric iodotoluenes were all prepared from the corresponding toluidines by Sandmeyer's reaction. The ortho and para isomerides were obtained pure and had b.ps. 205° and 211° respectively. The meta isomeride had b.p. 213° [Beilstein and Kuhlberg give 204° (Annalen, 1871, 158, 349)] and in view of the fact that this compound lost some of its iodine when subjected to the action of hydrogen iodide in glacial acetic acid a sample was prepared from an authentic specimen of m-toluidine specially obtained pure by the following series of reactions.



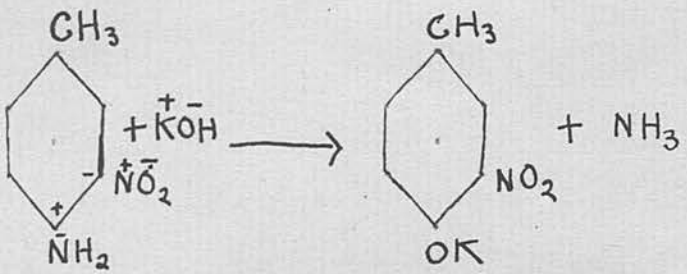


p-Toluidine (200 grams) was acetylated by boiling with 300 grams of acetic acid and 15 grams of anhydrous zinc chloride for 2 hours. At the end of this period the whole was poured into water and the solid acet-p-toluidide filtered off, thoroughly washed with water and carefully dried.

Acet-p-toluidide (100 grams) was then added to a mixture of 200 grams of concentrated H_2SO_4 and 200 grams of concentrated nitric acid. The temperature of the mixture rose to 35° and the toluidide was added in quantities necessary to maintain the temperature at 35-40° (About 20 mins. only was necessary for this. If the reaction is allowed to go more slowly hydrolysis of the toluidide takes place and the resulting product is very tarry.) The mixture was then almost immediately poured into a large excess of water and the solid which separated filtered off, pressed on a porous tile and then dried in a dessicator. The solid was then placed in a flask and melted on the water bath. The water which separated was poured away/

away and thus m-nitro-aceto-p-toluidide was obtained dry.

The nitro compound was then dissolved in about twice its own volume of alcohol, and the quantity of potassium hydroxide necessary to hydrolyse this to m-nitro-p-toluidine was added in solution in its own weight of water. When the odour of ammonia from this mixture was marked, hydrolysis was complete and the whole was cooled.



The solid which separated out at ordinary temperatures was filtered off and dissolved in three parts by weight of alcohol and the amino group replaced by hydrogen by diazotising the amine in presence of 3 parts of concentrated sulphuric acid, and then heating the reaction mixture on the water bath.

The crude m-nitrotoluene was distilled over in steam and separated in the usual manner. It was purified in the following way. (Reissert, Ber., 1897, 30, 1047).

Sodium (12.5 grms.) was dissolved in 310 cc. of absolute/

absolute alcohol and to the cold solution of sodium ethoxide so obtained, 40 gms. of diethyl oxalate (prepared by the method recommended by Clarke and Davis in Organic Syntheses Pt. II, pp. 23) and 45 gms. of the crude m-nitrotoluene were added. The reaction mixture assumed a deep red colour and was maintained at a temperature of 37° for 3 days. The alcohol was then distilled off and the residue extracted with ether. The ethereal solution was in turn extracted with 10 per cent aqueous sodium hydroxide, dried over $CaCl_2$ and the m-nitrotoluene then purified by distillation. It had m.p. 16° and b.p. 231° at 76° mm.

m-Nitrotoluene (40 gms.) was reduced to m-toluidine by means of 50 gms. of iron filings, 60 cc. of water and 4 cc. of glacial acetic acid in the apparatus already described. The m-toluidine so obtained had b.p. 202.5-3° and was colourless. The m-iodotoluene prepared from this in the usual manner had b.p. 213°. This proved the reliability of the m-toluidine used in the experiments, since all the m-iodotoluene prepared had b.p. 213°.

EXPERIMENTAL. QUANTITATIVE.

Hydrolysis of the isomeric methoxybenzyl bromides.

(a) Hydrolysis when emulsified with $\frac{N}{40}$ NaOH at 55°C.

This series of experiments is not strictly comparable with other series but is quoted because it shows quite clearly the similarity of the ortho to the para isomeride and also the sharp line of demarcation between the para and meta isomerides.

Method. Approximately 1 gram of the bromide was weighed by difference into 250 cc. of $\frac{N}{40}$ NaOH which was vigorously stirred with a Witt stirrer and maintained at a temperature of 55°. At regular intervals 25 cc. of this mixture were withdrawn (the stirring was not stopped during this operation) and run into 25 cc. of standard H_2SO_4. By this means hydrolysis was at once stopped and the excess of H_2SO_4 was then titrated rapidly. In this way an approximate measure of the rate of hydrolysis of the bromides was obtained. The results are summarised in Table I (see also table I.(i) publication I. pp.1398).

Table I

In which

t represents time in minutes from commencement of experiment, w the weight of bromide used and x the percentage of the bromide changed.

ortho compound		meta compound	para compound
w =	0.8824	0.831	0.934
t	x	x	x
2.5	34.0	-	45.4
4.5	62.0	1.6	90.8
14.5	90.0	13.3	94.8
34.5	98.4	24.0	94.9
44.5	90.0	43.0	99.4
154.5	99.0	66.4	-
234.5	99.0	-	

(b) Hydrolysis in solution.

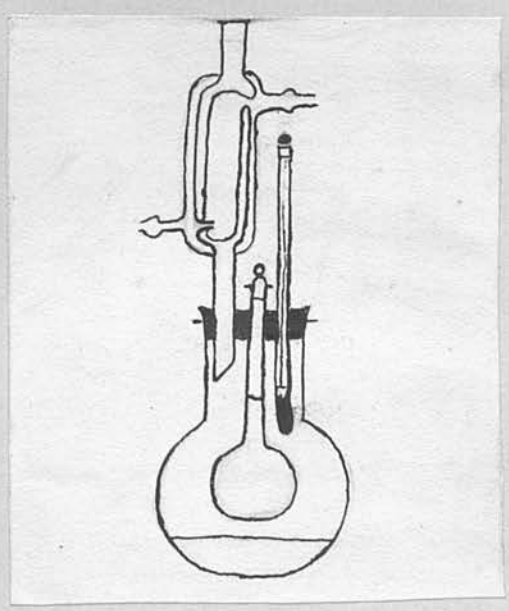
The second series of hydrolysis experiments which were carried out in solution in aqueous alcohol contains results strictly comparable with one another, and those obtained in other experiments. In this series the acid liberated by the hydrolysis of the bromide was estimated by direct titration with standard alkali.

Method. Approximately 1 gram of the bromide was weighed into a graduated 100 cc. flask and then sufficient aqueous alcohol (containing 80 per cent alcohol) added to make the volume 100 cc. This was then placed in a thermostat at 25° and the liberated acid determined by titrating aliquot portions of this solution. The results of this experiment are summarised/

summarised by saying that whilst the para isomeride is completely hydrolysed after 2.5 mins. and the ortho isomeride appears to be almost completely hydrolysed in that time, the meta isomeride was hydrolysed to the extent of 10, 20, and 33 per cent after 1, 2, and 3 days respectively.

The rate of hydrolysis of the meta isomeride was compared with that of benzyl bromide at a temperature of boiling chloroform vapour, i.e. 60°.

A weighed quantity of the bromide (either m-methoxybenzyl bromide or benzyl bromide) was dissolved in 105 cc. of absolute alcohol, 20 cc. of the solution placed in a graduated 25 cc. flask, 5 cc. of water added and the volume of the whole made up to 25 cc. with absolute alcohol. The contents of the flask were well mixed and then the flask placed in the vapour of boiling chloroform.



At the end of the intervals stated in the tables (an extra 5 mins. was allowed in each case for equilibration of the temperature) the contents of the flask were washed into a large excess of water and the liberated acid at once titrated with standard alkali. The results are summarised in Table II in which t represents time in minutes from the commencement of the experiment, w the weight of bromide taken, and x the percentage of bromide changed.

TABLE II.

Benzyl bromide		m-methoxybenzyl bromide.	
w = 0.4610 grams		w = 0.5430 gram.	
t	x	t	x
½	22.1	½	14.2
1	38.7	1	28.4
2	59.0	2	49.2
4	79.8	4	71.9
8	87.0	8	89.0

The rate of hydrolysis of the ortho and para compounds under these conditions is of course infinitely rapid.

Results similar to those in aqueous alcohol at 25° were obtained when the hydrolyses were carried out in $\frac{N}{50}$ aqueous alcoholic alkali and also $\frac{N}{10}$ aqueous alcoholic alkali at 25°.

Reduction of the methoxybenzyl bromides by dry hydrogen iodide in glacial acetic acid.

Preparation of the reagent.

Hydrogen iodide was prepared according to the method of Norris and Cottrell (Amer. Chem. J., 1896, 18, 97.). Iodine (80 grams) and dry red phosphorus (8 grams) both in a finely powdered condition were mixed together in a flask which was then gently warmed and shaken. The whole liquified and when all reaction had finished the flask was cooled and 30 cc. of water added. A small flame was placed under this and the stream of hydrogen iodide regulated by the size of the flame. The hydrogen iodide was passed through an empty Woulff's bottle which served as a trap, and then through a U tube containing glass wool and pumice which had been soaked in a paste of red phosphorus and water. The gas was dried by passing it through about 8 inches of P_2O_5 and then passed into cold glacial acetic acid until the acid was saturated.

Reduction of the methoxybenzyl bromides.

Approximately 0.5 cc. of 0.25 cc. of the bromide under investigation was weighed into a small 5 cc. stoppered/

stoppered measuring cylinder. Five ccs. of the hydrogen iodide solution were then added (the reducing agent contained 0.4464 gram of HI per cc.) and the cylinder placed in a thermostat at 25°. By means of a small pipette 1 cc. of the solution was withdrawn at definite intervals of time, run into a large excess of water and the iodine which had been liberated titrated with $\frac{N}{10}$ sodium thiosulphate solution. A blank experiment in order to determine the amount of oxidation which is due to the oxygen of the atmosphere was carried out at the same time.

The results are summarised in Table III (see also Table II of publication I, pp. 1399 and 1400.)

Table III

The symbols t, w and x have the same significance as before.

	ortho compound		meta compound		para compound	
w 1)	0·442 gm.		0·811 gm.		0·902 gm.	
2)	0·395 "		0·50 "		0·415 "	
t	x (i)	(ii)	x (i)	(ii)	x (i)	(ii)
5	1	0	50	34	1	2
15	3	3	81	80	1	2
35	11	4	90	93	2	1
75	16	11	94	99	4	3
195	34	24	100	99	6	4

Notes on the reductions. A very slight precipitate was noted in the reduction of the ortho compound, but this went completely into solution at

a/

a temperature of 25°. The accuracy of the method was apparent from the fact that 0.5 ccs. of solution was left in the cylinder at the end of the experiment. When this residual (0.5 cc.) was left in contact with the atmosphere, resin was formed in the case of the ortho and para isomerides.

Isolation of reduction products from the action of hydrogen iodide on m-methoxybenzyl bromide (see publication III).

m-Methoxybenzyl bromide (6.06 gram) was weighed into a graduated flask (capacity 50 cc.) which was then filled to the mark with glacial acetic acid containing 0.46 grams of hydrogen iodide per cc. and then placed in a thermostat which was maintained at a temperature of 25°. A sample of this withdrawn after 20 minutes indicated that 93.5 per cent of the bromide had been reduced. Samples withdrawn after the reaction had proceeded for one hour, and one hour and a half were identical, and indicated that reduction was complete (97.5 per cent) and that the liberation of iodine had ceased.

Separation of the reaction products.

The contents of the flask were poured into 200 ccs. of water containing 17 grams of $Na_2S_2O_3$ in solution. This acid solution was neutralised with solid sodium carbonate (during this operation the odour/

odour of methyl iodide was very marked), and then extracted with ether. The ethereal solution was in turn extracted thrice with 10 per cent caustic potash solution and then dried over anhydrous sodium sulphate. After distilling off the ether the residual oil was fractionated, and boiled mainly between 180° and 200°. This fraction weighed 0.90 grams. On refractionating 0.50 grams boiled between 175° and 185°. This alkali insoluble oil was m-tolyl-methyl ether (B.Pt.177°C.) and was further identified by oxidising a small portion with alkaline permanganate to m-methoxybenzoic acid, and also by demethylating it to m-cresol as described below.

From the caustic potash solution, acid precipitated an oil which after extracting with ether drying etc. and distilling was found to boil between 190° and 200° and weighed 0.70 gram. This oil had the peculiar odour of m-cresol (B. Pt. of pure m-cresol is 201°), gave a blue violet colour with ferric chloride solution and a white precipitate with bromine water. This compound crystallised from aqueous alcohol in white needles and had m.p. 81-2° and did not depress the melting point of an authentic specimen of tribrom-m-cresol.

Demethylation of m-tolylmethyl ether.

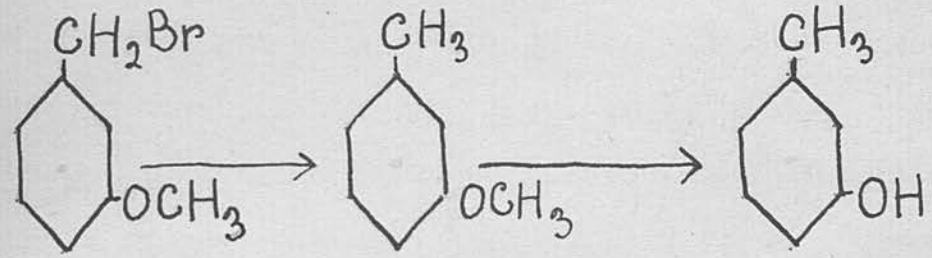
The ether obtained in the first experiment was dissolved in 5 cc. of the reducing agent and allowed to stand at 25° for 5 hours. Iodine was not liberated.

The/

The mixture was neutralised etc. as before when a small trace of the ether was detected unchanged and 0.17 gram of m-cresol was isolated and identified as before.

No liberation of iodine took place when 0.50 gram of methyl iodide was allowed to stand in solution in 5 cc. of the reducing agent for 4 hours at 25°.

Hence the reduction of m-methoxybenzyl bromide follows the course



Hydrolysis of the isomeric ω-Bromotoluic acids.

Systematic investigations on the hydrolysis of the ω-chlorotoluic acids have been undertaken by Olivier (Rec. trav. chim. 1923, 42, 515.) The method adopted by Olivier includes the extraction of unchanged material with ether from the hydrolysis mixture. In the present investigation the hydrobromic acid and the toluic acid were both estimated by direct titration and the correction to be applied for the acidity due to the carboxyl group was determined and applied in each experiment.

Salkind/

Salkind and Ssemenow (loc. cit.) have carried out systematic hydrolyses of the ω-bromotoluic acids in aqueous acetone solution at a temperature of 50°. Both these series of investigations are comparable, but for purposes of comparison with other investigations a complete series of hydrolysis was carried out in aqueous alcoholic solution at a temperature of 76°5, the boiling point of carbon tetrachloride. A small quantity of the acid (0.10 gram) was weighed into a 25 cc. graduated flask and then dissolved in 20 cc. of absolute alcohol, 5 cc. of distilled water added and the volume made up to 25 cc. with alcohol. The mode of procedure was then exactly as described before. The results are summarised in Table IV (see also Table I, publication IV, pp. 1315).

Table IV

	o-Compound.		*m*-Compound.		*p*-Compound.		Benzyl bromide.	
t.	*w.*	*x.*	*w.*	*x.*	*w.*	*x.*	*w.*	*x.*
½	0·1068	5·0	0·1019	27	0·1076	13	0·0804	57
1	0·1158	7·0	0·1010	42	0·1049	30	,,	81
2	0·1031	4·9	0·1207	70	0·1126	54	,,	92
4	0·1089	4·7	0·1001	87	0·1110	74	,,	96
8	0·1126	4·8	0·1149	90	0·1032	83	,,	97
16	—	—	0·1154	94	0·1207	90	0·0975	99
32	—	—	0·1199	98	0·0998	94	—	—

It is very important to note the peculiar behaviour of the ortho isomeride during this hydrolysis.

Reduction/

Reduction of the isomeric ω-bromotoluic acids.

The solubility of the ω-bromotoluic acids in cold glacial acetic acid is not high enough to permit the use of the reducing agent used in the previous experiments. For the reduction of the ω-bromotoluic acids therefore the following method was employed. A constant boiling mixture of hydrogen iodide and water was prepared in the usual way. Great care was exercised in the preparation of this reagent, all samples being distilled twice before use. Approximately 0.10 gram of the acid was dissolved in 15 cc. of glacial acetic acid, the whole being slightly warmed if necessary. Ten cc. of the constant boiling mixture of hydriodic acid and water were added and the flask placed in the vapour of boiling toluene. At the end of stated intervals the solution was washed out and the liberated iodine estimated by titration with sodium thiosulphate solution. A blank experiment to ascertain the amount of air oxidation was carried out on each occasion. The results are summarised in Table V (see also Table II, publication IV, pp. 1316).

Table V

	o-Compound.		*m*-Compound.		*p*-Compound.		Benzyl bromide.	
t.	*w.*	*x.*	*w.*	*x.*	*w.*	*x.*	*w.*	*x.*
1½	0·1026	11	0·1010	24	0·1044	49	0·1518	34
3	0·1223	24	0·1003	43	0·1033	73	0·1549	55
6	0·1161	42	0·1001	68	0·1001	91	0·0900	78
12	0·0931	51	0·1066	86	0·0901	99	0·1103	92

Reduction of the isomeric toluic acids under these conditions takes place to a negligible extent.

Hydrolysis of the isomeric nitrobenzyl bromides, 3-nitro-4-hydroxybenzyl bromide and 3-nitro-4-methoxybenzyl bromide.

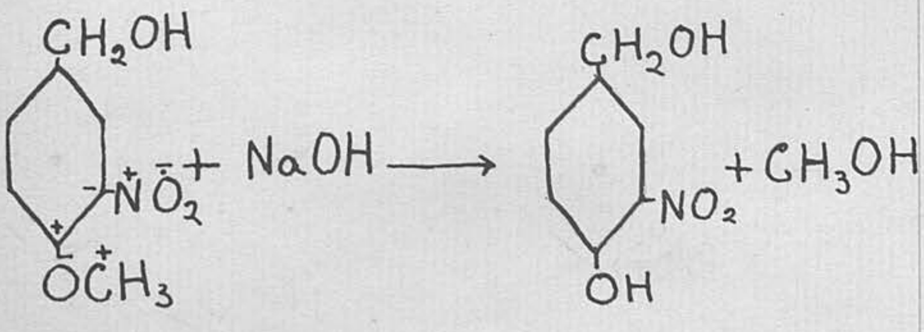
Preliminary experiments showed that when these compounds are hydrolysed by aqueous alcoholic alkali, a change takes place in the case of p-nitrobenzyl bromide and 3-nitro-4-methoxybenzyl bromide, which can only be attributed in the former case to a complex reaction of the type

$$NO_2C_6H_4C\ H_2Br \longrightarrow NO_2C_6H_4CH_2OH \longrightarrow$$

$$HOOC.C_6H_4\ \underset{\diagdown O \diagup}{N - N}.\ C_6H_4.\ COOH.$$

(o-nitrobenzyl alcohol with alkali gives azoxybenzene 2:2'- dicarboxylic acid - see Beilstein, Vol IV. pp. 1343).

and in the latter case to a reaction



Hence/

Hence these bromides were hydrolysed under the same conditions as were the ω-bromo-toluic acids. The hydrobromic acid liberated was estimated by titration with $\frac{N}{10}$ aqueous sodium hydroxide as before, save in the case of 3-nitro-4-hydroxybenzyl bromide. Here $\frac{N}{20}$ ammonium hydroxide solution was used and hydrolysis of unchanged bromide during the titration was avoided.

The results are summarised in Table VI (see also Table III, publication IV, pp. 1317).

Table VI

	Nitrobenzyl bromides							
	Ortho.		Meta.		Para.		3-Nitro-4-methoxy-benzyl bromide.	
t.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.
½	0·1267	10·8	0·1226	12·0	0·1168	11·0	0·1067	73·2
1	0·1190	19·2	0·1037	23·0	0·1045	19·5	0·1008	90·2
2	0·1022	32·4	0·1083	38·4	0·1147	32·8	0·1023	95·5
4	0·1010	54·7	0·1171	59·3	0·1015	54·6	0·1116	97·1
8	0·1081	78·9	0·1196	85·1	0·1146	78·9	0·1037	98·7
16	0·1040	93·9	0·1194	96·2	0·1068	95·3	0·1038	99·3
32	0·0998	99·1	0·1176	99·8	0·1041	99·5	0·1039	99·8

3-Nitro-4-hydroxybenzyl bromide.

t	¼	½	1	2
w	0·1008	0·1024	0·1031	0·1028
x	85	96	99	100

Hydrolysis of the isomeric ω-bromoxylenes.

Preliminary experiments showed that in order to obtain a series of results the compounds had to be hydrolysed at the temperature of the vapour of boiling chloroform. At 76° the para isomeride was almost completely hydrolysed in half an hour. Except in this particular the mode of procedure was as in the previous cases. The results are summarised in Table VII/

Table VII (see also Table I, publication V, pp. 2281). In this table the hydrolysis of ω-iodo-p-xylene is included.

Table VII

	Ortho-compound.		Meta-compound.		Para-compound.		Benzyl bromide.		ω-Iodo-*p*-xylene.	
t.	*w.*	*x.*	*w.*	*x.*	*w.*	*x.*	*w.*	*x.*	*w.*	*x.*
½	0·1060	55	0·0980	25	0·0983	66	0·1093	22	0·1335	38·8
1	0·1064	77	0·0996	42	0·1074	87	0·1056	37	0·1146	63·1
2	0·1030	89	0·1037	64	0·1019	96	0·1100	59	0·1280	78·8
3	0·1022	94	0·1011	77	0·0997	100	0·1078	71	0·1291	84·7

Reduction of the isomeric ω-bromoxylenes.

For the reduction of the ω-bromoxylenes at 25° a solution of hydrogen iodide in glacial acetic acid was used, which contained 0.70 gram of H I per cc. Approximately 0.5 gram of the bromoxylene was dissolved in sufficient glacial acetic acid to make the volume 1 cc. in a 5 cc. ground glass stoppered measuring cylinder. The reducing agent (4 cc.) was then added and the experiment continued as in the case of the methoxybenzyl bromides. The results of these experiments are summarised in Table VIII (see also Table II, publication V, pp. 2282). Benzyl bromide was subjected to the same treatment.

Table VIII

t.	Ortho-compound. $w=0{\cdot}5862$ gm. x.	Meta-compound. $w=0{\cdot}5537$ gm. x.	
$\frac{1}{2}$	—	17·9	The para-isomeride did not reduce under these conditions, and iodine corresponding to 2 per cent. reduction was liberated from benzyl bromide.
$1\frac{1}{2}$	2·5	25·6	
$3\frac{1}{2}$	4·2	36·5	
7	8·2	50·8	
20	12·1	83·9	

Identification of the products of the action of hydrogen iodide on the isomeric ω-bromoxylenes and benzyl bromide.

For this purpose approximately 6 grams of the ω-bromoxylene and 45 cc. of the reducing agent were used. The mixture was maintained at a temperature of 25° for forty hours and then poured into water. The solids which separated in the experiments with the ortho and para isomerides and also with benzyl bromide were filtered off, dried and recrystallised from light petroleum. They proved to be the corresponding iodo derivative. ω-Iodo-o-xylene melted at 33-4°, ω-iodo-p-xylene at 46-7° (c.g. Pavlovskii, J. Russ. Phys. Chem. Soc., 1911, 43, 214-8.) and benzyl iodide at 24°. Estimations of the hydrolysable iodine confirmed this.

In addition to the solid, which was obtained from the reduction product of the ortho compound, a small drop of oil was observed but it was not possible/

possible to identify it owing to the very small quantity which separated out.

m-Xylene was isolated from the reduced meta isomeride in the following way. The reduction mixture was poured into excess of water decolorised by the addition of sodium thiosulphate and the acid neutralised with sodium hydroxide. The whole was extracted with ether and from the ethereal extract an oil (1.5 gram) was obtained which distilled between 135° and 150°. When redistilled it boiled at 135-43°. It was identified by its density (0.857 at 16°) and its trinitro derivative of m.p. 181-2° which did not depress the melting point of an authentic specimen of trinitro-m-xylene.

Hydrolysis of the isomeric chlorobenzyl bromides at 76.5° (b.p. of CCl_4).

Approximately 0.5 grams of the bromide was weighed into a 105 cc. flask, and alcohol added to the graduation mark. The hydrolysis of the bromide was then carried out as was that of m-methoxybenzyl bromide, excepting that in this case the temperature was 76.5° (b.p. of CCl_4). The results are summarised in Table IX in which t represents the time in hours from commencement of experiment, w is the weight used in each titration, and x is the percentage changed.

TABLE IX.

	Ortho Compound.	Meta Compound.	Para Compound	Benzyl Bromide.
w =	0.1067 gm	0.1036 gm	0.1029 gm	0.0804 gm.
t	x	x	x	x
½	27.4	20.8	45.4	56.5
1	45.8	38.1	68.6	71.3
2	67.5	58.2	88.2	92.4
4	88.0	79.8	95.5	95.8
8	96.1	92.0	97.4	97.4

Reduction of the chlorobenzyl bromides.

These compounds were subjected to the action of hydrogen iodide in glacial acetic acid but at 25° the reduction which took place was very slight. From the para isomeride p-chlorobenzyl iodide m.p. 65° (van Raalte, Rec. trav. Chim., 1899, 18, 391) was isolated in the usual manner. The Bromides were then reduced at 110° in the acetic acid hydriodic acid reagent and the results are summarised in table X in which t, w and x have the usual significance.

TABLE X./

TABLE X.

	Ortho compound		Meta compound.		Para compound.	
t	w	x	w	x	w	x
1	0.1160 gm.	52	0.1192 gm	37	0.1168 gm	49
2	0.1208 "	69	0.1026 "	57	0.1036 "	70
4	0.1172 "	91	0.1164 "	81	0.1050 "	88
8	0.1080 "	102	0.1102 "	97	0.1048 "	98
Infin.	0.1085 "	106	0.1155 "	101	0.1083 "	100

The isomeric bromobenzyl bromides were then hydrolysed and reduced under conditions identical with those quoted in the above experiments save in the value of w which was altered so as to give approximately equivalent concentrations in the two series. The results of the hydrolyses are summarised in table XI and those of reduction in table XII.

TABLE XI.

	Ortho compound.	Meta compound.	Para compound.
w =	0.1276 gm.	0.1257 gm.	0.1275 gm.
t	x	x	x
½	23.3	20.9	40.0
1	43.7	38.7	62.1
2	66.1	60.0	84.6
4	86.8	82.2	95.2
8	95.8	94.7	98.1

TABLE XII.

	Ortho compound.		Meta compound.		Para compound.	
t	w	x	w	x	w	x
1	0.1287	51	0.1275	39	0.1243	409
2	0.1272	67	0.1272	57	0.1264	72
4	0.1320	91	0.1278	79	0.1273	89
8	0.1266	100	0.1254	97	0.1303	97
Infin.	0.1270	104	0.1268	100	0.1280	101

The isomeric bromobenzyl bromides were subjected to the action of hydrogen iodide in glacial acetic acid at a temperature of 37°. The order of reactivity was again o and p > m. After 12 days, reduction had taken place to the following extent; o = 31 per cent, p = 29 per cent and m = 16 per cent. From these experiments o-bromobenzyl iodide m.p. 47-8° and p-bromobenzyl iodide m.p. 72-3° were isolated, the oil from the reduction of the meta compound showing no tendency to crystallise after some weeks.

Reduction of the isomeric m and p-bromobenzyl iodides was carried out at 110° in the usual way and the results are summarised in table XIII. The reduction of the ortho compound was not carried out when it was seen that the reduction curves were those obtained by the reduction of the bromides, within the limits of experimental error (abt ± 1%)

TABLE XIII./

TABLE XIII.

	Meta compound.		Para compound.	
t	w	x	w	x
1	0.1564	41	0.1514	51
2	0.1534	59	0.1609	69
4	0.1518	81	0.1568	89

Hydrolysis of m and p-fluorobenzyl bromides.

These were hydrolysed under the usual condition at the boiling point of carbon tetrachloride, the results are summarised in Table XIV.

TABLE XIV.

	Meta compound.		Para compound.	
t	w	x	w	x
½	0.0955	21.2	0.0970	66.1
1	0.0984	40.5	0.1020	86.5
2	0.0984	61.3	0.0980	94.7
4	0.0969	82.9	0.0960	96.5
8	0.1047	94.0	0.0994	97.0

Reduction/

Reduction of m- and p-fluorobenzyl bromides.

The reduction of these compounds was carried out at a temperature of 110°, the b.p. of toluene and in table XV the slight difference of ease of reduction is shown.

TABLE XV.

	Meta compound.		Para compound.	
t	w	x	w	x
1	0.1025	34.0	0.1026	32.2
2	0.1042	49.3	0.1040	48.1
4	0.1107	82.3	0.1036	79.0

In table XVI the results from the hydrolysis of p-fluorobenzyl bromide and p-chlorobenzyl bromide at 60° are summarised. These experiments were undertaken with a view to discovering the manner in which the reactivity of the fluorobenzyl bromides is governed by general polar influences.

TABLE XVI.

	p-Fluorobenzyl bromide		p-Chlorobenzyl bromide.	
t	w	x	w	x
½	0.1088	20.9	0.1146	10
1	0.1024	38.8	0.1120	19.7
2	0.1089	59.1	0.1146	38.4
4	0.1060	80.9	0.1122	67.7
8	0.		0.	

Reduction of the halogenated phenols at 25°.

Approximately 0.6 gram of the phenol was dissolved in sufficient glacial acetic acid to make the volume 2.5 cc. in a small 5 cc. ground glass stoppered measuring cylinder. Glacial acetic acid (2.5 cc.) containing 0.40 gm. of H I per cc. was added, the whole well mixed and placed in a thermostat at 25°C. One cc. portions of this were withdrawn at definite intervals and the liberated iodine estimated with standard sodium thiosulphate solution. In this way reduction curves of p-iodophenol, o-iodophenol and p-bromophenol were obtained and the results are summarised in Table XVII (see also Table IV, publication IV, pp. 1319).

Table XVII

	o-Iodophenol. $w=$ 0·6104 gm.	*p*-Iodophenol. $w=$ 0·6394 gm.	*p*-Bromophenol. $w=$ 0·6070 gm.
t.	*x.*	*x.*	*x.*
15	28·2	69·0	4·4
45	56·2	88·8	8·7
105	75·6	95·4	15·9
225	90·0	100·0	28·7

A satisfactory reduction curve of o-bromophenol could not be obtained in this way so the isomeric ortho and para bromophenols were then reduced at 78° (temperature of vapour of boiling alcohol) in

a/

a mixture of acetic acid and constant boiling aqueous hydriodic acid. The results are summarised in Table XVIII (see also Table V, publication IV, pp. 1319).

Table XVIII

	o-Bromo-phenol. $w=$ 0·1730 gm.	*p*-Bromo-phenol. $w=$ 0·1719 gm.
t.	*x.*	*x.*
60	18·7	40·7
120	31·7	68·4
180	39·6	83·9
240	47·6	94·2
300	53·0	100·0

p-Chlorophenol was the only chloro isomeride which was reduced. A solution of hydrogen iodide in glacial acetic acid (0.37 gm. of H I per cc.) reduced the phenol to 10 per cent of the theoretical after four hours but reduction then stopped.

The meta halogenated phenols did not lose their halogen atoms under any circumstances.

4-Iodoresorcinol was completely reduced in half an hour at 25° in a solution of glacial acetic acid which contained 0.40 gram of H I per cc. The position of the iodine atom in this compound has not been ascertained but its behaviour with hydrogen iodide establishes it as in position 2 or 4 and thus the compound is regarded as containing the iodine atom in position 4.

Reduction/

Reduction of the isomeric iodotoluenes at 25°.

The results of these experiments carried out in the same way as the reduction of the halogenated phenols are summarised in Table XIX. (see also Table V, publication V, pp. 2283).

Table XIX

	Ortho-compound.	Meta-compound.	Para-compound.		Ortho-compound.	Meta-compound.	Para-compound.
u =	1·2150 gm.	1·1934 gm.	1·2051 gm.				
t.	x.	x.	x.	t.	x.	x.	x.
1	48·4	4·1	32·1	6	88·1	13·3	79·2
2	67·9	7·9	50·5	8	92·0	17·4	85·9
4	82·8	10·9	69·9				

From the ortho and para isomerides toluene was isolated by the method employed for the separation of m-xylene from the reduction of ω-bromo-m-xylene. It was quite free from halogen and its trinitro derivative (m.p. 82°) did not depress the melting point of an authentic specimen of trinitro-toluene.

Iodobenzene liberated iodine from hydrogen iodide in glacial acetic acid in quantities which represented 10 per cent reduction in 8 days.

G E N E R A L.

The results obtained during these investigations have substantiated the principle of induced alternate polarities in many ways. The systems investigated were simple ones and whilst many of the compounds have been known for a long period the notable differences in the manner in which they would react towards hydrolysing and reducing agents, especially the latter, have not been suspected, since these differences could only have been foreseen by an application of such a principle as that enunciated by Lapworth. In some cases, data did exist as to the reactivity of the isomerides but the same reagents had not been used throughout, and the series here recorded is comparative in that the reactivities have all been carried out in solution and with reagents of definite and standard concentration.

In addition to induced effects of an alternating character, the influence which an atom or group of atoms exerts on a molecule as a whole, and also the manner in which the course of a reaction may be determined by steric or spatial influence have all been investigated. The "general influence" is apparent in the order of ease of hydrolysis of the various isomerides in solution in aqueous alcohol when/

when a series of isomerides were found to be either more readily or less readily hydrolysed than the unsubstituted compound in such a solution. The methoxybenzyl bromides and fluorobenzyl bromides did not follow this general rule however, and here the unsubstituted compound was intermediate between the p and m isomerides. The complete series of hydrolyses therefore reads as follows

p-OCH_3 > o-OCH_3 > p-CH_3 > o-CH_3 > m-CH_3 > p-F > unsubs. > m-OCH_3 > p-Cl > p-Br > m-COOH > o-Cl and o-Br > m-F m-Cl and m-Br > p-COOH > m-NO_2 > o-NO_2 > and p-NO_2.

This order has been arrived at from a consideration of the times taken for 50 per cent hydrolysis of the bromide, the $-OCH_3$ and $-CH_3$ at 60°, and the remainder at 76°. Velocity constants were only obtained in the case of the nitro compounds where the reaction is very slow and hence are not recorded. A similar series to the above, for the corresponding benzyl chlorides, has been obtained by Olivier (loc. cit) but the methoxybenzyl chlorides and the fluorobenzyl chlorides were not examined by that investigator, and therefore the above series is the most complete on record for this type of reaction. The ease with which it was possible to trace the general effect in this way is no doubt due to the simplicity of the course of this reaction which is merely/

merely

$$R.C_6H_4\ CH_2Br + HOX \longrightarrow R.C_6H_4.\ CH_2\ OX + H\ Br$$

in which R is a substituent in the benzene nucleus and X is either H or $-C_2H_5$.

General remarks on the reductions.

When the different compounds were subjected to the action of hydrogen iodide, several reactions took place at the same time. These are due to (a) the effects detailed above and in addition, to (b) a mass action effect which results in the production of the corresponding iodide on account of the concentration of hydrogen iodide in the reducing agent, thus

1. $R.C_6H_4CH_2Br + HI \longrightarrow RC_6H_4\ CH_2\ I + H\ Br.$

Such an iodide formation may be followed by a reaction due to polar influences when iodine is liberated according to the equation

2. $R.C_6H_4\overset{-}{C}H_2\overset{+}{I} + \overset{+}{H}\ \overset{-}{I} \longrightarrow R\ C_6H_4\ CH_3 + I_2.$

The reactions due to polar influences however may take place concomitantly with iodide formation and then iodine will also be liberated in the following manner.

3. $R.C_6H_4.\ \overset{-}{C}H_2\overset{+}{Br} + \overset{+}{H}\ \overset{-}{I} \longrightarrow R.\ C_6H_4CH_3 + I\ Br.$

4. $I\ Br + H\ I \longrightarrow H\ Br + I_2$

The reactions which are governed by purely induced alternating polar influences are 2 and 3.

In general it may be said that the inducing polar influence of the substituent group R determines the course of the reaction. If the inducing influence is marked, as in the case of the methoxybenzyl bromides then reactions 3 and 4 are the main reactions, and if this influence is weak, e.g. the halogenated benzyl bromides then reactions 1 and 2 represent the course of the reduction. In all cases however reactions 1 and 2 take place to some extent.

In addition to these reactions there is a fifth which probably takes place during the reduction of a benzyl bromide when in solution in acetic acid and aqueous hydriodic acid, namely hydrolysis of the iodide to alcohol. Such a change however is a reversible one.

$$R.C_6H_4CH_2\,I + HOH \rightleftharpoons R.C_6H_4CH_2OH + H\,I.$$

and hence does not affect the completeness of the reduction. Reductions were carried out in this reagent when it was found impossible to obtain reduction curves at 25°, because of either the insolubility of the compounds, or the slowness of the reaction at that temperature.

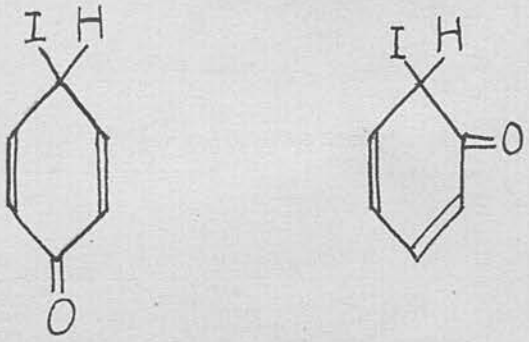
The influence of the oxygen atom.

The series investigated in this connection were the isomeric methoxybenzyl bromides, the halogenated phenols, the isomeric ω-bromotoluic acids and various nitrobenzyl/

nitrobenzyl bromides. On the investigation of the properties of the isomerides of the first series the marked alternating influence of the oxygen atom of the methoxyl group became apparent. The remarkable ease with which the para isomeride lost its bromine atom as bromidion in aqueous alcohol was almost paralleled by the ease with which the meta isomeride liberated iodine from hydrogen iodide at 25°. The order of ease of hydrolysis was p > o > unsubs > m and hence the general enhancing or inhibiting influence of the methoxyl group on the reaction must be small compared with its alternating influence. The order of ease of reduction however is m > o > p and unsubs., whereas it would be expected to be at least m > o and p and unsubs. The reducibility of the ortho compound is probably governed by the same factors which determine the occurrence of ortho derivative in the disubstitution products from a monosubstituted benzene, which, in virtue of its directing group would be expected to yield only meta derivative. Thus the unexpected rate of hydrolysis of the ortho compound would then be due to the same cause as that governing the reduction and not to a steric effect.

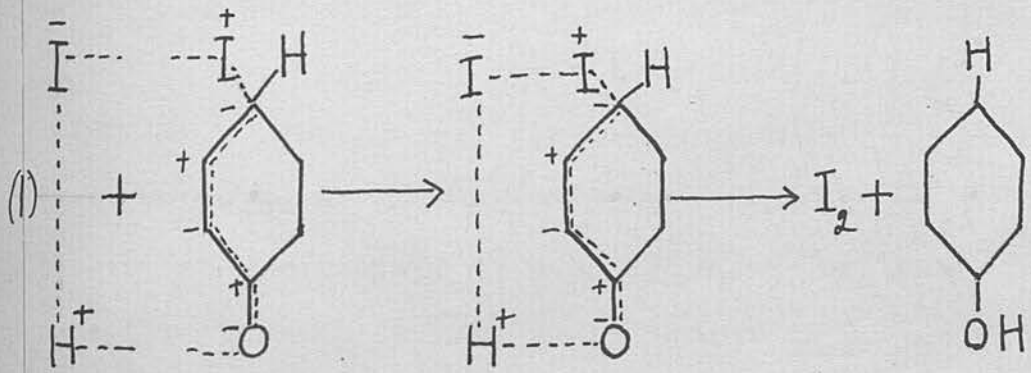
The differences observed in the halogenated phenols are no doubt due in some measure to structural changes which take place during the reaction. The more rapid reduction of the para isomerides as compared with the ortho suggests that reduction is here assisted/

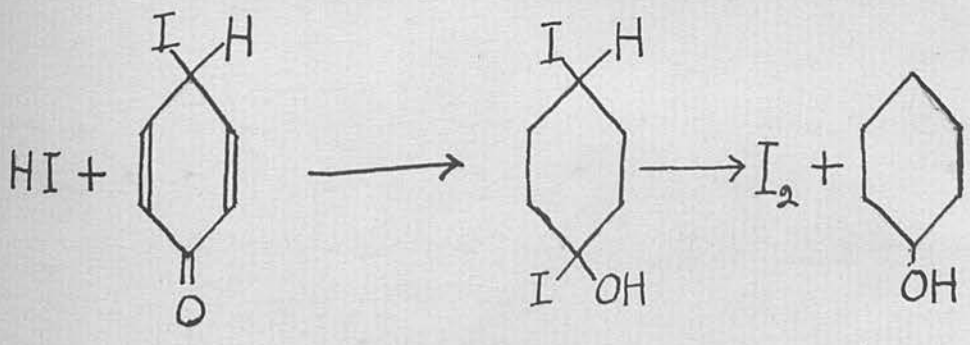
assisted by the formation of molecules of a quinonoid type.



The complete mechanism of reduction is then represented by one of the two following schemes,

(i) Robinson's (Men. Manchester Phil. Soc., 1920, 64, No.4) which involves partial dissociation of the reactants or (ii) Holleman's (Die direkte Einführung).





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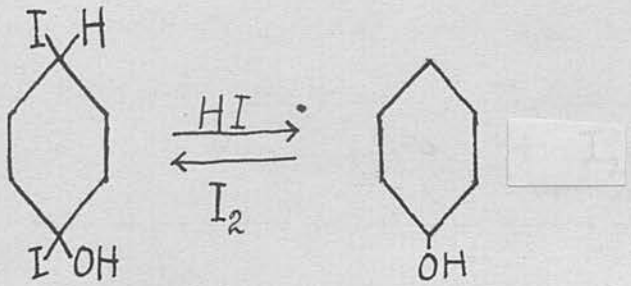
The formation of the type of compound quoted in the latter scheme is assumed to be the preliminary to substitution in the benzene nucleus by Holleman, and hence the following is probably the reversable reaction involved.



The suggestion that the formation of molecules of quinonoid type is a great factor in the ease with which para iodo phenol loses its iodine, is borne out in two ways, firstly by the extraordinary facility with which the iodine is eliminated from 4-iodoresorcinol [the formation of mols of quinonoid type in simple resorcinol derivatives is well known and has been described by many investigators including Baeyer, (Ber., 1886, 19, 163;) Perkin, (J., 1895, 67, 993;) Kostanecki, (Ber., 1899, 22, 1345;) Fuch and Elzner, (ibid, 1920, 53, 886;) and Herzig and Zeisel, (ibid, 1518)] and the reduction of the isomeric iodotoluenes in which case, the tendency to form quinonoid molecules probably does not assist reduction and therefore the iodine nearest to the key atom, i.e. that in the ortho derivative is eliminated most readily.

The reduction of the various halogenated phenols is therefore an example of the manner in which a

reaction/

reaction may be affected by structural changes, the remarks on such a reaction being summarised by saying that the halogen atoms in the ortho and para compounds all exhibit "positive polarity".

Whilst it is correct to say that the iodine in 4-iodoresorcinol is more "positive" than that in p-iodophenol owing to the presence of the second hydroxyl group, it is incorrect to say that the increased reactivity is due solely to the inducing influence of the second hydroxyl group, because investigation has shown the necessity for comparing the reactivity of isomerides when discussing purely alternating polar influences.

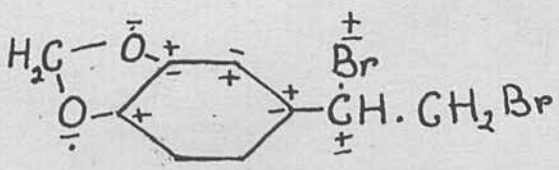
A second point of importance arises from this research. The iodophenols are more rapidly reduced than the corresponding bromophenols. Gotts and Hunter, (J., 1924, 125, 442) who pointed out that the relative stability of various dihalogeno-dinitromethanes in presence of reagents such as K I, KCN, $Na_2S_2O_3$ conforms to the general order Cl > Br > I in virtue of the more electro positive nature of the iodine in iodo derivatives, were criticised by Mrs Ingold (J., 1925, 125, 1532) for generalising on an isolated case of such stability, since it is the case that halogenated acetylenes do not conform to this order. The relative stability of the halogenated phenols in presence of hydrogen iodide however again conforms to the order Cl > Br > I and the results here recorded are another example/

example of the point stressed by Gotts and Hunter.

It was not found possible to obtain any data on the difference of ease of hydrolysis of the halogenated phenols, and it was seen that in such compounds the halogen is far more resistant to the action of hydrolysing than reducing agents. Thus an influence which is transmitted from an atom to a substituent in meta position is in some manner weakened and is not sufficient to overcome the usual tightening of the bond between the halogen and benzene nucleus.

It may here be stated that in an analogous manner, although the bromine in m-methoxybenzyl bromide is very reactive towards hydrogen iodide, it is not so reactive as that of the para isomeride is in aqueous alcohol, and hence it may be concluded that an effect transmitted through to a para position is more effective than one transmitted to a meta position.

As a direct example of this the hydrolysis of α- 3 : 4 - methylene-dioxyphenyl-$\alpha\beta$-dibromoethane in cold aqueous acetone solution to α-3:4-methylene dioxyphenyl-β-bromo-α-hydroxyethane (Barger and Jowett, J., 1905, 87, 970) may be quoted.



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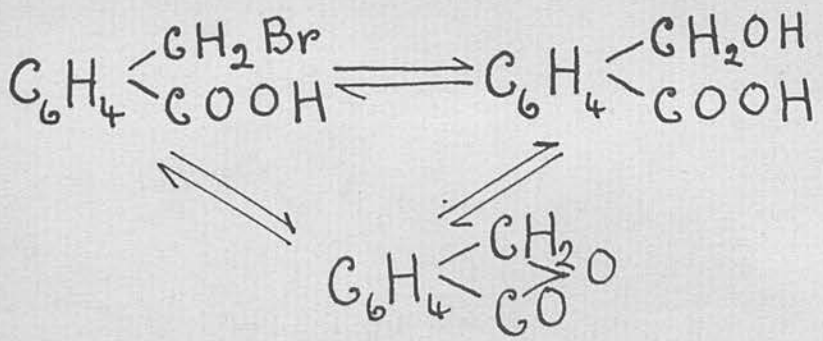
The retarding influence of the oxygen in meta position is not sufficient to overcome the enhancing influence of that in para position, which is in keeping with the remarks made above.

In the third series of isomerides examined in order to substantiate the inducing influence of the oxygen atom, the oxygen atoms were present in the carboxyl group, and here the first marked influence of a general character was met with. All the isomerides are more difficult to hydrolyse than benzyl bromide but the rates of hydrolysis of the meta and para isomerides are in an order the opposite of that found in the case of the methoxybenzyl bromides. Here the ortho isomeride certainly behaves in an abnormal manner since the figures recorded in table IV (pp. 63) represent the excess titration over the figure required for neutralisation of the carboxyl group. The sudden fall after rising to a maximum is due to the cycle of changes shown here.



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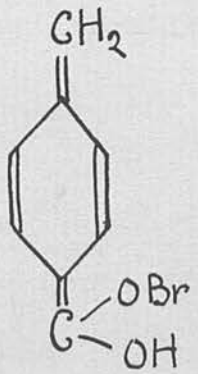
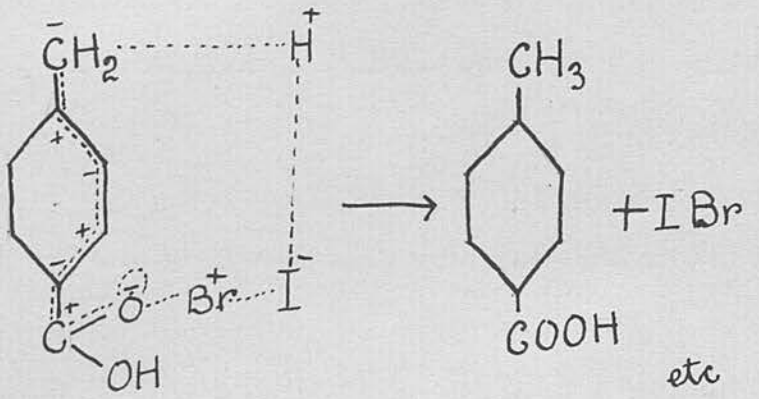
The hydrolysis of ω-bromo-o-toluic acid to ω-hydroxy-o-toluic acid is accompanied by the formation of hydrobromic acid and phthalide. The titration follows its abnormal course until equilibrium is reached in the production of phthalide. Thus the tendency to form phthalide is the predominant factor in the hydrolysis of ω-bromo-o-toluic acid.

The insolubility of these compounds in glacial acetic acid necessitated the use of a mixture of the constant boiling point mixture of water and hydriodic acid and acetic acid as reducing agent. Once more the tendency of ω-bromo-o-toluic acid to form phthalide became apparent in the fact that iodine representing only 50 per cent reduction was liberated. The removal of part of the bromine as hydrogen bromide is the obvious cause of this abnormality. The order of ease of reduction of the other isomerides was p>unsubs>m. It is quite conceivable that reduction of the para isomeride is somewhat assisted by the formation of molecules of the following type,



and/

the tendency towards complete conjugation being one of the recognised phenomena of organic chemistry. The course of the reduction is then again represented as follows



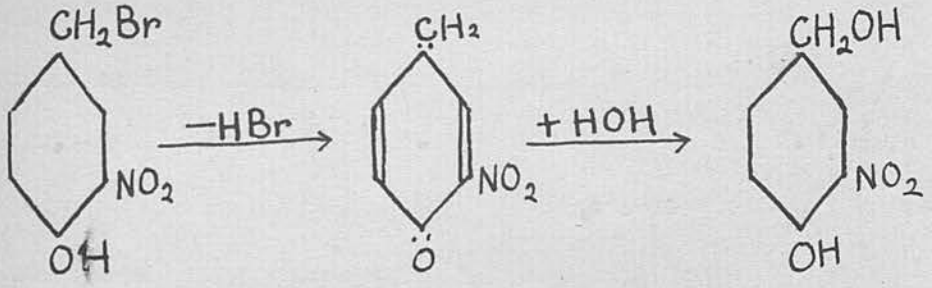
Owing to the low concentration in which these reductions were carried out it was not found possible to isolate any reduction products, but there was no reason to suppose the reductions had taken place in an abnormal manner as the carboxyl group was not affected by the reagent employed.

The next series investigated, namely the nitro-benzyl bromides, showed that the general inhibiting influence of this group is very large whilst the alternating influence is surprisingly small although the order of ease of hydrolysis was as expected, namely m> o and p. Even the steric effect due to the proximity of the nitro group in ortho position to the $-CH_2Br$ group was masked by the huge inhibiting influence, and it was possible to demonstrate how the general influence of such a group could be employed

to/

to stabilise a very reactive compound such as p-methoxybenzyl bromide or the corresponding p-hydroxybenzyl bromide.

3-Nitro-4-methoxybenzyl bromide, unlike p-methoxybenzyl bromide, is a stable crystalline compound which is hydrolysed moderately slowly and 3-nitro-4-hydroxybenzyl bromide is a similar compound which hydrolyses more rapidly than the corresponding methoxy derivative. This difference may be due to the ease with which the latter might lose H Br in accordance with the scheme.



Ionisation of the hydrogen of the hydroxyl group would also assist such a hydrolysis since the oxygen would then function as a stronger "key-atom" than when present in a methoxyl group.

The influence of the hydrogen atom.

The methyl group is analogous to the hydroxyl group in the way in which it directs substituents into the benzene nucleus. Carbon in such a group is merely a transmitter of induced polar effects and/

and hence any directive influence exerted by the methyl group is due to the hydrogen atoms which it contains. The difference of the acidity of the three cresols is a concrete example of this and particular interest attaches itself to the results obtained in the present investigation. That hydrogen does act as a positive "key-atom" is shown by the fact that the differences of reactivity observed in the ω-bromo-xylenes were the parallel of those observed in the case of the methoxybenzyl bromides save in one particular. The alternating influence of the methyl group is moderately large but is not sufficient in this case to mask the general polar effect. It was seen that the reductions follow the course represented by equations 1 and 2, pp. 80 . The ortho isomeride once more behaved in an unexpected manner and was reduced more rapidly than the unsubstituted compound. It was also possible to show that a benzyl iodide (in virtue of the more electro-positive nature of the iodine) is more difficult to hydrolyse than the corresponding bromide. This substantiates the correctness of the principle and emphasizes the remarks made on pp. 85 concerning Mrs Ingold's criticism of Gotts and Hunter.

The order of ease of reduction of the isomeric iodotoluenes bears out the suggestion advanced in this thesis that the reduction of the halogenated phenols is assisted by an isomeric change of the phenol,/

phenol, since in the case of the iodo-toluenes, in which the tendency to form molecules of a quinonoid type must not be in any way marked, the order of ease of reduction is o> p >m, that is the iodine atom nearest to the "key-atom" is the one which is most readily removed. In this series also the properties of the iodine of the meta isomeride approaches more nearly to that of the iodine in the other two isomerides than is the case in the halogenated phenols, and the important bearing this has on the question as to how far the "polarity" of the hydrogen atoms in the nucleus of phenol and toluene is responsible for the production of substituents of definite orientation is seen from the following table in which x and x' are the quantities of the various isomerides produced in the nitration of phenol and toluene respectively and y and y' the extent to which reduction of the corresponding iodo derivatives had taken place after 50 per cent of the halogen had been eliminated from the para isomeride.

		x			y
Phenol	o	52%	Iodophenols	o	17%
	m	-		m	-
	p	48%		p	50%

(i.e. no reduction of the meta isomeride and no substitution in meta position).

Toluene/

		x'			y'
Toluene	o	56%	Iodotoluenes	o	68%
	m	3%		m	8%
	p	41%		p	50%

The figures tabulated under x and x' are those quoted in Holleman.

It is convenient to summarise at this stage, certain of the results obtained in the series consisting of:-

(1) the methoxybenzyl bromides

(2) the halogenated phenols

(3) the ω-bromoxylenes and

(4) the iodotoluenes

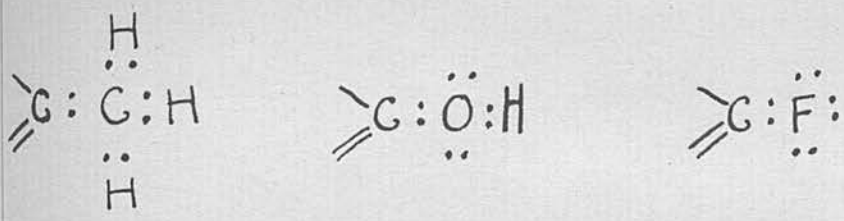
in order to show the parallel which exists between the hydroxyl group and the methyl group.

Hydrolysis	Methoxybenzyl bromides	p > o > unsubs > m
Reduction	Halogenated phenols	p > o > unsubs > m
Hydrolysis	ω-Bromoxylenes	p > o > m > unsubs.
Reduction	Iodotoluenes	o > p > m > unsubs.

The directive influence of the halogen atoms.

Lapworth (loc. cit.) has pointed out that the halogen atoms are probably the most weakly directing atoms, and the production of 2:4:6-tribromophenol in the bromination of phenol certainly bears out such a suggestion. The present investigations have shown that/

that as compared with methoxyl the influence of chlorine and bromine on the l ability of the bromine atom of the $-CH_2Br$ in the respective benzyl bromides, is very small indeed. The isomeric fluorobenzyl bromides differ from the chloro and bromo compounds in that there is a greater difference between the rates of hydrolysis of m and p fluorobenzyl bromides than between those of the corresponding chloro and bromo compounds. Fluorine is a more strongly directing atom than either chlorine or bromine and this point is stressed much better by examples quoted in this thesis than by those which involve substitution of a nuclear type where solvent action plays such an important role and often masks the true cause of differences of reactivity.
The importance of the fluorobenzyl bromide experiments lies in the comparison of influencing atoms or groups with the same electronic shell which is now possible, i.e.



The inducing power rises to a maximum at the oxygen atom and is lowest in the case of the fluorine atom, and in this latter case the power of reversing the order of reactivity when the reagent is changed from

a/

a hydrolysing to a reducing agent has almost disappeared. This reversal of reactivity has proved to be a valuable criterion of the truth of the principle and whilst it was discovered to take place in four cases there were two in which reversal did not take place, namely the chlorobenzyl bromides and the bromobenzyl bromides. The explanation of this is not easy to find, although it appears as if the magnitude of the differences of the reactivity of isomerides varies with the reagents employed. The unexpected rate of reduction may be due to the association of the reacting molecules with molecules of solvent, but whatever is the cause the halogens are sharply differentiated from oxygen and the methyl group in this respect.

Ingold in the Annual Reports (1924, pp. 110) regards the reducibility of the ω-bromotoluic acids and ω-bromoxylenes as explicable from other points of view since he says "experiments have been presented (in 1924) with reference to the polarity theory ..... which are capable of more than one interpretation." In publication III, pp. 2829 this reversal of reactivity has been pointed out as one that "could not have been foreseen with the aid of any general principles enunciated prior to the principle of induced alternate polarities."

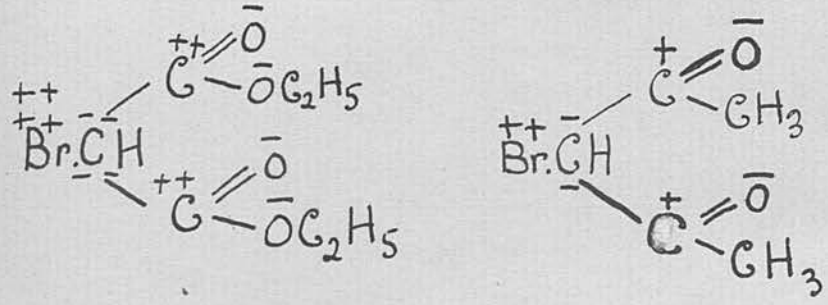
Other Theories.

Of the many theories which have been advanced in order to explain phenomena such as those recorded in this thesis, three may be discussed in particular. These are the tautomeric hydrogen hypothesis of Thorpe [vide Thole and Thorpe (J., 1911, 99, 2185,) Norris and Thorpe (J., 1921, 119, 1203) and Gupta and Thorpe (J., 1922, 121, 1896.)], the variable distribution of affinity as postulated by Flürscheim (refs. already given together with numerous articles to Chemistry and Industry) and the polarity of double bonds (Lowry J., 1923, 123, 822 et seq.)

The tautomeric hydrogen hypothesis suggests that the greater the tendency of a compound to acquire the hydrogen atom necessary to enable it to react in its enolic form the more readily it will be reduced, and it has been employed to explain differences in ease of reducibility shown by compounds which are known to be capable of existing in tautomeric modifications. Allsop and Kenner (J., 1923, 123, 2294) regard these suggestions as more widely applicable than the principle of induced alternate polarities, whilst Macbeth (J., 1922, 121, 1126) has pointed out that the bromine atom in bromodiethyl malonate is more readily removed by a reducing agent than that in bromoacetyl acetone, and whilst Macbeth suggests

that/-

that an explanation is forthcoming on account of the piling up of "key-atoms" in the former as compared with the latter, no explanation can be found on the basis of Thorpe's hypothesis

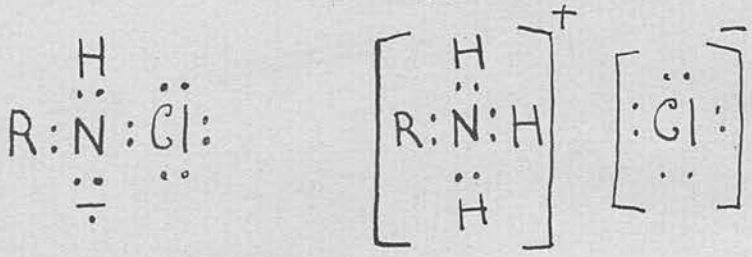


Although no explanation can be found on Thorpe's suggestion, Macbeth is incorrect also since it has been shown in these investigations that the mere piling up of "key-atoms" is not always accompanied by an increased reactivity in the molecule. Here the general polar influence is more probably responsible for the increased reactivity.

The hypothesis of Thorpe has reference for the most part to variations of reactivity within a very restricted range of the field covered by polarity principles. It obviously cannot be extended to explain the ready reducibility of the chloroamines or alkyl hypochlorites which are compounds of the simplest nature in which the reactivity of the halogens is due to the negative nature of the element to which halogen is attached.

i.e. $>\overset{\cdot\cdot}{N}\overset{+}{\cdot}Hal$ and $-\overset{\cdot\cdot}{O}\overset{+}{\cdot}Hal$

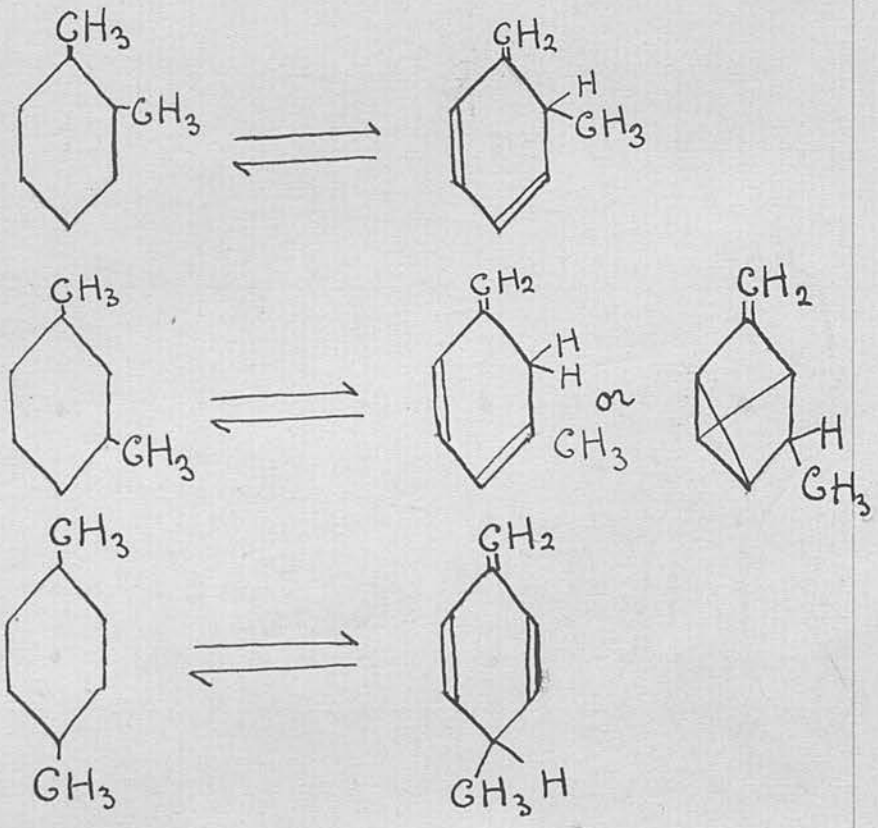
(The reactivity of the halogen in the former of these is different from that in compounds of the type R. $NH_2H.Cl$. and the cause is at once apparent from the electronic formulae of the two types.



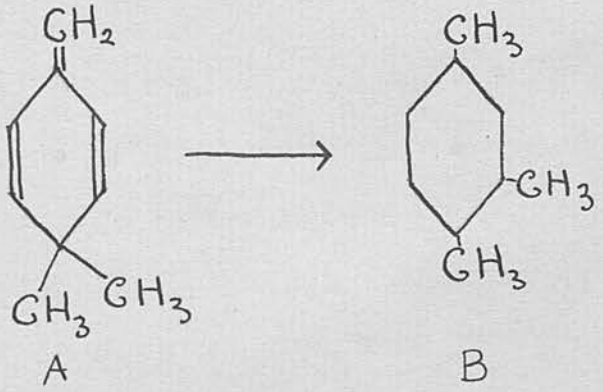
In the former the halogen is attached by two electrons to the nitrogen whilst in the latter the halogen is ionised.)

Since the tautomeric hydrogen hypothesis was put forward in order to explain differences in ease of reducibility, it cannot be used in the cases of hydrolysis of the various benzyl bromides, a series of differences which are exactly what would have been expected from the application of polarity principles (that is, if the peculiar position of the ortho compounds be excepted). When the ease of reducibility of the isomeric iodotoluenes, isomeric ω-bromo-xylenes, and also the methoxybenzyl bromides are considered in the light of this hypothesis, no information is forthcoming as to the differences observed. It would be necessary in the first place to establish the existence of tautomeric forms of these compounds and then to/

to show that one isomeride more easily reverts to its tautomeric modification than the others. Thus in the case of the ω-bromoxylenes such systems as the following would have to be shown to exist,



and it would also be necessary to show that the ω-bromoxylenes had a constitution corresponding to the ketonic form during reduction. There is nothing to substantiate the assumption as to the existence of a system in the literature beyond compounds of type A below (Anwers and Zeigler Ann., 1921, 425, 217) which however are very readily transformed into compounds of type B.



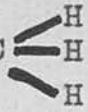
These arguments obviously hold in the other examples cited, and hence the hypothesis is to be regarded as unsatisfactory.

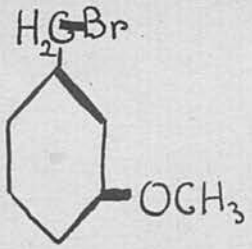
Flüorscheim (loc. cit.) is of the opinion that differences in the acidity of substituted and unsaturated carboxylic acids may be explained by assuming an abnormal affinity demand of the substituting or unsaturated atom present in the chain or nucleus attached to the carboxyl groups. This results in a redistribution of the valency forces in the whole molecule, with an increase or decrease in the strength with which the ionisable hydrogen is attached to the molecule, according to the nature of the substituent, or the position of the double bond. He has also employed such views to explain the phenomena of aromatic substitution. Hence it follows that such suggestions ought to be capable of explaining the results recorded in these investigations. They fail to do so in many instances the most important being the reductions of the isomeric methoxybenzyl bromides, the ω-bromotoluic acids, and all the differences met with/

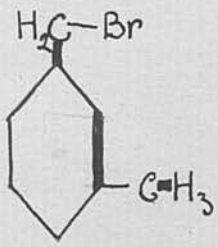
with in the halogenated hydrocarbons in publication V. It might be possible to explain the differences met with in the halogenated phenols but the difficulty attached to a correct application of the views of Flürscheim is shown by the fact that even Cohen, Vol.I, 1923, pp. 177, says that according to Flürscheim's hypothesis the halogens in meta halogenated phenols should be loosened. As these investigations have shown, this is not so.

Again if Flürscheim's views were correct there should be no difference in the order of reactivity whatever reagent is employed, a fallacy which was noted four times. That the "kind" of affinity must be considered as opposed to the postulation of a mere loosening of the bond is shown by comparing the differences of ease of hydrolysis of benzyl bromide, ω-bromo-m-xylene and m-methoxybenzyl bromide with the differences of ease of reduction. These three compounds do not vary greatly in the time during which 50 per cent of the compound is hydrolysed at 60° under equivalent conditions. The figures read benzyl bromide, 1 hr. 30 mins.; ω-bromo-m-xylene, 1 hr. 20 mins. and m-methoxybenzyl bromide, 2 hrs. The same quantity of reduction takes place at 25° in the case of benzyl bromide not at all, ω-bromoxylene, 7 hrs., and m-methoxybenzyl bromide, 5 mins.

It is also difficult to see in what manner the methyl group makes an increased or decreased affinity demand/

demand on the carbon atom to which it is attached and actually the hydrogens ought to be regarded as being capable of making increased affinity demands in virtue of the recognition of compounds of the type $H-\left[F-H-F\right]$ (vide Sidgwick, J., 1923, 123, 725; Lowry and Burgess, J., 1923, 123, 2111; Lowry J. Soc. Chem. Ind., 1923, 42, 1048). This however would lead to the representation of the methyl and hydroxyl groups as follows  and , and the formulation of the respective benzyl bromides thus:-





That is m-methoxybenzyl bromide should be stable when ω-bromo-m-xylene is unstable.

Thus Flürscheim's views, which have been so fruitful in many fields of organic chemistry are incapable of application in several cases here recorded, since in such views no cognisance is taken of the possible polarities of any of the atoms in an organic molecule.

Lowry (loc. cit.) suggests that a double bond in organic chemistry usually reacts as if it consisted of the ordinary co-valency and one polar valency, that/

that is there is a definite migration of an electron from one atom to the other, represented as follows:-

$>C=X$ is really $>\overset{+}{C}-\overset{-}{X}$ or $>\overset{+}{C}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\overset{-}{X}}}:$

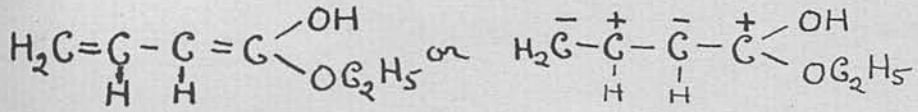
– is equivalent to :, 2 electrons.

Several of the difficulties attending this suggestion have been pointed out by Sugden (J., 1923, 123, 1861). Sidgwick (Faraday Soc. discussion 1923, 471), Lapworth and Robinson (ibid, 1923, 503), Flürscheim (ibid 534), Aucken (Chem. and Ind. 1925, pp. 72).

If Lowry's assumption were correct, then alternate polarity effects could only be transmitted along a completely conjugated chain of carbon atoms. The experiments on the ω-bromo-xylenes and the methoxy-benzyl bromides however show that perfect conjugation is not a vital necessity for the transference of such effects, although it is probable that the examples quoted contain the limiting number of singly bound carbon atoms over which the effect will be transmitted, and also that the "amplifying" influence of the benzene nucleus compensates the damping effect of the single bonds. Whilst it appears logical to assume that the more the electrons are shared the more they tend to be definitely orientated under the influence of the "key-atom" with the appearance of enhanced positive and negative characteristics on the atoms in the chain, still it appears illogical to say at present that/

that such an influence will stop at once when the atoms are singly bound, that is according to Lewis, when they mutually share two electrons. It is however a matter for further experiment to see how far such an influence, when passed through a benzene nucleus will extend over single bonds. Recent work by Conant and Kinner, (J.A.C.S. 1924, 46, 232) appears to support the view that the influence is not transmitted over single bonds in an aliphatic chain, and that general and steric influences are the predominating factors governing reactivity in such compounds.

In order to explain the reactivity of ethyl crotonate Lowry assumes the formation of an enolic modification and hence the reactive form of the ester has the composition



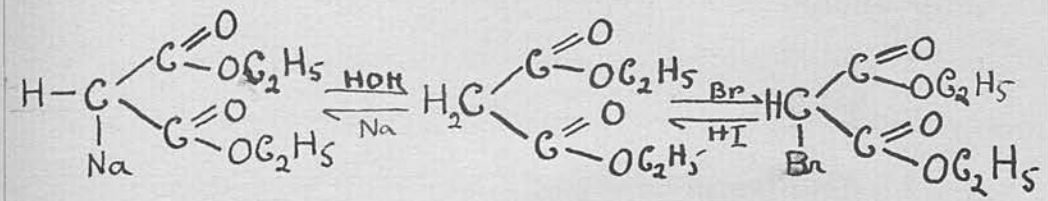
The extension of such a view to the ω-bromoxylenes etc. leads to the assumption of compounds necessary for the explanation of the reactivity of these compounds by means of the tautomeric hydrogen hypothesis, and hence to the conclusion that Lowry's view cannot be harmonised with the experimental data.

Lowry is of the opinion that a system in which the polarities are concordant is more stable than one in which they are crossed (such states correspond

to/

to homogenity and heterogenity of polarity respectively as defined by Lapworth some years before Lowry's suggestion was put forward). When the isomeric ω-bromoxylenes (or methoxybenzyl bromides) are considered from the point of view of such a suggestion, it will be seen that the polarities are crossed in the meta isomeride but are concordant in the ortho and para isomeride. The meta is the least stable isomeride in the presence of hydrogen iodide but most stable in the presence of a hydrolysing agent. The difference in the two reactions lies in the fact that the former case a "concordantly polarised molecule" is produced whereas in the latter the molecules produced still contain "crossed polarities". Hence this hypothesis is only applicable in part and reciprocal attraction of the reactive atoms of the molecules, such as that of the bromine of the benzyl bromide for the hydrogen of the hydrolysing agent must always be taken into account. In addition to this it must be remembered that the reversibility of the reaction plays a large part in determining the course of a reaction and thus we find that a series of reactions such as the following takes place according to the conditions*

* In a series of reactions not quoted in the thesis it was hoped to show that the hydrogen of the CH_3 group of m-tolylmethyl ether the molecule of which is "concordantly polarised" is more reactive towards amyl nitrite than the corresponding hydrogen atom in the ortho and para isomerides, but this expectation was not realised owing to tarring during the condensation.



Homogeneous or Concordant

Heterogeneous or Crossed

Lowry's suggestions hold good for the examples quoted in the original paper, but they must always be dependant on the type of reaction studied as is seen from the behaviour of the benzyl bromides recorded here.

Suggested causes of the property of induced alternate polarities.

Lapworth (J., 1922, 121, 416), Robinson and Kermack (ibid, 427), Thomson (Phil. Mag. 1923 (VI) 46, 497-514) and Hjendahl (J., 1924, 125, 1381) have in turn been able to arrive at theoretical explanations of the property of induced alternate polarities of atoms, and all agree that in some way or other it is the configuration of the electrons in the molecule, which is responsible for the setting up of the alternation, and also for its maintenance along a chain.

Thomson's suggestions have been adversely criticised by Lapworth and Robinson (Nature, 1923, 112, 722) since whilst the existence of an electrostatic doublet between a carbon atom and an atom such as/

as chlorine or oxygen would cause an electronic shift, as Thomson says, the electrons would be expected to move in a continuous manner under such circumstances and hence the effect would be, not an alternation of properties along a chain of carbon atoms but a gradual change such as is to be regarded as the cause of the general effect.

Hjendahl bases his explanation on the Bohr theory of the atom and on Sidgwick's suggestion (Trans. Faraday Soc., 1923, 19, 459) that shared electrons pursue looped or figure-of-eight orbits round the nuclei of two atoms joined by a non-polar link. The positive or negative nature of the atom depends on the shorter or longer period an electron spends in the neighbourhood of the nucleus of the atom, a period determined by the size of the loop round the inducing atom. The value of this suggestion lies in the attempt to correlate the well known phenomena of alternation and the most modern mathematical conceptions of the structure of the atom. It is open to objections however and one that has arisen from these researches, is that an effect transmitted from para position is greater than from meta position, whilst Hjendahl arrives at figures - 0.360 and + 0.408 for the magnitude of such effects. This once more emphasises the peculiar amplifying influence of the benzene ring about which so little can be said with certainty.

Robinson/

Robinson and Kermack (loc. cit.) point out that whilst all the carbon atoms in an organic compound must be surrounded with an octet of electrons (according to the Lewis Langmuir theory) these octets cannot all be of equal stability unless the substance is symmetrically constituted. The stability or instability of these octets determines the negative or positive nature of the atoms. Thus in a hydrocarbon chain, a strain is set up by reason of the great stability or instability of the octet surrounding the substituent atom, thatis the "key-atom". From this it might at once be said that if the reaction which is taking place is one which is not assisted or retarded by steric or structural changes in the molecule, then the more stable the octet round the "key-atom" the greater the strain set up along the chain, and therefore the greater the effectiveness of the "key-atom". The order of effectiveness of the different octets as demonstrated in these investigations is oxygen > methyl group > fluorine > chlorine and bromine. Octet stability certainly must be regarded as the reason why the influence of the methyl group is so marked. The tendency of the hydrogen atoms to surrender their electrons to the octet round the carbon atom would produce a very stable octet which would then cause the marked variations of reactivity observed in the ω-bromoxylenes and iodophenols. Again the greater stability of the fluorine octet/

octet would account for the greater inducing influence of fluorine as compared with bromine and chlorine. As little can be said as regards the respective stability of the other halogen octets except that they ought to be more unstable than that of fluorine, correspondingly little can be said about expectations as regards their inducing power. The position of oxygen is however quite unique. It is still difficult to say why this atom should be so powerful in its inducing influence. A different mechanism of reaction or transmission of the effect, such as conjugation of the oxygen atom with the nuclear carbon atoms must be postulated. The influence would then be transmitted along three electrons, a configuration through which induced effects are most effectively transmitted.

The difference between the influence of oxygen and fluorine however emphasises an important point, namely that the electro-negative nature of an atom does not determine the strength with which it acts as a key atom, and therefore Ingold's assumption that when nitrogen and oxygen are combined, the oxygen is the "key-atom" (J. 1924, 125, 93) receives no confirmation whatever from these investigations.

Lapworth suggests (loc. cit) that if, in an organic molecule, one of the atoms (the "key-atom") rises or falls in co-valency, then a "constraint" is/

is readily set up in the molecule with a resulting redistribution of the valency forces, and appearance of increased and decreased partial valencies on alternate atoms. The most effective "key-atoms" are those which readily rise or fall in co-valency such as nitrogen and oxygen, and this has been substantiated in the case of the oxygen atom. The halogens are admittedly much weaker, a fact which also receives a full explanation from Lapworth's suggestions with perhaps the exceptional position of fluorine once more, the tendency of which to rise in covalency is almost nil. Compounds of the type $H - \left[F - H - F\right]$ may be regarded as cases where F exerts a covalency greater than one, but it is doubtful if this type of association takes place during the reactions investigated here. The marked influence of the hydrogen of the methyl group is due to the tendency of the hydrogen atoms to contribute their electrons to the octet surrounding the carbon atom. This results in the setting up of the "constraint" and a redistribution of the valency forces in the molecule, a view which is quite in keeping with the experimental results and the views of Robinson and Kermack.

The theoretical derivation of the principle is a matter of difficulty, since the cause of valency is not yet finally agreed upon. In conclusion a recent suggestion of Robinson (Chemistry and Industry 1925, pp. 113) may be considered. He points out that in the/

the course of activation of a reacting molecule the electronic changes involved are equivalent to the passage of a small electric current from the key atom to the reacting atom or vice versa, which may however be side tracked by systems of high capacity. This suggestion receives support in many instances in these investigations and as an example the case of p-methoxybenzyl bromide may be quoted. Here the current is very effectively transmitted to the bromine atom [this probably means the appearance of an electron (Kermack and Robinson) or of a partial valency (Lapworth) on the reacting atom] unless a system of high capacity (a nitro group) is present to side track it, as in 3-nitro-4-methoxybenzyl bromide. Such an influence is apparently most effectively transmitted through a benzene nucleus which as these investigations have shown appears to act as an "amplifier", and the fact that in benzene the carbon atoms are to be regarded as joined together by three electrons (Thomson Phil. Mag., 1921, (VI), 41, 535, Robinson and Kermack loc. cit.) again suggests that this arrangement is the one which most efficiently transmits polarity effects along a series of carbon atoms.

Summary of Subsidiary Thesis presented

for the degree of D.Sc.

THE CONDENSATION OF DIPHENYLFORMAMIDINE WITH PHENOLS.

An investigation carried out in collaboration with John Haldane, Ph.D., directed by

JOHN B. SHOESMITH, M.Sc.(Vic.)

under the supervision of

Prof. Sir Jas. Walker, F.R.S.

Department of Chemistry

Edinburgh University.

May 1925.

The condensation which takes place between diphenylformamidine and compounds containing an active methylene group has been extended to various phenols, and in this way a new synthesis of aromatic ortho-hydroxyaldehydes brought about. The reaction which takes place was found to be as follows

$$(HO)_x\ R.H + CH(NC_6H_5)(NHC_6H_5) \longrightarrow (HO)_x\ R.CH = NC_6H_5 + C_6H_5NH_2$$

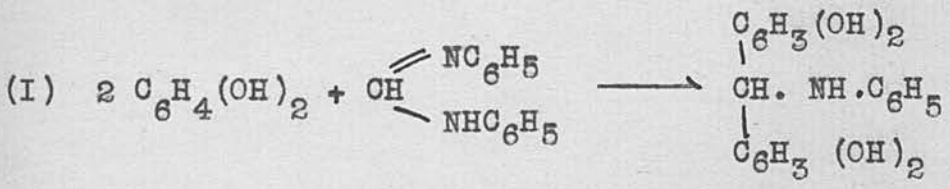
in which R is a benzene or naphthalene nucleus and x is 1 to 3.

The intermediate compounds isolated were 4:6-dihydroxyisophthalylidenebisaniline from resorcinol and diphenylformamidine and 2-hydroxy-1-naphthylidene-aniline from β naphthol and diphenylformamidine. Intermediate compounds were not isolated from resorcinol monomethyl ether, guaiacol, pyrogallol, phenol, the isomeric cresols and α naphthol, although the reaction products in all these cases and also resorcinol and β naphthol gave the corresponding hydroxy aldehydes on hydrolysis

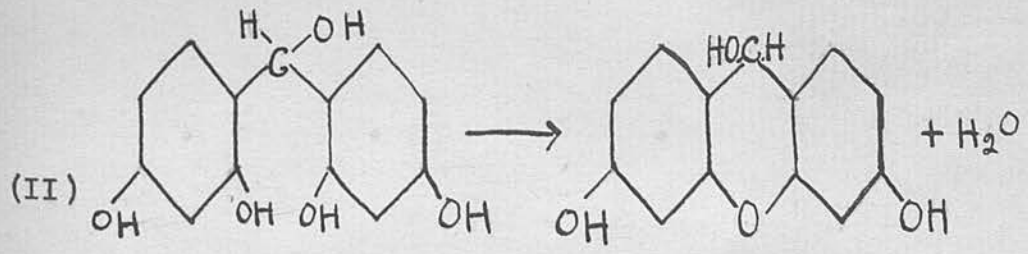
$$(HO)_x\ R.CH = NC_6H_5 + H_2O \longrightarrow (HO)_x\ R.CHO + C_6H_5\ NH_2$$

A long series of experiments were undertaken and the best conditions for isolating aldehydes in all these cases determined. The preparation of β-resorcylaldehyde received special attention as the formation of resin and isophthalaldehyde can be avoided when special precautions are taken.

The condensation of diphenylformamidine and resorcinol might conceivably take place between two molecules of resorcinol and one of the formamidine. This would result in a reaction as follows



This on hydrolysis would give 2:4:2':4' tetrahydroxydiphenylcarbinol which might then go over into the corresponding 3:6-xanthhydrol as follows



This suggestion is borne out by the deep red-green fluorescence noticable in all the alkaline solutions of the condensation products from diphenylformamidine and/

and resorcinol. In order to see if this is so, the compound was synthesised by the reduction of 3:6-dihydroxyxanthone prepared from 2:4:2':4'-tetrahydroxybenzophenone which was in turn synthesised as in publication VIII. The resulting compound dissolved in alkali with a very deep red green fluorescence showing that the xanthhydrol is actually produced during this condensation.

Publication I

RECIPROCAL INDUCED POLARITY EFFECTS IN CRESOLS AND THEIR DERIVATIVES. PROPERTIES OF THE ISOMERIC METHOXYBENZYL BROMIDES.

BY

ARTHUR LAPWORTH

AND

JOHN BALDWIN SHOESMITH.

From the Transactions of the Chemical Society, 1922. Vol. 121.

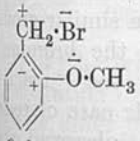
IV.—*Reciprocal Induced Polarity Effects in Cresols and their Derivatives. Properties of the Isomeric Methoxybenzyl Bromides.*

By Arthur Lapworth and John Baldwin Shoesmith.

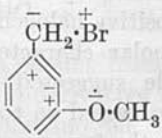
tal influence which one atom or group exerts on the pro- of another elsewhere in the same molecule is doubtless complex and probably the resultant of several simultaneous . There appear to be, for example, (*a*) general polar effects, atoms tending to raise or lower the affinity of the molecule ole for an electric charge (Flürscheim, T., 1909, **49**, 1627;

droxyl groups the induced polarities are in the opposite sense
e natural polarities; this is in agreement with the measure-
of Dawson and Mountford (T., 1918, **113**, 937), who found
m-cresol has a higher ionisation constant than either *o*- or
sol. It was further suggested that, as the *o*-hydroxyl group
arated from the methyl group by fewer intervening atoms
the *p*-hydroxyl group, the lower ionisation of *o*-cresol as
ared with *p*-cresol is explained; the authors now think,
ver, that much value must not be attached to this point, since
her cases, including those dealt with in the present paper,
der which di-derivatives of benzene showing induced polar
usually take is para-ortho-meta, whilst an induced polar
alone would be expected to give rise to the order, ortho-para-
The frequent displacement of the ortho-compounds from
would appear to be their natural positions may be due, either
special force of steric effects in the ortho-positions or to a
cy of activated forms to assume *p*-quinonoid rather than
inoid configurations.

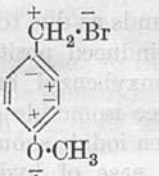
agreement between the requirements of the principle of
alternate polarities and the observed properties of the three
being so striking, the authors decided to direct their attention
possibility of demonstrating that such effects may be recip-
and that the elements of the hydroxyl group—more particu-
the oxygen atom—may in turn affect the properties of the
groups in similar alternating manner. Thus the hydrogen
of the methyl group in *m*-cresol should exhibit an enhanced
e polar character in virtue of the position of the strongly
ely polar oxygen. Definite polar character in hydrogen
y attached to carbon is, however, not easy to detect except
ciation with certain complexes, and it appeared likely that
nt could be demonstrated more readily by studying the pro-
s of halogen in a similar position. Great practical difficulties
ted with the properties of hydroxybenzyl haloids also made
ssary to use their methyl ethers, the methoxybenzyl bromides.



Ortho.



Meta.

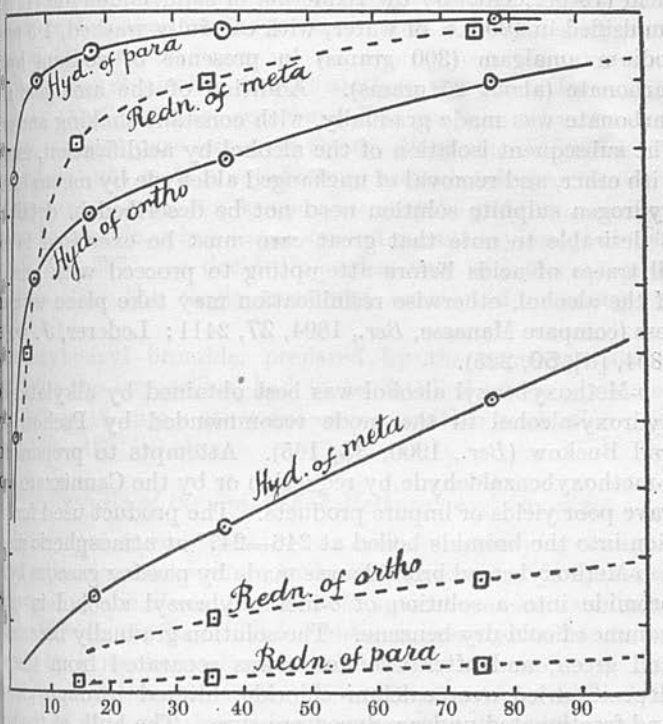


Para.

ese three compounds the oxygen atoms, acting as negative
oms, were expected to give rise to the induced polarities
ted in the formulæ. The *o*- and *p*-isomerides thus contain

principle of induced alternate polarities when sources of con- can be to a considerable extent eliminated.

he following figure are shown in continuous lines curves which spond with one series of measurements made on the hydrolysis three isomerides under comparable conditions, and three , in interrupted lines, corresponding with a series of measure- on their reduction by hydrogen iodide. The inversion



Time (minutes).

Methoxybenzyl bromides.
Full lines—Curves of hydrolysis.
Interrupted lines—Curves of reduction.

order of reactivity in passing from one reaction to the other, ar separation of the *m*-derivative from its isomerides, which greatly differ from one another in both reactions, is clearly

EXPERIMENTAL.

Preparation of the Methoxybenzyl Bromides.

g series of experiments which were made by one of us with ject of preparing the three isomeric methoxybenzyl alcohols

(50 per cent. of the theoretical) by reducing the aldehyde, nded in water, with sodium amalgam. The methylation ydroxybenzyl alcohol (1 mol.) by the action of methyl sulphate nols.) and potassium hydroxide dissolved in methyl alcohol gave yields approximating to 50 per cent. of the theoretical; a larger proportion of alkylating agent, a product contaminated much dialkyl derivative is formed.

Methoxybenzyl bromide was prepared in much the same way at above described for the preparation of the ortho-compound. ed at 127°/16 mm.*

Methoxybenzyl alcohol (anisyl alcohol) was made from anis- yde by the Cannizzaro reaction. The product, after one such ent, was not pure (compare Späth, *Monatsh.*, 1913, **34**, 1995) and did not yield a satisfactory bromide; it was therefore necessary to treat it a second time with 25 per cent. alcoholic ium hydroxide, when the recovered *p*-methoxybenzyl alcohol at 255—257°—or decidedly higher and within a narrower than after the single treatment considered necessary by (*loc. cit.*).

Methoxybenzyl bromide, prepared by the same method as sed for the isomerides, had to be distilled under a pressure ceeding 16 mm., otherwise decomposition took place. It at 128—129°/16 mm.

(a) *Hydrolysis of the Emulsified Methoxybenzyl Bromides.*

following data were obtained by merely emulsifying the three ides with standard sodium hydroxide at constant temperature termining the diminution in titre against standard acid after intervals of time. The emulsions were agitated during lysis by a mechanical stirrer of constant efficiency. As the ns were not homogeneous, the results cannot be utilised for lation of true relative velocity constants, but the numbers te very clearly the great differences in reactivity of the three ides and cannot be explained by differences in solubility

the following tables, the numbers under t are the intervals e in minutes which had elapsed since the initial mixing and withdrawal of the samples for analysis, whilst those under x e percentage quantities of the compound hydrolysed during intervals, calculated on the assumption that one molecular tion of sodium hydroxide is neutralised by the hydrolysis olecule of the bromide—an assumption justified by the results

* It is worthy of note that of the three methoxybenzyl bromides, the compound has the most marked lachrymatory properties.

nutes, but being less rapid with the *o*- than with the *p*-com-
A regular curve of hydrolysis was obtained in this as in
lowing instance and all previous ones, with the *m*-isomeride,
, and 59 per cent. being hydrolysed in thirty-five, one hundred
fty-five, and three hundred and fifteen minutes, respectively.
same remarks apply to the observations made with $N/10$-
hydroxide in 95 per cent. alcohol; but all the changes took
more rapidly; with the *m*-isomeride, 37, 80, and 96 per cent.
ydrolysed in thirty-five, one hundred and fifty-five, and three
ed and fifteen minutes, respectively.

duction of the Methoxybenzyl Bromides by Means of Hydrogen Iodide.

tendency of these bromides, especially the para-compound,
nify in presence of moist hydrogen iodide led to the use of
ous acetic acid as solvent. Hydrogen iodide was prepared
ght modification of the method recommended by Norris and
ll (*Amer. Chem. J.*, 1896, **18**, 97), freed from iodine by passing
ugh a U-tube containing moist red phosphorus distributed
ss-wool, and dried by means of phosphoric oxide. The
n employed in the reductions contained 0·4464 gram of
r c.c.

reactions were carried out as follows in a thermostat main-
at 25°.

uantity of the methoxybenzyl bromide was weighed in a small
ed vessel, 5 c.c. of the hydrogen iodide solution were added,
duction was allowed to proceed. Aliquot portions of the
n were removed at intervals, diluted with a large bulk of
and titrated with $N/10$-sodium thiosulphate.

he following tables are given, under t, the time, in minutes,
had elapsed between the initial mixing and the withdrawal
sample of solution, and, under x, the percentage quantity
ide reduced, calculated on the assumption that the iodine
ed was produced in accordance with the equation.

o-Methoxybenzyl bromide. Weight taken in gram. (i) 0·772; (ii) 0·395.

(i)		(ii)	
t.	*x.*	*t.*	*x.*
5	1·0	5	0
15	2·7	15	3·2
35	10·5	35	7·0
75	16·3	75	10·9
195	26·8	275	23·5

Publication II.

THE PREPARATION OF THE ISOMERIC METHOXYBENZYL BROMIDES.

BY

JOHN BALDWIN SHOESMITH

From the Transactions of the Chemical Society, 1923. Vol. 123.

VIII.—*The Preparation of the Isomeric Methoxybenzyl Bromides.*

By John Baldwin Shoesmith.

Isomeric methoxybenzyl bromides were first obtained by (*Monatsh.*, 1913, **34**, 1995), who employed in their preparation actions summarised in the following scheme :

$$C_6H_4\langle^{OH}_{CHO} \xrightarrow[KOH]{Me_2SO_4} C_6H_4\langle^{OMe}_{CHO} \xrightarrow[KOH]{25\%} C_6H_4\langle^{OMe}_{CH_2\cdot OH} \xrightarrow{HBr} C_6H_4\langle^{OMe}_{CH_2Br}$$

present communication gives details of methods which were ed in order to obtain the intermediate compounds in better

possible
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nate at 170—180° until a gain in weight of 60 per cent. of the
l compound had taken place. Slight hydrolysis of the
nate occurred in all cases, and an odour of carbonyl chloride
erceptible. To prevent unnecessary tarring at this stage, the
nates had been freed from chloroformate by recrystallisation
alcohol. The chlorinated compounds show a tendency to
llise when kept at room temperature for some time, but
pts to separate pure compounds have met with little or no
ss.

Methoxybenzyl Bromide. Hydrolysis of Dichlorinated o-Tolyl
nate.—This product was found to contain 36·6 per cent. of
ne hydrolysable with alcoholic potash ($C_{15}H_{10}O_3Cl_4$ requires
37·3 per cent.).

Hydrolysis with formic acid. Twenty-five grams of the
s chlorinated carbonate were boiled with 200 c.c. of 80 per
formic acid for two hours, hydrogen chloride being evolved.
eep red solution was diluted with 500 c.c. of water, and the
aldehyde * distilled in steam and purified by extraction with
and conversion into the bisulphite compound. A yield of
cent. of the theoretical was thus obtained.

Hydrolysis with formic and oxalic acids. Twenty-five grams
oil were boiled with a mixture of 75 c.c. of 80 per cent. formic
nd 35 grams of anhydrous oxalic acid. The aldehyde was
separated and purified as before. The yield was slightly
red.

Hydrolysis with sodium acetate. Twenty-five grams of the
re boiled with 75 c.c. of alcohol, 15 grams of anhydrous sodium
te, and 25 grams of sodium acetate crystals for two hours,
m chloride being precipitated. The alcohol, now contaminated
thyl acetate, was as far as possible distilled off, the residue
d with five parts of water and acidified, and the aldehyde
ed in steam. This method gave by far the best yield (60 per
of purified aldehyde.

Hydroxybenzyl Alcohol.—Twelve grams of redistilled salicyl-
de were emulsified by shaking with 100 c.c. of water, and
rams of 1·5 per cent. sodium amalgam added in small quantities.
pent amalgam was continuously removed and excessive
ity was avoided by the gradual addition of 25 grams of
m bicarbonate. When the yellow colour due to the presence

* When this aldehyde and related aldehydes derived from resorcinol are
with Schiff's reagent, the normal reaction appears to be the precipita-
yellow hydrated Schiff's bases, and not the formation of the usual
red dye (Wieland and Scheuing, *Ber.*, 1921, **54**, [*B*], 2527). This
is undergoing further investigation.

cralic acids gave in each case a yield of 40 per cent. of the
etical. Sodium acetate and alcohol gave a yield of 50 per cent.
Methoxybenzaldehyde (*Anisaldehyde*). — Nitric acid alone
urs, *Annalen*, 1845, **56**, 307) or diluted with acetic acid
le, *Bull. Soc. chim.*, 1899, [iii], **21**, 1076) oxidised anethole too
ily to produce anisaldehyde in good yield.
ly grams (3 mols.) of anethole, emulsified in 500 c.c. of water
0 grams of kieselguhr, were oxidised by adding a solution of
ams (more than 4 mols.) of chromic acid in 80 c.c. of water so
that the temperature did not rise above 28°. A faint odour
taldehyde was perceptible. The mixture having been stirred
alf an hour, when the temperature was once more normal, a
ooled solution of 80 grams (6 mols.) of sulphuric acid in 100 c.c.
ter was added during one and a half hours. The temperature
mixture gradually rose to 27° and the colour changed to green.
the temperature had fallen to 16—18°, the kieselguhr was
d off and washed twice with ether. The main solution was
n four times with ether, the mixed ethereal extracts were
d free from anisic acid with 5 per cent. caustic soda solution,
of the ether was evaporated, and the residual impure anis-
yde converted into the bisulphite compound, which was filtered,
ed, and washed free from unoxidised anethole with alcohol.
ldehyde, liberated from a warm, aqueous solution of the
hite compound by concentrated sodium carbonate solution,
xtracted with ether, dried, and distilled. Half the expected
yde was obtained in a pure condition.
e semi-oxidised mixture which was extracted by alcohol from
isulphite compound gave a further 5 per cent. of aldehyde.
ic acid (8 per cent.) was liberated by acid from the alkali
ings above.
idation of Anethole by Sodium Chlorate.—A solution of 4·5 grams
ethole (3 mols.) in a mixture of 80 c.c. of acetone, 40 c.c. of
cent. sodium chlorate solution (2 mols.), and 4 c.c. of 2 per
osmic acid solution was boiled at 65° for ten hours, 2 c.c. of the
ion being titrated at regular intervals with silver nitrate
ion. At the end of the time stated, the quantity of chloride
dark solution was constant, that is, the reaction

$$\text{MeO}\cdot\text{C}_6\text{H}_4\cdot\text{CH}:\text{CHMe} + 2\text{NaClO}_3 \longrightarrow 3\text{OMe}\cdot\text{C}_6\text{H}_4\cdot\text{COH} + 3\text{CH}_3\cdot\text{CHO} + 2\text{NaCl}$$

complete. The acetone was then evaporated off and the
yde isolated from the residue as in the previous case, 2·2 grams
pure aldehyde being obtained along with a trace of anisic acid.
periments carried out since the last communication (Lapworth

Publication III

REDUCTION OF *m*-METHOXYBENZYL BROMIDE BY HYDROGEN IODIDE.

BY

JOHN BALDWIN SHOESMITH.

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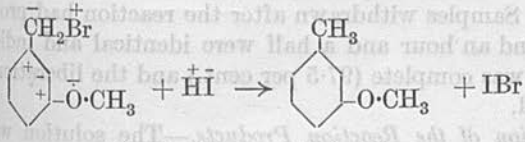
rom the Transactions of the Chemical Society, 1923. Vol. 123.

XXIX.—*Reduction of* m-*Methoxybenzyl Bromide by Hydrogen Iodide.*

By John Baldwin Shoesmith.

recent paper (Lapworth and Shoesmith, T., 1922, **121**, 1391), ase of replacement of bromine in the three isomeric methoxy- l bromides was considered from the point of view of the ple of induced alternate polarities. It was shown that whilst alogen in *m*-methoxybenzyl bromide was less readily removed kali than was the halogen in the *o*- and *p*-isomerides, yet the meride was the most readily attacked by hydrogen iodide, e being especially rapidly liberated when *m*-methoxybenzyl ide was dissolved in glacial acetic acid containing hydrogen e at 25°. The liberation of free iodine was interpreted as due to tion of the methoxybenzyl bromide in accordance with the ions—

(I.)



(II.) $$IBr + HI \longrightarrow HBr + I_2.$$

ralised with solid sodium carbonate (during this operation the r of methyl iodide was very marked), and then extracted with The ethereal solution was extracted thrice with 10 per cent. potash solution, dried over anhydrous sodium sulphate, the removed, and the residual oil fractionated. The main fraction, 180—200°, weighed 0·90 gram. On refractionating, 0·50 gram between 175° and 185°. This alkali-insoluble oil was *m*-tolyl ether (b. p. 177°) and was further identified by oxidising a portion with alkaline permanganate to *m*-methoxybenzoic and by demethylating to *m*-cresol as described below.

m the caustic potash solution 0·70 gram of *m*-cresol, b. p. 200°, was isolated in the usual way. It gave a bluish-violet with ferric chloride solution, and a precipitate with bromine which crystallised from aqueous alcohol in white needles ng at 81—82°, alone or mixed with an authentic specimen of mo-*m*-cresol.

thylation of the m-*Tolyl Methyl Ether.*—The 0·50 gram of obtained in the first experiment was mixed with 5 c.c. of the acid–hydriodic acid solution and kept for five hours at 25°. odine was liberated. The mixture was neutralised, etc., as and a small trace of the ether was still unchanged; 0·17 of *m*-cresol was isolated and identified as previously described. liberation of iodine took place when a mixture of 0·50 gram of iodide with 5 c.c. of the acetic acid–hydriodic acid solution ept for four hours.

author wishes to thank Prof. A. Lapworth for valuable sions *re* the communication of this note, and also the Earl of Research Fund Committee for a grant which defrayed the some of the chemicals and apparatus used.

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EDINBURGH UNIVERSITY. [*Received, August 27th,* 1923.]

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Publication IV

POLARITY EFFECTS IN AROMATIC HALOGEN COMPOUNDS.

BY

JOHN BALDWIN SHOESMITH,

ARTHUR CLEMENT HETHERINGTON,

AND

ROBERT HENRY SLATER.

From the Transactions of the Chemical Society, 1924. Vol. 125.

XIII.—*Polarity Effects in Aromatic Halogen Compounds.*

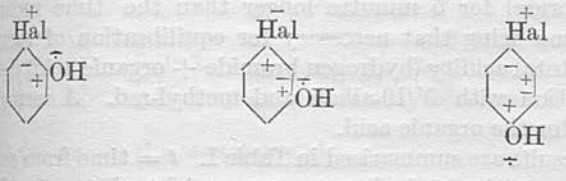
By John Baldwin Shoesmith, Arthur Clement Hetherington, and Robert Henry Slater.

investigations of Lapworth and Shoesmith (J., 1922, **121**, and Shoesmith (J., 1923, **123**, 2828) have been continued and s been found possible to predict differences in reactivity as ds hydrolysis and reduction by hydrogen iodide of the position erides of a number of halogen-substituted benzenoid compounds simple application of the principle of induced alternate ities.

addition to the induced alternate polarity influences in a ule two other factors must be considered: (*a*) general polar nces, which are due to substituent atoms or groups and affect olecule as a whole (Flürscheim, J., 1909, **95**, 718; Lapworth, *Manchester Phil. Soc.*, 1920, **64**, No. 3; Kermack and Robin- J., 1922, **121**, 428; Lapworth and Shoesmith, *loc. cit.*; nson, *Ann. Reports*, 1922, 99), and (*b*) spatial and steric factors operate generally in the aromatic series in the ortho-iso- es. When discussing differences in reactivity, it is therefore sary to consider closely related compounds such as isomerides er to eliminate (*a*) and meta- and para-isomerides to elimi- (*b*).

has also been possible to show that 3-nitro-4-hydroxybenzyl ide is more easily hydrolysed by aqueous alcohol than tro-4-methoxybenzyl bromide (Table III). Hydriodic acid ces the nitro-group and therefore the change of order of tivity with change of reagent could not be investigated.

he halogen atoms in the halogenated phenols are to be regarded eing situated one place nearer the " key-atom " than are those e corresponding methoxybenzyl bromides. Thus the order of of reduction of such phenols should be, and actually is, *p* and , the reverse of that already found in the latter series.



he order in which halogen atoms are removed from such com- ds is *p*-iodo > *o*-iodo > *p*-bromo > *o*-bromo > *p*-chloro (Tables IV V). The meta-isomerides show no tendency to reduce.* 4-Iodo- inol reduces far more rapidly than the iodophenols. It is, of se, recognised that in this series a quinonoid change could t or addition of reducing agent might precede reduction, but ltimate result is that which would be expected on the theory duced alternate polarities.

EXPERIMENTAL.

[With A. C. HETHERINGTON.]

motoluic Acids.—The ω-bromotoluoyl bromides from which rresponding ω-bromotoluic acids were obtained were prepared vies and Perkin's method (J., 1922, **121**, 2202). The reactions mmarised as follows.

$$Me{\cdot}C_6H_4{\cdot}CO_2H \xrightarrow{SOCl_2} C_6H_4Me{\cdot}COCl \xrightarrow{Br} CH_2Br{\cdot}C_6H_4{\cdot}COBr \xrightarrow{HCO_2H} CH_2Br{\cdot}C_6H_4{\cdot}CO_2H.$$

romo-*m*-toluoyl bromide has b. p. 160—165°/14 mm. and 23—25°. *ω-Bromo-p-toluoyl bromide* has b. p. 165—170°/12 and m. p. 39—40° (Found : Br = 54·55. $C_8H_6OBr_2$ requires 57·55 per cent. The low result is due to hydrolysis by spheric moisture).

nzen and Stäuble (*J. pr. Chem.*, 1921, [ii], **103**, 352) have prepared o-α-naphthol from 2 : 3 : 4-trichloro-α-naphthol by reduction with ic acid. The resulting monochloro-compound is quite stable to the g agent.

—Approximately 0·10 gram of the acid, dissolved in 15 c.c. of
l acetic acid, was heated with 10 c.c. of constant-boiling
odic acid in the vapour of boiling toluene. After a definite
val the liberated iodine was titrated with thiosulphate. A blank
riment to ascertain the amount of air oxidation was carried
n each occasion.
e results are summarised in Table II; t, w, and x have the same
icance as before.

TABLE II.

o-Compound.		m-Compound.		p-Compound.		Benzyl bromide.	
w.	x.	w.	x.	w.	x.	w.	x.
0·1026	11	0·1010	24	0·1044	49	0·1518	34
0·1223	24	0·1003	43	0·1033	73	0·1549	55
0·1161	42	0·1001	68	0·1001	91	0·0900	78
0·0931	51	0·1066	86	0·0901	99	0·1103	92

e behaviour of the *o*-compound is again abnormal owing to
lide formation.
duction of the isomeric toluic acids for 6 hours under the same
itions as those in the previous experiment takes place to the
wing extents: *o*- 0·16, *m*- 0·49, *p*- 0·43 per cent.
rrections for such small quantities have not been applied to
romo-acid reduction figures.

Nitrobenzyl Bromide.—*o*-Nitrobenzyl chloride (Haeussermann
Beck, *Ber.*, 1892, **25**, 2445) (1 part) was boiled with concentrated
ous sodium acetate (2 parts) and the *o*-nitrobenzyl acetate
rted into *o*-nitrobenzyl alcohol by boiling 50 per cent. sulphuric
. This alcohol was crystallised from hot water and, when mixed
the calculated quantity of phosphorus pentabromide, readily
o-nitrobenzyl bromide, light yellow plates, m. p. 45·5°, from
petroleum (Found: Br = 36·82. $C_7H_6O_2NBr$ requires
37·00 per cent.).

Nitrobenzyl bromide was prepared from *m*-nitrobenzyl alcohol
hydrogen bromide in dry benzene, two layers forming. The
als that separated from the lower layer and the further quantity
ned by evaporating the benzene were recrystallised from light
leum; the product had m. p. 57°.

Nitrobenzyl bromide, prepared by Lyons and Reid's method
mer. Chem. Soc.*, 1917, **39**, 1729) and recrystallised several
from light petroleum to remove benzal bromide, melted at

Nitro-4-hydroxybenzyl bromide was obtained from the corre-
ing alcohol, which was prepared by Stoermer and Behn's
od (*Ber.*, 1901, **34**, 2459). The alcohol crystallised from water
ight yellow needles, m. p. 97°. A solution of these in the

am and obtained in 50 per cent. yield from the dried, ethereal t of the distillate. Its solution was diazotised (Varnholt, *Chem.*, 1887, **36**, 27), heated, filtered, and the chlorophenol ted with ether and purified by distillation.

Bromophenol, prepared in a similar manner from *m*-bromo-benzene [bromination of nitrobenzene (Wheeler and McFarland, *Chem. J.*, 1897, **19**, 366) is much more satisfactory than ation], distils at 125—127°/12 mm. (Diels and Bunzl, *Ber.*, 38, 1495, give b. p. 135—140°/12 mm.).

Iodophenol was obtained from *m*-nitroaniline (Nölting and er, *Ber.*, 1887, **20**, 3020), the intermediate *m*-iodonitrobenzene reduced with iron and hydrochloric acid.

Iodoresorcinol was prepared by Stenhouse's method (*Annalen*, 171, 311). The compulsory use of 220 grams of litharge mate 20 grams of resorcinol prevents reduction of the iodo-inol by the hydriodic acid produced in the reaction.

action of the Halogenated Phenols.—Approximately 0·6 gram phenol was made up to 2·5 c.c. with glacial acetic acid in a stoppered measuring cylinder, 2·5 c.c. of glacial acetic acid ining 0·410 gram of hydrogen iodide per c.c. (Lapworth and mith, *loc. cit.*) were added, and the whole was well mixed and in a thermostat at 25°. One c.c. portions were withdrawn inite intervals and the liberated iodine was estimated with iphate. A comparison of the ease of reduction of *o*-iodo-, *p*-iodophenol and *p*-bromophenol was thus obtained. The s are summarised in Table IV.

s method did not furnish a satisfactory reduction curve for ophenol, but the above results having been obtained for the enols and *p*-bromophenol at 25° a series of experiments at 78° ted the comparison : 10 c.c. of a standard solution of the ated phenol in glacial acetic acid and 10 c.c. of constant-hydriodic acid were heated together in the vapour of boiling ; the liberated iodine was estimated as before. The results marised in Table V.

ables IV and V, x has the same significance as before, and t time in minutes from the commencement of the experiment. le IV, w is the total weight of the phenol used, whilst in Table resents the weight used in each reduction.

lorophenol was the only one of the chloro-isomerides to show uction under the different conditions described, and this was ght. A solution of the phenol in glacial acetic acid con-0·37 gram of hydrogen iodide per c.c. showed a reduction 10 per cent. after 4 hours. Complete reduction was never d.

Publication V

POLARITY EFFECTS IN THE ISOMERIC ω-BROMOXYLENES AND ISOMERIC IODOTOLUENES.

BY

JOHN BALDWIN SHOESMITH

AND

ROBERT HENRY SLATER.

From the Transactions of the Chemical Society, 1924. Vol. 125.

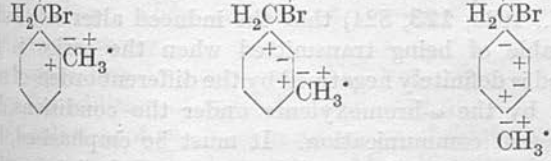
Reprinted from the Journal of the Chemical Society,
Volume 125, 1924.

CV.—*Polarity Effects in the Isomeric ω-Bromoxylenes and Isomeric Iodotoluenes.*

By John Baldwin Shoesmith and Robert Henry Slater.

n investigations of this series (Lapworth and Shoesmith, J., 121, 1392; Shoesmith, J., 1923, **123**, 2838; Shoesmith, erington, and Slater, this vol., p. 1312), which have so far n confined to the influence which oxygen exerts as a "key-m" on halogen atoms in various benzenoid compounds, have n extended and the influence of the hydrogen atoms in a methyl p in such compounds ascertained.

y the same methods as were employed in the first investigations, s now been possible to show that the isomeric ω-bromoxylenes t in an anticipated order. The order of ease of hydrolysis should and $o>m$ and of reduction by hydrogen iodide $m>o$ and p.



10-Chloro-5-benzoyl-5 : 10-dihydrophenarsazine, $C_6H_5\cdot CO\cdot N(C_6H_4)_2AsCl$, ot been previously described. It is prepared from 10-chloro-5 : 10-di-phenarsazine in an excess of boiling benzoyl chloride, diluted with dry e, for 10 hours. After removal of excess xylene the dark coloured s oil is allowed to stand for 2 days and the solid material filtered off. ubstance is obtained in colourless, hard crystals, m. p. 180—181° on isation from benzene (Found : As = 19·7. $C_{19}H_{13}ONClAs$ requires 19·64%).

Thorpe (J., 1911, **99**, 2185, and onwards) cannot be extended to trace the observations on the differences of ease of reducibility the methoxybenzyl bromides (Lapworth and Shoesmith, *loc. cit.*) of the halogen compounds described in the present communic-ation.

EXPERIMENTAL.

Preparation of the ω-Bromoxylenes.—These were all obtained by general method summarised as follows :—

$$\underset{\text{(I.)}}{CH_3\cdot C_6H_4\cdot NH_2} \longrightarrow \underset{\text{(II.)}}{CH_3\cdot C_6H_4\cdot CN} \xrightarrow[\text{alcohol}]{\text{Na in}} \underset{\text{(III.)}}{CH_3\cdot C_6H_4\cdot CH_2\cdot NH_2} \xrightarrow{HNO_2} \underset{\text{(IV.)}}{CH_3\cdot C_6H_4\cdot CH_2\cdot OH} \xrightarrow[\text{dry benzene}]{\text{HBr in}} \underset{\text{(V.)}}{CH_3\cdot C_6H_4\cdot CH_2Br}$$

The toluidines (I) were converted into the corresponding toluo-nitriles (II) in the usual manner, and the latter purified by dis-tillation in steam. They had b. p., *o*- 202—204°, *m*- 210—212°, and *p*- 215—217°, respectively.

The nitriles were reduced to the tolylmethylamines (III) by means of sodium and alcohol (compare Kröber, *Ber.*, 1890, **23**, 3; Sommer, *ibid.*, 1900, **33**, 1073). Sodium (100 gms.) was added, through an upright condenser, to a boiling solution of the nitrile (30 gms.) in perfectly dry alcohol (1 litre). When all the sodium had dissolved, the reduction mixture was diluted with water, acidified with hydrochloric acid, and the alcohol distilled in steam. The tolylmethylamine liberated from the residual acid solution by sodium hydroxide was distilled in steam, extracted with ether, and the distillate with ether, dried over sodium sulphate, and purified by distillation.

The yields of the *o*-, *m*-, and *p*-tolylmethylamines obtained by the general method were, *o*- 50%, *m*- 30%, and *p*- 60% of the theoretical quantity. They distilled at 200—202°, 198—200°, and 196—196°, respectively.

The corresponding tolylcarbinols (IV) were obtained from the diazo-compounds by the addition of twice the necessary quantity of sodium nitrite to a solution of the base in an excess of dilute hydrochloric acid. Nitrogen was evolved at once. After 12 hours, the reaction was completed on the water-bath. The carbinol, removed from the reaction mixture with ether, was distilled in steam, and obtained crystalline from the ethereal extract of the distillate. The yields were *o*- 50%, *m*- 70%, and *p*- 40%. *o*-Tolylcarbinol, m. p. 33°, b. p. 113—114°/9 mm.; *m*-tolylcarbinol, b. p. 108—111°/10 mm.; *p*-tolylcarbinol, m. p. 60°. The poor yields of the ortho- and para-

TABLE II.

Ortho-compound. $w=0{\cdot}5862$ gm. x.	Meta-compound. $w=0{\cdot}5537$ gm. x.	
—	17·9	The para-isomeride did not reduce
2·5	25·6	under these conditions, and iodine
4·2	36·5	corresponding to 2 per cent. reduc-
8·2	50·8	tion was liberated from benzyl
12·1	83·9	bromide.

ed to be the corresponding iodo-derivatives; ω-iodo-*o*-xylene, 33—34°, ω-iodo-*p*-xylene, m. p. 46—47° (compare Pavlovsky, *Phys. Chem. Soc.*, 1911, **43**, 214), and benzyl iodide, m. p. Estimations of the hydrolysable iodine confirmed this.

addition to the solid which was obtained from the reduction ct of the ortho-compound a small drop of oil was observed, it was not possible to identify it owing to the very small ntity which separated out.

Xylene was isolated from the reduced meta-isomeride in the ving way. The reduction mixture was poured into excess of , decolorised by the addition of sodium thiosulphate, and the neutralised with sodium hydroxide. The whole was extracted ether and from the ethereal extract an oil (1·5 gm.) was ed which distilled between 135—150°. When redistilled, it d at 135—143°. It was identified by its density (0·857 at 16°) s trinitro-derivative, m. p. 181—182°, which did not depress melting point of an authentic specimen of trinitro-*m*-xylene.

Reduction of the Iodotoluenes at 25°.

e iodotoluenes were prepared from the toluidines. The ortho- ide distilled at 205° and the para at 211° (m. p. 35°).

order to obtain the meta-isomeride perfectly free from ortho- ound, *m*-nitrotoluene was purified by means of ethyl oxalate odium methoxide as described by Reissert (*Ber.*, 1897, **30**,). The pure *m*-nitrotoluene (m. p. 16°, b. p. 231°) was reduced iron filings and a small quantity of acetic acid (see also mith, Hetherington, and Slater, *loc. cit.*). The toluidine, distilled at 203°, was converted into *m*-iodotoluene, b. p. in the usual way. The explosions which took place during ast preparation, especially when it was carried out on a ately large scale, are noteworthy, and small-scale experiments s. of *m*-toluidine) are to be recommended.

e iodotoluenes were reduced under the same conditions as the ω-bromoxylenes, and in Table III, t is the time in days

Publication VI

NDENSATION OF DIPHENYLFORMAMIDINE WITH PHENOLS. PART I. A NEW SYNTHESIS OF β-RESORCYLALDEHYDE.

BY

JOHN BALDWIN SHOESMITH

AND

JOHN HALDANE.

From the Transactions of the Chemical Society, 1923. Vol. 123.

CIX.—*Condensation of Diphenylformamidine with Phenols. Part I. A New Synthesis of β-Resorcylaldehyde.*

By John Baldwin Shoesmith and John Haldane.

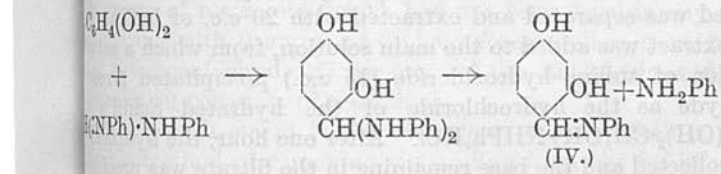
s condensation which takes place when diphenylformamidine is ted with compounds containing an active methylene group s first pointed out by Dains (*Ber.*, 1902, **35**, 2504). As an mple of this may be quoted the condensation of the amidine with acetylacetone, which probably takes place in two stages. e intermediate compound (II) is never isolated, aniline being nted at once.

$$CH(NPh)\cdot NHPh + CH_2(COMe)_2 \longrightarrow CH(NHPh)_2\cdot CH(COMe)_2 \text{ (II.)}$$
$$\longrightarrow CH(NHPh):C(COMe)_2 \text{ (III.)} + NH_2Ph.$$

ino methyleneacetylacetone (III) is isolated in almost quanti- ve yield.

his type of reaction appears to be a very general one and has n extended by Dains and his co-workers (*J. Amer. Chem. Soc.*, , onwards) to a large number of similar compounds.

he present investigation has shown that condensation also takes e between diphenylformamidine and resorcinol. Aniline is nted and a solid compound results. The course of the reaction presented thus :



(IV.)

e crude condensation product, which consists essentially of the iff's base (IV) of β-resorcylaldehyde, unchanged resorcinol, and enylformamidine, is hydrolysed by boiling caustic soda and sorcylaldehyde can thus be obtained in a very simple manner.

is, however, necessary to say that the structure to be assigned ompound (IV) is not yet decided. Its physical and chemical erties show that it is slightly different from the Schiff's base of ldehyde which was prepared by Dimroth and Zoeppritz (*Ber.*, , 35, 995) by another method.

he present communication details the method of preparing sorcylaldehyde in appreciable yield; the extension of the hod to other phenols and the constitution of the intermediate pound are reserved for further investigation.

The method of purification adopted is very much better than any olving the use of sodium bisulphite solution.

Condensation under other Conditions.—The same quantities of rcinol and diphenylformamidine were heated at 130° for one a half hours, and the hydrolysis was carried out as before. d, however, precipitated a considerable quantity of red needles, ch were characterised as the dialdehyde of resorcinol, $H_2(OH)_2(CHO)_2$, m. p. 126° (Tiemann and Lewy, *Ber.*, 1877, **10**, 1). They represented 25 per cent. of the resorcinol; a smaller ntity (25—30 per cent.) of monaldehyde was isolated from the solution, whilst the resin present represented 30—40 per cent. aldehyde was difficult to purify.

When the condensation was effected at 100° for nine hours, 40 per t. of the expected monaldehyde, a trace of dialdehyde, and 30 per cent. of the resinous compound were produced.

n increase in the quantity of resorcinol used caused a corre- ding increase in the amount of aldehyde produced.

he effect of moisture on this condensation is remarkable. The hydrated Schiff's base which is probably formed in the con- sation in presence of moisture was found to decompose at 100° he impure condition into aniline and a resin. This caused the d of monaldehyde to be very poor whenever precautions were aken to dry the resorcinol before use. Under these conditions, interesting to point out the as yet inexplicable formation of dehyde.

ive grams of resorcinol (which had not been dried in any way), ondensing with 9 grams of diphenylformamidine, gave 25 per t. of the monaldehyde, 27 per cent. of the dialdehyde, and resin esenting 20 per cent. of resorcinol.

stillation with steam in the absence of caustic alkali is not a icable method of removing the aniline from the Schiff's base uced in the condensation. This is due to the decomposition of lydrated Schiff's base by moisture at 100°, as already stated. resin obtained dissolves afterwards in caustic alkali with a deep olour, but does not appear to be a definite compound.

Summary.

Diphenylformamidine and resorcinol condense together on ng with liberation of aniline. The condensation product, olysed by caustic alkali, yields aniline and β-resorcylaldehyde. The method by which the best yields of β-resorcylaldehyde be obtained is described and the deleterious effect of moisture, long heating, and condensation at too high a temperature ied out.

Publication VII

Reprinted from the Journal of the Chemical Society, Volume 125, 1924.

CXXVIII.—*Condensation of Diphenylformamidine with Phenols. Part II. The General Nature of the Reaction.*

By JOHN BALDWIN SHOESMITH and JOHN HALDANE.

Part I (J., 1923, **123**, 2704), it was shown that the products ed by condensing resorcinol with diphenylformamidine yield, hydrolysis, β-resorcylaldehyde and 4 : 6-dihydroxy*iso*phthal- hyde. The reaction has now been extended to resorcinol omethyl ether, guaiacol, pyrogallol, phenol, the isomeric cresols, - and β-naphthols. The aldehydo-group enters in the ortho- ion to a hydroxyl group, and the yield of hydroxyaldehyde s from 60% in the case of β-naphthol to 10% from phenol, ough, in general, the primary condensation appears to be plete. The chief by-products are resins of a "bakelite" re. By this means 1-hydroxy-2-naphthaldehyde is more readily inable than by Friedländer's process (*Ber.*, 1908, **41**, 1037). rther, it is shown that the reaction takes place as assumed dy (*loc. cit.*), the intermediate products, 2-hydroxy-1-naphthyl- aniline, $OH{\cdot}C_{10}H_6{\cdot}CH{:}NPh$, and 4 : 6-dihydroxy*iso*phthalyl- bisaniline, $C_6H_2(OH)_2(CH{:}NPh)_2$, having been isolated in condensation of diphenylformamidine with β-naphthol and rinol, respectively.

EXPERIMENTAL.

insure constancy of temperature, the condensation flasks immersed in vapour from a boiling liquid. To obtain a tem- ture between 80° and 140°, a mixture of benzene, toluene, xylene was distilled until the temperature was reached and the condenser was tilted back and used as a reflux. This od is especially useful when the condensation is very susceptible ight temperature changes, as the diphenylformamidine con- tions have proved to be.

ndensations with β-Naphthol.—A mixture of diphenylformamid- 7 g.) and β-naphthol (5 g.) was heated at 130° for 6 hours, ht excess (16 c.c.) of 10% aqueous sodium hydroxide added, liberated aniline distilled in steam, the solution cooled, the anged diphenylformamidine (0·6 g.) filtered off, and the filtrate fied. The precipitate of β-naphthol and 2-hydroxy-1-naphth- yde was boiled with alcoholic aniline, the Schiff's base of the yde, which separated from the cooled solution, was hydrolysed aqueous sodium hydroxide as before, the aniline removed steam, and the aldehyde (2·9 g.), precipitated as a yellow-

henylformamidine and β-naphthol was dissolved in warm cohol containing a small quantity of aniline (diphenylformamidine very soluble in such a mixture). The yellow needles of 2-hydroxy-naphthylideneaniline that separated from the cooled solution re almost identical with a sample prepared from 2-hydroxy-1-phthaldehyde by Gattermann and Horlacher's method (*Ber.*, 32, 286), and when purified by Manchot and Palmberg's thod (*Annalen*, 1912, **388**, 112) melted at 92—93°.

4 : 6-Dihydroxy*iso*phthalylidenebisaniline. It has not been sible to isolate the intermediate compound from pure dry rcinol and diphenylformamidine in a state of purity which would tify speculation as to its composition. When ordinary resorcinol used, however, the pure intermediate 4 : 6-dihydroxy*iso*-thalylidenebisaniline was obtained. The crude reaction product washed free from diphenylformamidine with aniline, pressed porous tile, and recrystallised from alcohol. It had m. p. 202— and was identical with the Schiff's base of 4 : 6-dihydroxy-phthalaldehyde prepared from the aldehyde as described by mann and Lewy (*Ber.*, 1877, **10**, 2212; they give m. p. 199°).

ldehydes could not be isolated from the products of reaction ween diphenylformamidine and catechol, quinol, phloroglucinol, p-nitrophenol. The very marked odour of phenylcarbylamine h was observed in the reaction product suggests that the reaction ssentially a decomposition of the diphenylformamidine into ine and phenylcarbylamine : $NHPh{\cdot}CH{:}NPh \rightarrow NH_2Ph + Ph{\cdot}N{:}C$. his decomposition also takes place when the formamidine is ed alone at 250°.

phenylformamidine appears to be stable in presence of resorcinol thyl ether or *o*-nitrophenol under all conditions.

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Publication VIII

PREPARATION OF 2:4:2′:4′-TETRAHYDROXYBENZOPHENONE.

BY

JOHN BALDWIN SHOESMITH

AND

JOHN HALDANE.

From the Transactions of the Chemical Society, 1924. Vol. 125.

[illegible].—*Preparation of 2 : 4 : 2′ : 4′-Tetrahydroxybenzophenone.*

By John Baldwin Shoesmith and John Haldane.

[illegible]:2′ : 4′-Tetrahydroxybenzophenone was first prepared by [illegible]er and Conzetti (*Ber.*, 1897, **30**, 971), who fused fluorescein [illegible]ride with caustic soda at 270—280°. The present investigation [illegible]shown that the method used first by Hoesch (*Ber.*, 1915, **48**, [illegible]) to prepare aromatic hydroxyketones is also applicable to the [illegible]hesis of this ketone.

[illegible]:4-Diacetoxybenzonitrile, $C_6H_3(OAc)_2{\cdot}CN$, and resorcinol con[illegible]e in presence of hydrochloric acid. 2 : 4-Diacetoxy-2′ : 4′-[illegible]droxybenzophenoneimine hydrochloride,

$$(OAc)_2C_6H_3{\cdot}C(:NH,HCl){\cdot}C_6H_3(OH)_2,$$

[illegible]formed, is moderately easily hydrolysed in acid solution to [illegible]xpected benzophenone. From the reaction product, resaceto[illegible]one, $C_6H_3(OH)_2{\cdot}CO{\cdot}CH_3$, and β-resorcylamide may also be [illegible]ted. The former is produced by the condensation of acetyl [illegible]ride (from diacetoxybenzonitrile and hydrochloric acid) with [illegible]rcinol, and the latter by the hydrolysis of unchanged diacetoxy-[illegible]nitrile.

[illegible]e compound described by Marcus (*Ber.*, 1891, **24**, 3652) as [illegible]rcylonitrile will not condense with resorcinol.

Experimental.

[illegible]:4-Diacetoxybenzonitrile (7 grams), prepared as described by [illegible]us (*loc. cit.*), and carefully dried resorcinol (2·5 grams) were

this ketone did not depress the melting point of an authentic specimen of resacetophenone.

Attempts were made to prepare β-resorcylonitrile. 2 : 4-Diacetoxybenzonitrile was boiled with caustic alkali (or dilute sulphuric acid) of different concentrations for varying periods of time. The hydrolysed mixtures were extracted with ether and the solid fractionally precipitated by the addition of ligroin. Analysis showed that the nitrogen content varied with the conditions of hydrolysis and a pure β-resorcylonitrile could not be isolated. The white needles obtained would not condense with resorcinol under the same conditions as those used in the condensation of 2 : 4-diacetoxybenzonitrile.

The authors wish to thank the Advisory Council of the Department for Scientific and Industrial Research for a grant to one of them (J. H.) which enabled this investigation to be carried out.

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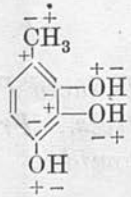
compare also *Mem. Manchester Phil. Soc.*, 1920, **64**, ii, 1 *et seq.* and Kermack and Robinson, this vol., p. 428 *et seq.*), (*b*) induced polar effects, and (*c*) steric effects. It is as yet scarcely possible to define precisely the proportion attributable to each of these in any single instance, but there is some reason to suppose that the range and periodicity peculiar to each type of effect may furnish a means of doing so. Thus a property which is found to rise and fall alternately in proceeding from one atom to another in order may be suspected to be one influenced by induced polarity effects. Steric effects are likely to recur at longer intervals, probably five or six atoms in saturated, open-chain compounds; whilst general polar effects are likely to be periodic only when associated with steric effects, with which, therefore, they would probably agree in periodicity.

Systematic measurements, therefore, may ultimately make it possible to foretell the total result of the combined general and induced polar effects produced on replacement of one atom or group in a molecule by another, but at present the data are insufficient and comparisons of properties are best restricted to those of positional isomerides or to those of different atoms in one and the same compound. Even as it is, general polar and steric influences cannot wholly be eliminated in studying the operations of induced alternate polarities, but some assistance may be derived from the circumstance that steric influence appears to be very effective only when the atoms concerned occupy certain relative positions—for example, ortho-positions in benzene di-derivatives, and α-positions in open-chain carbonyl compounds.

Attention was recently directed by one of us to the properties of the isomeric cresols (*Mem. Manchester Phil. Soc.*, 1920, **64**, 10). Using the generalised diagram



and assuming that the hydrogen atoms of a methyl group attached to an aromatic nucleus can act as "positive key atoms"—the assumption conveyed by the dots attached to their polar signs—the induced polarities to be expected are indicated. In the case of the *m*-hydroxyl group, the natural relative polarities of the atoms (with which the capacity for ionisation is associated) are, as the above diagram shows, enhanced by the induced ones, whilst in the *o*-

halogen with their natural negative polarity enhanced, whilst in the *m*-isomeride the opposite is the case.

The test on which the authors relied for comparing the negative polarity of the bromine atoms was based on the double decomposition of the halogen compounds with alkalis

$$\overset{-}{X}—\overset{+}{Br} + \overset{-}{Na}—\overset{+}{OH} \longrightarrow X{\cdot}OH + \overset{+}{Na}—\overset{-}{Br}.$$

In accordance with this polar reaction, the compounds with more " negative " halogen, namely, the *o*- and *p*-compounds were expected to react most readily with alkalis, and the experiment confirmed this expectation in full, for the *m*-compound reacted very much more slowly than did the other two, which, except as emulsions (in which case relative solubilities are confusing factors), lost their bromine as bromidion so rapidly that the velocity of reaction could not be measured. There was evidence that the *o*-compound was slightly less reactive than the *p*-compound either when emulsified or when in solution.

Halogen, as one of us has previously shown, may exhibit reactions in which it appears to behave as with a positive polar character (*Mem. Manchester Phil. Soc.*, 1920, **64**, ii, 8). Thus, when situated in the α-position in ketones, and even more markedly in that position in 1 : 3-diketones, 1 : 3-ketonic esters, and malonic esters, it is known to be very readily replaced by hydrogen. This sometimes happens when hydrogen bromide is present, as in the case of α-bromo-acetoacetic ester,

$$\overset{-}{X}—\overset{+}{Br} + \overset{-}{Br}—\overset{+}{H} \longrightarrow X{\cdot}H + Br{\cdot}Br$$

and more frequently with hydrogen iodide, in which case the preceding equation may, of course, be modified thus :

$$\overset{-}{X}—\overset{+}{Br} + \overset{-}{I}—\overset{+}{H} \longrightarrow X—H + Br—I$$
$$Br—I + I—H \longrightarrow HBr + I_2$$

More recently Nicolet (*Amer. Chem. J.*, 1921, **43**, 2081) has interpreted replacement of iodine by hydrogen in certain aromatic compounds as due to " positive halogen " on similar grounds.

The induced positive polar character of the bromine atom in *m*-methoxybenzyl bromide suggested that the " reactivity " of the three isomerides when tested as to their ease of reduction by hydrogen iodide should be the inverse of that observed when tested by the ease of hydrolysis. Experiment entirely confirmed this surmise. Whilst the contrast between the *m*-compound and the other two isomerides was not so very great as before, it was still very decided; and this fact provides, in combination with the other data given in this paper, a striking example of the applicabili-

and the corresponding bromides in quantity from the cresols will be dealt with in another communication. In the present paper will be described only the more important observations made in connexion with the conversion of the isomeric hydroxybenzaldehydes into the corresponding methoxybenzyl bromides, and the properties of the latter.

o-Hydroxybenzyl alcohol was obtained in the most satisfactory yield (70 per cent.) by the reduction of salicylaldehyde (12 grams), emulsified in 100 c.c. of water, with carefully washed, 1·5 per cent. sodium amalgam (300 grams) in presence of sodium hydrogen carbonate (about 25 grams). Addition of the amalgam and bi carbonate was made gradually, with constant shaking and cooling. The subsequent isolation of the alcohol by acidification, extraction with ether, and removal of unchanged aldehyde by means of sodium hydrogen sulphite solution need not be described in detail, but it is desirable to note that great care must be exercised to remove all traces of acids before attempting to proceed with purification of the alcohol, otherwise resinification may take place with serious loss (compare Manasse, *Ber.*, 1894, **27**, 2411; Lederer, *J. pr. Chem.*, 1894, [ii], **50**, 225).

o-Methoxybenzyl alcohol was best obtained by alkylation of the hydroxy-alcohol in the mode recommended by Pschorr, Wolfe and Buckow (*Ber.*, 1900, **33**, 165). Attempts to prepare it from *o*-methoxybenzaldehyde by reduction or by the Cannizzaro reaction gave poor yields or impure products. The product used for conversion into the bromide boiled at 246—247° at atmospheric pressure.

o-Methoxybenzyl bromide was made by passing gaseous hydrogen bromide into a solution of *o*-methoxybenzyl alcohol in twice its volume of cold dry benzene. The solution gradually became turbid and green, and after two hours was separated from the water deposit, dried over calcium chloride, filtered through glass-wool and fractionated under reduced pressure. The bulk of the bromide boiled at 118°/18 mm., and analysis for ionisable bromine showed it to be pure.

m-Hydroxybenzyl alcohol was readily obtained in 80 per cent. yield by reduction of the corresponding aldehyde with sodium amalgam, as described in the case of the corresponding ortho derivative.

m-Methoxybenzaldehyde was made in 86 per cent. yield by the interaction of *m*-hydroxybenzaldehyde, aqueous sodium hydroxide and methyl sulphate in molecular proportions, the reaction being completed by boiling for several hours.

m-Methoxybenzyl alcohol was obtained by the action of 25 per cent. ~~aqueous~~ alcoholic potassium hydroxide on the aldehyde, or in bett

obtained by following the hydrolysis of samples of the three bromide to completion.

(*a*) o-*Methoxybenzyl bromide.*

	(i)			(ii)	
Temperature	55°			20°	
Wt. of bromide	0·8824 gram			0·6785 gram	
Alkali used	250 c.c. of *N*/40-NaOH			100 c.c. of *N*/10-NaOH	
t.	*x.*	*t.*	*x.*	*t.*	*x.*
2·5	37·0	77·5	90·0	15	96·5
7·5	62·0	157·5	99·0	30	100·0
17·5	70·0	237·5	99·0	45	100·0
37·5	78·7	7·5	64·7		

(*b*) p-*Methoxybenzyl bromide.*

Temperature	55°		20°	
Wt. of bromide	0·831 gram		0·7850 gram	
Alkali used	250 c.c. of *N*/40-NaOH		100 c.c. of *N*/10-NaOH	
t.	*x.*	*t.*	*x.*	
2·5	75·4	37·5	97·9	The substance was almo
7·5	90·8	77·5	99·4	completely hydrolyse
17·5	94·8			after 2·5 minutes.

(*c*) m-*Methoxybenzyl bromide.*

Temperature	55°			20°	
Wt. of bromide	0·934 gram			0·8988 gram	
Alkali used	250 c.c. of *N*/40-NaOH			100 c.c. of *N*/10-NaOH	
t.	*x.*	*t.*	*x.*	*t.*	*x.*
7·5	1·6	77·5	43·0	45	2·4
17·5	13·3	157·5	66·7	105	4·0
37·5	24·0	15	1·0	185	5·4

(*b*) *Hydrolysis of Dissolved Methoxybenzyl Bromides.*

Owing to the extremely high speed at which alkalis act on th *o*- and *p*-bromides, it has not been found possible to measure th speed of the reaction in dilute alcohol at 25°.

Using as solvent alcohol, containing about 20 per cent. of wate *p*-methoxybenzyl bromide, initially at concentration about 1 p cent., was almost completely hydrolysed in five minutes after bei dissolved, even in absence of alkali; the *o*-isomeride was not con pletely hydrolysed in the same time, but no satisfactory determin tions of the small quantity of unchanged bromide could be pra ticable. Under the same conditions, *m*-methoxybenzyl bromi (0·1824 gram per 100 c.c. of dilute alcohol) was hydrolysed to th extent of 10, 20, and 33 per cent. in 24, 48, and 72 hours, respectivel

With excess of *N*/50-sodium hydroxide (solvent = alcohol about 90 per cent.), the results with the *o*- and *p*-isomerides we much as in absence of alkali, hydrolysis being almost complete

(*b*) p-*Methoxybenzyl bromide.* Weight taken in gram. (i) 0·902; (ii) 0·415.

(i)		(ii)	
5	0·7	5	1·5
15	1·4	15	2·3
35	2·0	35	1·0
75	3·9	75	3·0
195	5·8	195	3·9

(*c*) m-*Methoxybenzyl bromide.* Weight taken in gram. (i) 0·811; (ii) 0·50.

(i)		(ii)	
5	49·8	5	37·0
15	80·6	15	79·5
35	89·7	35	93·3
75	97·4	75	98·5
175	99·8	175	98·0

The authors' thanks are due to the Department of Scientifi and Industrial Research for a grant to one of us (J. B. S.) whic enabled the work to be done.

CHEMISTRY DEPARTMENT,
UNIVERSITY OF MANCHESTER. [*Received, June 2nd*, 1922.]

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yields and with greater certainty than was formerly possible. Improved methods are given for the preparation of the hydroxybenzaldehydes, *o*-hydroxybenzyl alcohol (saligenin), and *p*-methoxybenzaldehyde (anisaldehyde).

The hydroxybenzaldehydes are obtained by hydrolysing the dichlorinated tolyl carbonates with formic acid, with a mixture of formic and oxalic acids, or with sodium acetate in alcoholic solution. The ortho-compound hydrolyses directly to salicylaldehyde, whilst the meta- and para-compounds yield the aldehyde carbonates, $CO(O{\cdot}C_6H_4{\cdot}CHO)_2$. Boiling sodium bisulphite solution completes the hydrolysis. These reagents are much more convenient than the calcium carbonate and water at 5 atmospheres pressure recommended by Raschig (D.R.-P. 233631).

Salicylaldehyde is best converted into *o*-methoxybenzyl alcohol by reduction to saligenin and subsequent methylation. In the case of the meta- and para-compounds the order of the reactions is reversed.

p-Methoxybenzaldehyde (anisaldehyde) is prepared by oxidising anethole with chromic and sulphuric acids. Anethole is oxidised by sodium chlorate directly to anisaldehyde, the intermediate glycol not being produced. This is in agreement with the results of similar oxidations carried out by Hofmann (*Ber.*, 1912, **45**, 3329; 1913, **46**, 1657).

Direct halogenation of the tolyl methyl ethers results in the formation of a mixture of nuclear and side-chain substituted halogen compounds from which methoxybenzyl halides cannot be isolated.

Experimental.

Chlorination of the Tolyl Carbonates.

The tolyl carbonates were prepared by the general method of Holleman and Hoeflake (*Rec. trav. chim.*, 1916, **36**, 261). Carbon chloride was passed into a 10 per cent. solution of the sodium tolyoxide until precipitation of the carbonate was complete. The ortho- and para-compounds gave the carbonates at once. *m*-Cresol gave the intermediate tolyl chloroformate, $C_6H_4Me{\cdot}O{\cdot}COCl$, which was converted into the carbonate by heating it with the equivalent amount of *m*-cresol dissolved in rather more than the theoretical quantity of caustic soda. The carbonates were all carefully crystallised from alcohol.

When the ω-chlorotolyl carbonates, $CO(O{\cdot}C_6H_4{\cdot}CH_2Cl)_2$, were hydrolysed, the resulting hydroxybenzyl alcohols were never isolated, owing to their remarkable tendency to resinify in presence of acid. Chlorine was therefore passed into the vigorously stirred, molten

of aldehyde had disappeared and the evolution of hydrogen was marked, the solution was cooled in ice and the saligenin, which crystallised in almost the theoretical yield, was filtered off and purified by shaking it in water solution with animal charcoal for three hours. After filtration, extraction with ether, and recrystallisation from ligroin, the sample melted at 86°. The method of purification was that adopted by Hart and Hirschfelder (*J. Amer. Chem. Soc.*, 1920, **42**, 2680). The saligenin was methylated and converted into *o*-methoxybenzyl bromide by the methods of Lapworth and Shoesmith (T., 1922, **121**, 1392). The bromide thus prepared crystallised from light petroleum in colourless, six-sided plates, m. p. 46°.

m-*Methoxybenzyl Bromide. Hydrolysis of Chlorinated* m-*Tolyl Carbonate.*—*m*-Tolyl carbonate after chlorination was found to contain 35·5 per cent. of hydrolysable halogen. The details set out below must be followed carefully to ensure a good yield of *m*-hydroxybenzaldehyde.

(*a*) Hydrolysis with formic acid. Twenty-five grams of the ester were hydrolysed with 100 c.c. of 80 per cent. formic acid as in the case of the *o*-tolyl compound. The impure *m*-aldehydophenyl carbonate, which was completely precipitated by addition of 150 c.c. of water to the cooled solution, was rapidly hydrolysed by freshly prepared, boiling aqueous sodium bisulphite. The filtered solution was acidified and steam-distilled to remove sulphur dioxide, the aldehyde extracted with ether, and the ethereal solution evaporated after neutralisation with sodium carbonate to destroy any trace of acid. The *m*-hydroxybenzaldehyde (yield 40 per cent.) was recrystallised from boiling water (yield 25 per cent.) and it then melted at 103—104°. A sample prepared from *m*-nitrobenzaldehyde melted at 104°.

(*b*) Hydrolysis with formic and oxalic acids. The same quantities were used as in the case of the ortho-compound; hydrolysis, yielding the aldehyde carbonate, was complete in one and a half hours. Subsequent hydrolysis with bisulphite solution gave the hydroxyaldehyde in slightly better yield than that obtained in (*a*).

(*c*) Hydrolysis with sodium acetate. The same quantities were used as in the preparation of salicylaldehyde, but the improvement in the yield was not so marked in this case.

There are no further details to add to those already communicated on the conversion of this aldehyde into *m*-methoxybenzyl bromide.

p-*Methoxybenzyl Bromide. Hydrolysis of Chlorinated* p-*Tolyl Carbonate.*—A summary of the yields given by methods employed is all that is necessary in this case. Formic acid alone and form-

and Shoesmith, *loc. cit.*) on the conversion of this aldehyde into *p*-methoxybenzyl bromide * bear out the necessity for a second reduction with alcoholic potash of the anisyl alcohol produced from this aldehyde by Cannizzaro's method. A solid anisyl alcohol was thus obtained. The bromide itself, which resulted on passing dry hydrogen bromide into the benzene solution of anisyl alcohol, was found to be very pure and crystallised in long needles. These needles are extremely sensitive to the action of moist air, and the bromide only existed as such for a few moments after removing into the atmosphere.

Chlorination of the Tolyl Methyl Ethers.—Chlorine was passed in a slow stream into the tolyl methyl ethers for half an hour. The introduction of cold air with the chlorine maintained the temperature at 40°. The quantity of hydrogen chloride not carried away mechanically was found in no case to exceed 0·10 per cent. The total halogen was estimated by the method of Carius, the hydrolysable halogen by boiling for half an hour with 10 per cent. alcoholic potash and estimating volumetrically the potassium chloride so produced.

The results are summarised.

Compound chlorinated.	Free HCl.	Total chlorine.	Chlorine hydrolysable compared with	
			Total Cl.	Total compound.
	Per cent.	Per cent.	Per cent.	Per cent.
ortho.	Nil	31·4	19·0	5·98
meta.	0·01	22·3	8·8	1·96
para.	0·10	29·2	24·8	7·20

When the ethers were exposed to the glare of a mercury vapour lamp the results were unaltered.

The author wishes to express his gratitude to Prof. A. Lapworth, F.R.S., who supervised his work in the Manchester University, and to the Advisory Council of the Department of Scientific and Industrial Research for a grant which enabled him to undertake the investigation.

* The marked difference in lachrymatory properties between *m*-methoxybenzyl bromide and the very easily hydrolysed, non-lachrymatory para isomeride finds a parallel in the vesicant properties of $\beta\beta'$-dichlorodiethyl sulphide and its non-vesicant, easily hydrolysed isomeride, $\alpha\alpha'$-dichlorodiethyl sulphide (Bales and Nickelson, T., 1922, **121**, 2137).

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The quantity of iodine liberated corresponded with that expected from such a reduction.

The result, namely, that the lability of the halogen atoms in *m*-methoxybenzyl bromide is least when alkali but greatest when hydrogen iodide is the reagent, is one that could not have been foreseen with the aid of any general principles enunciated prior to the principle of induced alternate polarities, and therefore was one to which the authors attached great importance. They had considered all other explanations of the course of the reaction and were satisfied that the preceding equations were the only ones which could account for the liberation of iodine in the experiment with hydrogen iodide. Since the publication of the original paper, however, the conclusions were privately criticised on the ground that it had not been established that the equations given represented the true course of the reaction; the assumed reduction product, namely, *m*-tolyl methyl ether, had not been isolated. In view of this, the experiments described in the present paper were made and the results are now communicated, as they remove any serious doubt which might otherwise be entertained of the course of the reaction in question

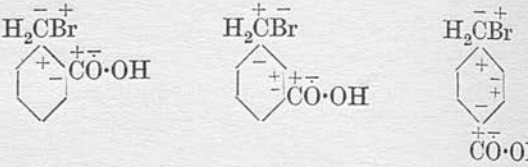
When *m*-methoxybenzyl bromide is dissolved in a solution of hydriodic acid in glacial acetic acid (0·46 gram of HI per c.c.) iodine is at once liberated. In an hour's time the amount of iodine present represents complete reduction of the $-CH_2Br$ group to $-CH_3$. From such a reduction mixture *m*-tolyl methyl ether and *m*-cresol may be isolated. The ether, which is obviously the intermediate compound in the scheme $OMe\cdot C_6H_4\cdot CH_2Br \xrightarrow{HI} OMe\cdot C_6H_4Me \xrightarrow{HI} OH\cdot C_6H_4Me$, is demethylated in the solution with no liberation of iodine.

EXPERIMENTAL.

A solution of 6·06 grams of *m*-methoxybenzyl bromide in glacial acetic acid, containing 0·46 gram of HI per c.c. (compare Lapworth and Shoesmith, *loc. cit.*), the total volume being 50 c.c., was maintained at 25°. After the reaction had proceeded for twenty minutes 1 c.c. of the mixture was withdrawn and the iodine which had been liberated titrated in about 100 c.c. of water with standard sodium thiosulphate solution; 93·5 per cent. of the bromide had been reduced. Samples withdrawn after the reaction had proceeded for an hour and an hour and a half were identical and indicated that reduction was complete (97·5 per cent.) and the liberation of iodine had ceased.

Separation of the Reaction Products.—The solution was poured into 200 c.c. of water containing 17 grams of sodium thiosulphate

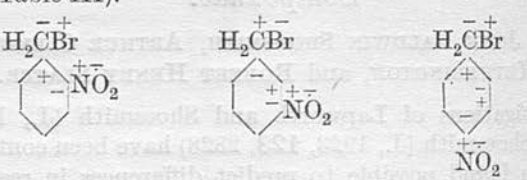
In the three isomeric ω-bromotoluic acids,



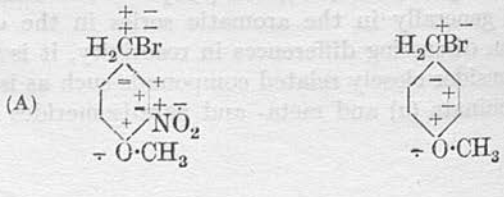
the bromine which has acquired an induced negative character is present in the meta-isomerides; thus the order of ease of hydrolysis should be $m>p$, and of reduction by hydrogen iodide, $p>m$, the reverse of that found in the methoxybenzyl bromides. Both these predictions were borne out by experiment (see Tables I and II).

Reduction of the carboxyl group under the conditions of the experiment is so small that it may be ignored.

Unsubstituted benzyl bromide is more easily hydrolysed (Table I) than any of the ω-bromotoluic acids. The introduction of the carboxyl group therefore stabilises the benzyl bromide molecule as a whole, a condition even more pronounced in the case of the nitrobenzyl bromides, where the general polar influence (*a*) is very marked. The ease of hydrolysis of the latter compounds still follows the same rule, and the meta is the most readily hydrolysed isomeride (Table III).



The introduction of the nitro-group into a very reactive molecule such as *p*-methoxybenzyl bromide diminishes the reactivity of the latter to the order of that of the unsubstituted compound. It is thus seen that the restriction that differences in reactivity can be predicted only for very closely related compounds such as isomerides is necessary, otherwise 3-nitro-4-methoxybenzyl bromide (A) (which was the compound investigated) might be expected to be more reactive than the very reactive *p*-methoxybenzyl bromide (B) in virtue of the enhanced induced negative character of the bromine atom in the former. This induced effect is more than balanced by that of the strong general inhibiting influence of the nitro-group.



A mixture of 25 grams of the ω-bromotoluoyl bromide and 300 c.c. of 80 per cent. formic acid (*d* 1·2) was warmed at 30—35° for 1 hour and poured into water, and the precipitated acid was dried and crystallised from benzene. The m. p.'s of the acids are, *o*- 146°, *m*- 150°, and *p*- 223° (compare Zalkind, *J. Russ. Phys. Chem. Soc.*, 1914, **46**, 508; Zalkind and Semenov, *ibid.*, p. 512).

Hydrolysis of the ω-Bromotoluic Acids.—Approximately 0·10 gram of the acid was dissolved in 20 c.c. of absolute alcohol, 5 c.c. of water were added, and the volume was made up to 25 c.c. with alcohol. The solution was heated at 76° (vapour of boiling carbon tetrachloride) for 5 minutes longer than the time recorded, the extra time being that necessary for equilibration of temperature, and the total acidity (hydrogen bromide + organic acid) determined by titration with *N*/10-alkali and methyl-red. A correction was applied for the organic acid.

The results are summarised in Table I. t = time from commencement of experiment in hours. w = weight of compound used in grams. x = percentage changed.

TABLE I.

	o-Compound.		*m*-Compound.		*p*-Compound.		Benzyl bromide.	
t.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.
½	0·1068	5·0	0·1019	27	0·1076	13	0·0804	57
1	0·1158	7·0	0·1010	42	0·1049	30	,,	81
2	0·1031	4·9	0·1207	70	0·1126	54	,,	92
4	0·1089	4·7	0·1001	87	0·1110	74	,,	96
8	0·1126	4·8	0·1149	90	0·1032	83	,,	97
16	—	—	0·1154	94	0·1207	90	0·0975	99
32	—	—	0·1199	98	0·0998	94	—	—

In the case of ω-bromo-*o*-toluic acid, x denotes, not the percentage of acid hydrolysed, but that calculated from the excess titration over the quantity required for neutralisation of the carboxyl group. The fall from the maximum is due to the following changes:

$$C_6H_4\!<\!\begin{matrix}CH_2Br\\CO_2H\end{matrix} \rightleftharpoons C_6H_4\!<\!\begin{matrix}CH_2\\CO\end{matrix}\!>\!O \rightleftharpoons C_6H_4\!<\!\begin{matrix}CH_2\cdot OH\\CO_2H\end{matrix}$$

(I.) (II.) (III.)

The hydrolysis of ω-bromo-*o*-toluic acid (I) to ω-hydroxy-*o*-toluic acid (III) is accompanied by the formation of hydrobromic acid and phthalide (II). In the titrations, which estimate both the halogen acid and the carboxylic acid, the values fall until equilibrium is reached in the production of phthalide. This is due to the spatial influences classified under heading (*b*).

Reduction of the Isomeric ω-Bromotoluic Acids at 110° *by Hydriodic*

minimum of dry benzene was saturated with dry hydrogen bromide, the benzene evaporated, and the residue crystallised from light petroleum, 3-*nitro*-4-*hydroxybenzyl bromide* being obtained in yellow prismatic needles, m. p. 82° (Found: Br = 34·46. $C_7H_6O_3NBr$ requires Br = 34·44 per cent.).

3-*Nitro*-4-*methoxybenzyl bromide*, prepared by methylating 3-nitro-4-hydroxybenzyl alcohol with methyl iodide and potassium hydroxide, recrystallising the product from hot water, and converting it (m. p. 69°) into the bromide as above, crystallised from light petroleum in pale yellow needles, m. p. 108° (Found: Br = 32·84. $C_8H_8O_3NBr$ requires Br = 32·49 per cent.).

These bromides were hydrolysed under the same conditions as the ω-bromotoluic acids. The hydrobromic acid liberated was titrated with *N*/10-caustic alkali as before, except in the case of 3-nitro-4-hydroxybenzyl bromide, where *N*/20-ammonium hydroxide was used and any hydrolysis of the unchanged bromide during the titration avoided.

The results are summarised in Table III.

TABLE III.

Nitrobenzyl bromides

	Ortho.		Meta.		Para.		3-Nitro-4-methoxybenzyl bromide.	
t.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.
½	0·1267	10·8	0·1226	12·0	0·1168	11·0	0·1067	73·2
1	0·1190	19·2	0·1037	23·0	0·1045	19·5	0·1008	90·2
2	0·1022	32·4	0·1083	38·4	0·1147	32·8	0·1023	95·5
4	0·1010	54·7	0·1171	59·3	0·1015	54·6	0·1116	97·1
8	0·1081	78·9	0·1196	85·1	0·1146	78·9	0·1037	98·7
16	0·1040	93·9	0·1194	96·2	0·1068	95·3	0·1038	99·3
32	0·0998	99·1	0·1176	99·8	0·1041	99·5	0·1039	99·8

3-Nitro-4-hydroxybenzyl bromide.

t	½	½	1	2
w	0·1008	0·1024	0·1031	0·1028
x	85	96	99	100

[With ROBERT HENRY SLATER.]

The *o*- and *p*-halogenated phenols were prepared from the corresponding aminophenols by the usual methods.

m-Chlorophenol was most conveniently obtained from *m*-chloronitrobenzene, 100 grams of which at 50° were dropped into a mechanically stirred mixture of 200 grams of iron filings, 400 c.c. of water, and 15 c.c. of concentrated hydrochloric acid (compare Morgan, J., 1900, **77**, 1204), the heat of reaction, after slight preliminary warming, maintaining the temperature at 95°. After an hour's heating at 90°, the whole was cooled, neutralised with 30 grams of sodium bicarbonate, and the chloroaniline distilled

TABLE IV.

	o-Iodophenol. $w =$ 0·6104 gm.	*p*-Iodophenol. $w =$ 0·6394 gm.	*p*-Bromophenol. $w =$ 0·6070 gm.
t.	*x.*	*x.*	*x.*
15	28·2	69·0	4·4
45	56·2	88·8	8·7
105	75·6	95·4	15·9
225	90·0	100·0	28·7

TABLE V.

	o-Bromophenol. $w =$ 0·1730 gm.	*p*-Bromophenol. $w =$ 0·1719 gm.
t.	*x.*	*x.*
60	18·7	40·7
120	31·7	68·4
180	39·6	83·9
240	47·6	94·2
300	53·0	100·0

The meta-halogenated phenols did not reduce in any circumstances.

4-Iodoresorcinol was completely reduced in $\frac{1}{2}$ hour at 25° in glacial acetic acid solution containing 0·40 gram of hydrogen iodide per c.c.

The authors desire to acknowledge a grant from the Earl of Moray Research Fund and also their indebtedness to Prof. Sir James Walker, F.R.S., Prof. A. Lapworth, F.R.S., and Mr. W. O. Kermack for their interest in these investigations.

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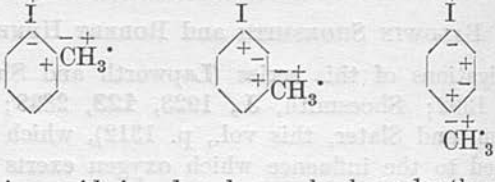
Experiment has fully borne out this prediction. It has, in fact, been found that under conditions by which ω-bromo-*m*-xylene is almost quantitatively reduced by hydrogen iodide to *m*-xylene, the isomeric ω-bromo-*p*-xylene is converted into ω-iodo-*p*-xylene.

The complete order of hydrolysis is $p>o>m$, and of reduction $m>o>p$.

The general polar influence exerted by the methyl group is quite marked and all the ω-bromoxylenes are more easily hydrolysed than the unsubstituted benzyl bromide. It must also be pointed out that the meta- and ortho-isomerides are more reactive than the unsubstituted compound to both reagents. As expected, ω-bromo-*p*-xylene is more easily hydrolysed than ω-iodo-*p*-xylene.

The order of ease of reduction of the iodotoluenes, in which the halogens are one place nearer to the "key-atom" than those present in the ω-bromoxylenes, was again as expected, namely, *o* and $p>m$, the reverse of the previous order, except that the ortho-isomeride is the isomeride most easily reduced to toluene.



The meta-isomeride is reduced very slowly under the experimental conditions, and therefore this series differs slightly from that of the halogenated phenols, in which the meta-isomeride is not reduced.

The possibility of the formation of reactive molecules of quinonoid type in any of the compounds here investigated is remote and the two series of experiments are of importance by reason of their simplicity.

It must be pointed out that the suggestion put forward by Lowry (J., 1923, **123**, 824) that the induced alternate influence only capable of being transmitted when the series is perfectly conjugated is definitely negatived by the different orders of reactivity displayed by the ω-bromoxylenes under the conditions described in the present communication. It must be emphasised, however, that the benzene ring is certainly a very efficient transmitter and possibly even an amplifier of induced polarity effects. In all probability, however, similar effects will not be observed in aliphatic compounds which contain a series of consecutive single bonds. This has recently been stressed by Lapworth (*Far. Soc. Disc.*, 1923, p. 505).

In addition, it is obvious that the tautomeric hydrogen hypothesis

isomerides are due to the fact that appreciable resinification took place during steam distillation of the tolylcarbinols.

The isomeric ω-bromoxylenes (V) were obtained from the corresponding tolylcarbinols by the usual method of saturating the dry benzene solution of the latter with dry hydrogen bromide. The *o*-isomeride, b. p. 102°/11 mm., m. p. 20°; *m*-, b. p. 97—99°/8 mm.; *p*-, b. p. 100°/9 mm., m. p. 35·5°.

Hydrolysis of the ω-Bromoxylenes at 60°.

The isomerides were hydrolysed at the temperature of the vapour of boiling chloroform, since this was found to be the most satisfactory temperature at which a series of results could be obtained. The method was that used in a previous communication (Shoesmith, Hetherington, and Slater, *loc. cit.*). The results are summarised in Table I,* where *t*, *w*, and *x* represent time in hours from commencement of experiment, weight of compound used, and percentage changed, respectively.

TABLE I.

	Ortho-compound.		-Meta-compound.		Para-compound.		Benzyl bromide.		ω-Iodo-*p*-xylene.	
t.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.	*w*.	*x*.
½	0·1060	55	0·0980	25	0·0983	66	0·1093	22	0·1335	38·8
1	0·1064	77	0·0996	42	0·1074	87	0·1056	37	0·1146	63·7
2	0·1030	89	0·1037	64	0·1019	96	0·1100	59	0·1280	78·8
3	0·1022	94	0·1011	77	0·0997	100	0·1078	71	0·1291	84·7

Quantitative Reduction of the ω-Bromoxylenes by Hydrogen Iodide at 25°.

A solution of hydrogen iodide in glacial acetic acid was used which contained 0·70 gm. of HI per c.c. Approximately 0·5 gm. of the bromoxylene was dissolved in sufficient glacial acetic acid to make the volume 1 c.c. in a 5-c.c. ground glass-stoppered measuring cylinder. The reducing agent (4 c.c.) was then added and the cylinder immersed in the thermostat. The rate at which the reduction took place was determined as in a previous communication (Lapworth and Shoesmith, *loc. cit.*). The results are summarised in Table II, where *t*, *w*, and *x* have the same significance as before.

Identification of the Reduction Products.—Approximately 6 grams of the ω-bromoxylene and 45 c.c. of the reducing agent were used. The mixture was maintained at 25° for 40 hours and then poured into water. The solids which separated in the experiments with the ortho- and para-isomerides and also with benzyl bromide were filtered off, dried, and recrystallised from light petroleum. They

* For convenience, the results for ω-iodo-*p*-xylene (for preparation, see p. 2282) are included.

from the commencement of the experiment, whilst w and x have the same significance as before.

TABLE III.

	Ortho-compound.	Meta-compound.	Para-compound.		Ortho-compound.	Meta-compound.	Para-compound.
	$w = 1{\cdot}2150$ gm.	$1{\cdot}1934$ gm.	$1{\cdot}2051$ gm.				
t.	x.	x.	x.	t.	x.	x.	x.
1	48·4	4·1	32·1	6	88·1	13·3	79·2
2	67·9	7·9	50·5	8	92·0	17·4	85·9
4	82·8	10·9	69·9				

From the *o*- and *p*- isomerides toluene was isolated by the method employed for the separation of *m*-xylene. It distilled at 105—118°, had density 0·876 at 16°, was quite free from halogen, and its trinitro-derivative (m. p. 81—82°) did not depress the melting point of an authentic specimen of trinitrotoluene.

Under the above conditions iodobenzene liberated iodine in a quantity which represented 10% reduction in 8 days.

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Experimental.

Diphenylformamidine.—This was prepared by boiling together aniline and formic acid (Weith, *Ber.*, 1876, 9, 454). Forty grams (1 mol.) of 80 per cent. formic acid were mixed with 160 grams (2½ mols.) of aniline. The water which was present in the original acid together with that produced in the reaction was distilled away through a fractionating column. The head of the column was fitted with a device for trapping the water so soon as it reached the top. After four hours' gentle boiling, the temperature was raised until 60 c.c. of aniline had distilled over. The residual diphenylformamidine solidified on cooling and after recrystallisation from alcohol melted at 137° (yield 63 grams).

Condensation of Diphenylformamidine with Resorcinol.—A long series of experiments has shown the following to be the best conditions for the preparation of β-resorcylaldehyde by this method.

A finely powdered mixture of 5 grams (1 mol.) of carefully dried resorcinol with 9 grams (1 mol.) of diphenylformamidine was heated in a small, thin-walled flask,* totally immersed in the vapour of boiling water to ensure a temperature of 100°. The mixture first liquefied; solid appeared after five hours' heating. At the end of six hours, the condensation product was dissolved in 50 c.c. of hot 12—15 per cent. caustic soda solution, the liberated aniline distilled with steam, and the cooled filtered solution made slightly acid with dilute hydrochloric acid. The small quantity of resin here precipitated was separated and extracted with 20 c.c. of boiling water. The extract was added to the main solution, from which a saturated solution of aniline hydrochloride (15 c.c.) precipitated β-resorcylaldehyde as the hydrochloride of the hydrated Schiff's base, $C_6H_3(OH)_2{\cdot}CH(OH){\cdot}NHPh,HCl$. After one hour, the hydrochloride was collected and the base remaining in the filtrate was precipitated by adding a saturated solution of sodium acetate. The free base was filtered off, mixed with the hydrochloride, and the whole hydrolysed with caustic soda solution. The liberated aniline was removed with steam, the bright red solution acidified, and the aldehyde, extracted with ether (yield 45—50 per cent. of the theoretical), was recrystallised from hot water. It was identified by mixed melting-point determinations (135—136°), the deep brown colour given by ferric chloride to its aqueous solution, the feathery needles of its phenylhydrazone, the oxime of melting point 192°, and the peculiar yellow precipitate which it gives with Schiff's reagent.

* It is hoped to publish details of this simple thermostat shortly.

The authors wish to state that the suggestion that such a condensation might take place was due to Prof. A. Lapworth, F.R.S. They also wish to thank the Advisory Council of the Department of Scientific and Industrial Research for grants which enabled each of them in turn to undertake these investigations.

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brown solid on addition of hydrochloric acid, crystallised from alcohol, separating in yellow prisms, m. p. 81°.

Condensation with α-Naphthol.—Diphenylformamidine (7 g.) and α-naphthol (5 g.) were heated together at 95° for 6 hours. The reaction product was hydrolysed as before. The dark green resin that appeared during the steam distillation was removed, a saturated solution of sodium chloride added to the green filtrate, the sodium salt of the aldehyde, which separated in yellow-green, leafy crystals, was washed with a saturated solution of common salt, decomposed with hydrochloric acid, and the 1-hydroxy-2-naphthaldehyde distilled in steam (yield 1·4 g., m. p. 58—59°, after crystallisation from alcohol).

Condensation with Resorcinol Monomethyl Ether.—This was carried out at 183—184° for 2 hours. After hydrolysis of the condensation product with sodium hydroxide and distillation of the aniline in steam, 2-hydroxy-4-methoxybenzaldehyde was extracted from the cooled, acidified solution with ether, separated from the extract with sodium bisulphite solution, and recrystallised from dilute alcohol (m. p. 41°; yield 20%).

Condensation with Guaiacol.—Temperature 210°; time 6 hours. 2-Hydroxy-3-methoxybenzaldehyde was isolated as in the preceding case (yield *ca.* 10%).

Condensation with Pyrogallol.—Temperature 110°; time 4 hours. 2 : 3 : 4-Trihydroxybenzaldehyde was separated by the bisulphite method (yield 20%).

Condensations with the Isomeric Cresols.—*o*-Cresol: temperature 183°; time 6 hours. The aniline was distilled in steam, the intermediate product hydrolysed as before, the liberated aniline distilled in steam, unchanged diphenylformamidine removed, the filtrate acidified with hydrochloric acid, and 2-hydroxy-3-methylbenzaldehyde isolated therefrom by distillation with steam and extraction of the distillate with ether (yield 25%).

m-Cresol: temperature 210°; time 6 hours. The yield of 2-hydroxy-4-methylbenzaldehyde, m. p. 59°, was *ca.* 20%.

p-Cresol: temperature 193°; time 6 hours. Under the best conditions, the yield of 2-hydroxy-5-methylbenzaldehyde, m. p. 56°, was only 15%.

Salicylaldehyde (yield 10%) was obtained from phenol in a similar manner. The condensation was carried out at 183° for 6 hours. Sodium bisulphite was used in order to extract the aldehyde from the ethereal solution; otherwise it was found to be contaminated with phenol. The method cannot be recommended in this case.

Isolation of the Pure Intermediate Compounds.—(1) 2-Hydroxy-1-naphthylideneaniline. The crude condensation product from

dissolved in 40 c.c. of dry ether, powdered anhydrous zinc chloride (1 gram) was added, and a slow stream of hydrogen chloride gas passed into the reaction mixture. Turbidity was apparent after four hours, and a crystalline precipitate formed almost immediately afterwards. The hydrogen chloride gas was passed for eight hours and after that the mixture allowed to stand for another twelve hours. The ether was then poured off from the crystals and from it, after standing some days, an additional quantity of the crystals separated out. The crystals were dissolved in cold water and precipitated with concentrated hydrochloric acid. The solid was purified by the repetition of this process at least twice, and after having been dried decomposed at 195° and proved to be 2 : 4-*diacetoxy*-2′ : 4′-*dihydroxybenzophenoneimine hydrochloride* (Found : Cl = 9·7. $C_{17}H_{16}O_6NCl$ requires Cl = 9·5 per cent.). The hydrochloride was hydrolysed by boiling 25 per cent. aqueous sulphuric acid, the operation being complete in about fifteen minutes. The cooled solution deposited a syrup which was then boiled with dilute sodium carbonate solution for half an hour. From this solution yellow crystals separated (2 grams) which were recrystallised from boiling water and animal charcoal and possessed all the properties of the 2 : 4 : 2′ : 4′-tetrahydroxybenzophenone obtained by the method of Meyer and Conzetti (*loc. cit.*).

β-*Resorcylamide.*—The acid solution from the hydrolysis of the imine hydrochloride was extracted with ether several times and the combined extracts were mixed with the ether from which the imine hydrochloride had separated. When the ether was distilled away from the extract, a syrup remained from which white, needle-shaped crystals were at once precipitated on the addition of water. This solid was recrystallised from water, when it melted at 221–222°. Its aqueous solution gave a reddish-brown coloration with ferric chloride. Ammonia was evolved (*a*) slowly from a boiling caustic soda solution of the solid, (*b*) more rapidly if the solid was first hydrolysed with 50 per cent. sulphuric acid and then boiled with caustic soda, (*c*) immediately when the solid was heated alone. The compound was classified as β-resorcylamide (Found : C = 55·14 ; H = 5·02 ; N = 9·03. Calc. for $C_7H_8O_3N$, C = 54·90 ; H = 4·58 ; N = 9·15 per cent.). After the hydrolysis of the amide a small quantity of β-resorcylic acid was isolated from the solution.

Resacetophenone.—The aqueous solution from which the β-resorcylamide had been precipitated was extracted with ether and the syrup remaining after the ether had been distilled off boiled with dilute hydrochloric acid and animal charcoal. From this solution white needles crystallised out which when purified melted at 141–142° and easily gave a phenylhydrazone with melting point 158°