Thesis for the Degree of Ph.D.

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

POLARITY EFFECTS IN AROMATIC HALOGEN COMPOUNDS.

by

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Within recent years it has become more and more apparent that the formulae employed in organic chemistry only give a very limited and inadequate representation of the mode of reactivity of any compound which may be considered. Thus, to take a simple example, isopropyl bromide is found to be produced by the addition of hydrobromic acid to propylene,

$$CH_3 - CH = CH_2$$

but there is nothing suggested by the above formula as to why the normal bromide is not the product of the reaction. A similar state of affairs exists as regards substitution of which the best known example is substitution in the benzene nucleus.

Attempts to modify the methods of graphical representation, with a view to indicating the differences in the reactivity of the constituent atoms in a molecule, have been made from time to time with more or less satisfactory results. Thus Thiele (Annalen, 1899, 306, 87.) has made use of dotted lines to express residual partial valencies, and his suggestions have been successfully expanded by Robinson and his collaborators (T., 1916, 109, 1029; 1917, 111, 958; etc.) to include trivalent nitrogen. Flürscheim (J. pr. Chem., 1902, 66, 321; 1905, 71, 497; 1907, 76, 165,/

165, 185; T., 1909, 95, 718; 1910, 97, 84.) has used thick and thin lines to represent increased and diminished affinities; whilst Fry (J. Amer. Chem. Soc., 1912, 34, 644; and onwards) attaches plus and minus signs to reactive and non-reactive hydrogen atoms respectively. Vorländer (Ber., 1919, 52, 263.) has recently used modifications of a similar nature in suggestions on substitution in the benzene nucleus.

The essential drawback to the adoption of such methods of notation is the lack of a sound physical basis without which a concrete understanding of the principle is impossible. It was only to be expected that the recent work of Kossel (Ann. Physik, 1916, (4), 49, 229.) and of Thomson (Silliman Lectures, 1903; Phil. Mag., 1921, (6), 41, 510.) on the electron, and its application to the theory of atomic structure by Lewis (J. Amer. Chem. Soc., 1916, 38, 763.) and by Langmuir (ibid, 1919, 41, 868; etc.) would have its influence on the theories of the molecular constitution of organic compounds; and the principle of induced alternate polarities gradually evolved by Lapworth (Mem. Manchester Phil. Soc., 1920, 64, (2), 1.; T., 1922, 121, 416.) took on a new aspect as the result of such considerations*. In this theory the carbon/

* Compare also Kermack and Robinson, T., 1922, 121, 428.

carbon atoms in a ring or chain are looked upon as tending to exhibit alternate homogeneity of polarity, thus:-

$$-\overset{-}{C}-\overset{+}{C}-\overset{-}{C}-\overset{+}{C}-$$

The influence of a strongly electropositive or negative atom attached to a carbon atom of such a chain would be expected to increase such a tendency, and for this reason the electropositive or negative atom is termed a "key-atom", and is represented in the formula by a dot attached to its polar sign. It would be expected that such atoms as divalent oxygen, trivalent nitrogen, hydrogen, and, to a lesser extent, the halogens would act as "key-atoms" under suitable conditions, and this has been shown to be the case. This is probably the simplest way of representing reactive and non-reactive atoms in an organic molecule.

The principle of induced alternate polarities includes and supersedes all earlier theories, and is capable of very wide application in many fields of organic chemistry. It has, however, not escaped criticism principally on the ground that, whilst it explains, it fails to predict reactivity (see the report of the discussion[*] at the Faraday Society's conference on the electronic theory of valency, July 1923, p.527.). This accusation is, however, without foundation for it has/

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[*] A short account of this discussion is given in Nature, 1923, <u>112</u>, 179.

has been shown that the induced polarity theory differs from all other theories which depend on activation produced from a distance in so far that it is possible by its aid to predict a reversal in the order of reactivity which ought to accompany a change in the character of the reagent used to demonstrate such effects (compare the results of the investigation of the reactivity of the halogen atoms in the methoxybenzyl bromides, mentioned below). The object, therefore, of the present research was to determine in how far it was possible to predict the existence of reactive as well as of non-reactive halogen atoms in the compounds examined. The application of a theory to predict a non-reactive atom is as of great importance as a prediction of a reactive atom.

The investigations described here may be divided into three sections:-

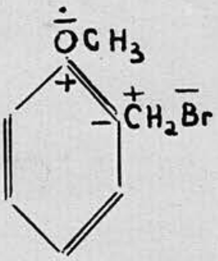
1. The influence of substituents on halogen atoms directly attached to carbon atoms of the benzene nucleus.
2. The influence of substituents on halogen atoms attached to the carbon atom in the shortest side-chain.
3. The influence of substituents with respect to the mode of addition at an ethylenic side-chain.

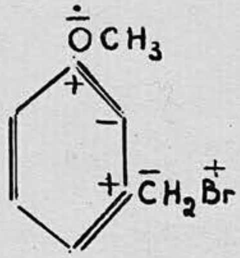
The/

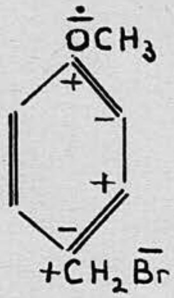
The influences exerted by an atom or group of atoms on the other atoms in the molecule may generally be grouped under three heads, namely, (a) steric or structural influences, (b) general polar influences, and (c) induced polar influences (vide Lapworth and Shoesmith, T., 1922, 121, 1391). The steric or structural effects are generally apparent in aromatic organic compounds when the substituents are in ortho-position to one another, and may be eliminated by confining attention to meta and para-derivatives.
The general polar effect, which is due to the influence of the substituent on the molecule as a whole (compare Flürscheim, T., 1909, 95, 718; Lapworth, Mem. Manchester Phil. Soc., 1920, 64, No.3; Kermack and Robinson, loc. cit.; Robinson, Ann. Reports, 1922, 19, 98.), may be eliminated by confining attention to isomerides only.

A striking example of the influence of a group on a side-chain halogen atom is to be found in the systematic examination of the methoxybenzyl bromides (Lapworth and Shoesmith, loc. cit.). Here the negative oxygen atom of the methoxyl group is the "key-atom", and it would be expected, on an examination of the formulae, that the negative character of the halogen atom would be enhanced in the ortho and para-compounds, but/

but that in the case of the meta-compound the halogen atom should possess induced positive properties.







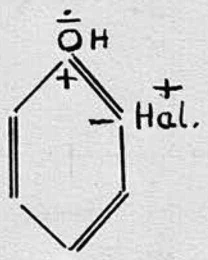
In order to ascertain whether this induction of polarity was actually taking place, the above investigators subjected the compounds, in turn, to hydrolysis and to hydriodic acid reduction. In such isomerides the halogen atom, which is in such a position with regard to the "key-atom" that its negative nature is enhanced, would be more easily removed on hydrolysis than that in which the negative nature is diminished. On the other hand the halogen atom, which is in such a position with regard to the "key-atom" that it receives an induced positive charge, would be the more readily removed on reduction, thus:-

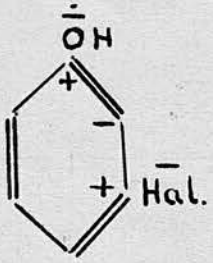
$$R - \overset{+}{CH_2} - \overset{-}{Br} + \overset{+}{H}\text{-}\overset{-}{OH} = R\text{-}\overset{+}{CH_2} - \overset{-}{OH} + \overset{+}{H}\text{-}\overset{-}{Br}$$

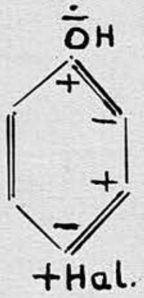
$$\left\{\begin{array}{l} R - \overset{-}{CH_2} - \overset{+}{Br} + \overset{+}{H} - \overset{-}{I} = R\text{-}\overset{-+}{CH_3} + \overset{-}{I}\text{-}\overset{+}{Br} \\ \quad I - Br + H - I = H - Br + I_2 \end{array}\right.$$

The results of the investigation are in absolute accordance with the theory; the order of reduction by hydriodic acid of the series was found to be meta > para and ortho, and the order of hydrolysis, para and ortho > meta.

From these results it is evident that the oxygen atom has a marked influence on the reactivity of the halogen atom attached to the carbon atom in the shortest side-chain; and it was now decided to determine whether a similar activation was produced when the halogen was moved one place nearer the "key-atom" and directly attached to a carbon atom of the benzene nucleus. Thus in the mono-halogenated phenols it would be expected from an examination of the formulae, modified in the above manner, that, this time, the halogen atoms in the ortho and para-positions should be more readily removed by a reducing agent than that in the meta-position, but that the reverse should be the case on hydrolysis. No systematic investigation of a nature which might enable this point to be settled without further examination could be found in the literature save that of Nicolet (mentioned below) who, however, did not examine isomerides.







Reduction of the monohalogenated phenols.

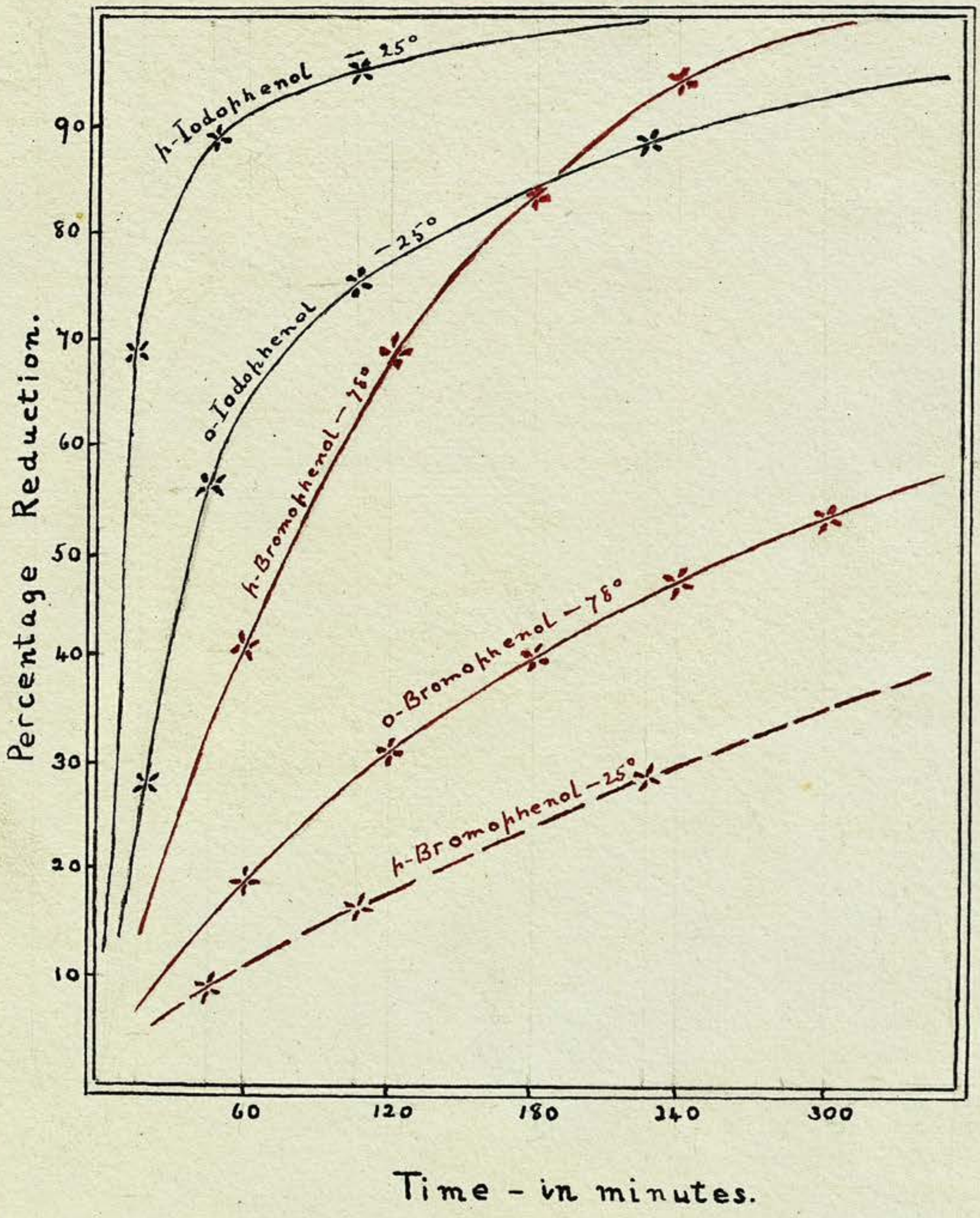
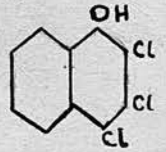


Figure I.

The action of hydriodic acid on the monohalogenated phenols showed that this first prediction was correct. The order of reduction to phenol of the series was found to be p-iodo > o-iodo > p-bromo > o-bromo > p-chloro > o-chloro; the meta-isomerides were unchanged under the same conditions*. The above order of reducibility of the halogens (I > Br > Cl) is to be expected since iodine has the greatest natural positive polar properties and chlorine the least, that is the greatest natural negative polar properties (compare Gotts and Hunter, T., 1924, <u>125</u>, 446.). 4-Iodoresorcinol, under the same conditions, loses its halogen atom still more readily than p-iodophenol.

Nicolet (J. Amer. Chem. Soc., 1921, <u>43</u>, 2081.) has shown that the halogen atoms in ortho and para-substituted iodoanilines and bromoanilines, and also in 3-iodo-4-hydroxybenzoic acid are removed when the compounds are boiled with hydrochloric acid, and he attributes this to the presence of "positive" halogen. He/

* It is interesting to note in this connection that Franzen and Staübe (J. pr. Chem., 1921, (2), <u>103</u>, 352.) have prepared 3-chloro-α-naphthol from 2-3-4-trichloro-α-naphthol,

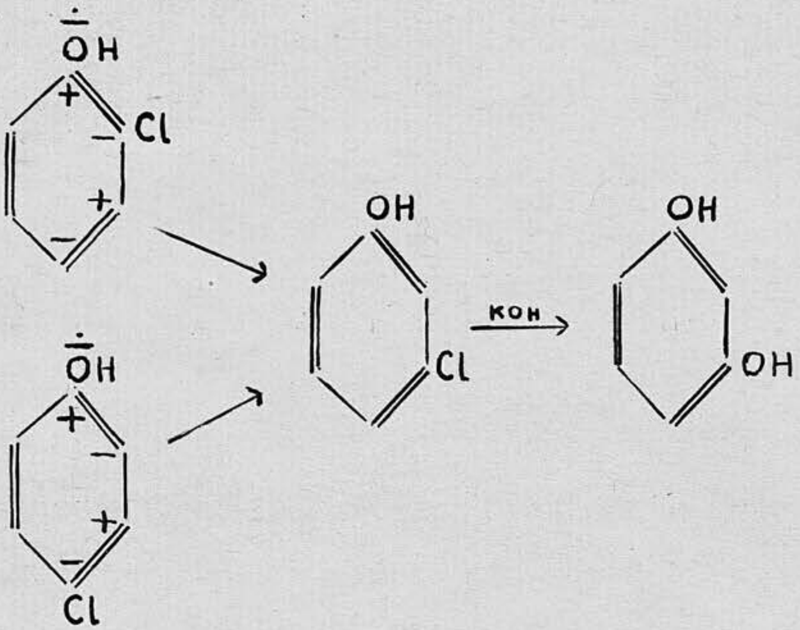


by reduction with hydriodic acid. The resulting mono-chloro-compound is quite stable to the reducing agent.

He has not shown, however, that the compounds which contain halogen in meta-position to such negative groups are not removed by a reducing agent. He also states that halogen atoms which are ortho to an amino or hydroxyl group are more positive than those in para-position to such groups. The present investigation has shown the reverse to be true.

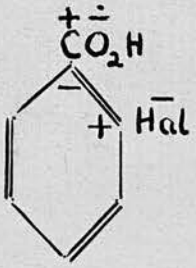
It was never found possible to remove any of the halogen atoms in the mono-halogenated phenols by hydrolysis with aqueous or alcoholic potassium hydroxide at the boiling point*. This must be attributed to the strong linkage which exists between a nuclear carbon atom and an attached halogen. It is rather interesting to note, however, that on fusion with potassium hydroxide the three isomeric mono-chlorophenols yield the same end-product, namely resorcinol (Blanksma, Chem. Weekblad, 5, 93; Tijmstra, ibid, 96.). This intramolecular change, in the case of the ortho and para-compounds, is believed to take place prior to the replacement of the halogen by hydroxyl, and may be explained as a result of the production of homogeneity of polarity. That is to say the chlorine atoms in ortho and para-chlorophenol, at the temperature of the fusion, are attracted to the carbon atom whose induced polarity is opposite to the natural polarity of the halogen.

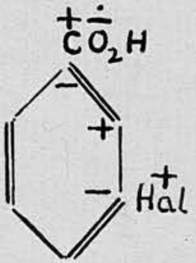
* The halogen atoms in compounds of this nature are only removed very slowly on hydrolysis with alcoholic soda under pressure at 180° (De Lange, Rec. trav. chim., 1919, 38, 103; Holleman, ibid, 1923, 42, 373; Meyer, Ber., 1921, 54, 2264.).

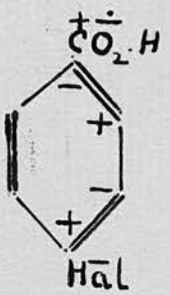


This state of greater stability is one to which all molecules tend (Lapworth, T., 1922, <u>121</u>, 416; Lowry, ibid, 1923, <u>123</u>, 822.).

The results of the hydriodic acid reductions of the mono-halogenated phenols clearly show that the oxygen atom of the hydroxyl group has a strong influence on the reactivity of the nuclear halogen atom. It would not, however, be expected that the influence of this atom would only be manifest in the hydroxyl group, but that a similar activation might be found in other groupings which contain that atom. Such a grouping might be found in the carboxyl radicle,and the mono-halogenated benzoic acids were accordingly examined.



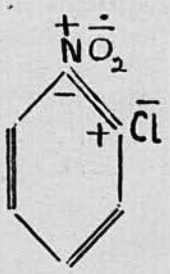


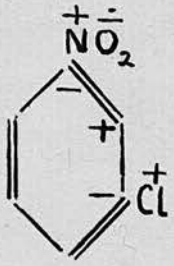


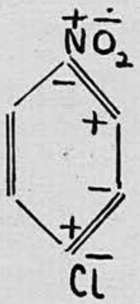
It was not, however, found possible to remove any of the halogen atoms in these compounds either by hydrolysis or by reduction with hydriodic acid. This non-reactivity* must again be attributed to the effect of the strong nuclear carbon-halogen linkage which completely counterbalances any such influence the carboxyl group may possess.

It is well known that the halogen atoms in the mono-chloronitrobenzenes are hydrolysed off in the order para and ortho > meta, that is in accordance with the principle of induced alternate polarities (compare Blanksma, Rec. trav. chim., 1905, 24, 320; Burton and Kenner, T., 1922, 121, 675; Ibbotson and Kenner, ibid, 1923, 123, 1260.).

[*] Rosenmund and Harms (Ber., 1920, 53, 2226.) have shown that the halogen atoms in similar compounds may be removed by the action of aqueous sodium acetate under pressure at 140°. The presence of a trace of copper acetate is, however, essential for the success of the reaction.





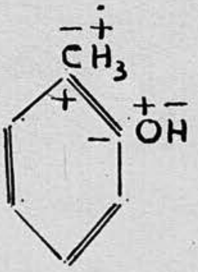


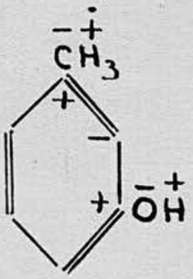
Experiments undertaken to determine whether this order was reversed (i.e. m > p and o) by the action of hydriodic acid were unsuccessful, owing to the reduction of the nitro-group.

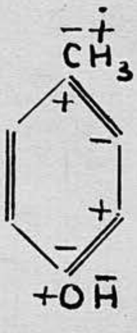
The reactivity of the halogen atoms in the compounds examined so far has been investigated from the point of view of activation induced by the negative oxygen atom. The inducing action of a hydrogen atom has not been investigated before with a view to establishing the correctness of the principle. Experiments were, therefore, carried out in order to determine to what extent hydrogen is capable of influencing a halogen atom both attached to a carbon atom of the nucleus and to a carbon atom in the shortest side-chain. Should the hydrogen atom under these conditions exhibit this ability for inducing activation, the mechanism of the reaction must necessarily be of a very simple nature since the tendency towards formation of complex intermediate compounds, depending on an increase in the affinity of constituent atoms, is/

is almost if not entirely eliminated. An examination of isomeric compounds which contain a methyl group appears to offer the most satisfactory method of demonstrating whether this activation can be produced by positive hydrogen atoms, and, accordingly, the compounds examined were of this nature.

Previous to this Lapworth (Mem. Manchester Phil. Soc., 1920, 64, (2), 10.) had pointed out, on an examination of the formulae of the three isomeric cresols, that the meta-compound should be the strongest acid for in that compound the positivity of the hydrogen attached to the oxygen atom is enhanced by virtue of the induction of polarity produced by the hydrogen atoms of the methyl group.







Reference to the literature showed that these were the precise experimental results of Dawson and Mountford (T., 1918, 113, 937.), who found that the ionisation constants of ortho and para-cresol were smaller/

Reduction of the mono-iodotoluenes.

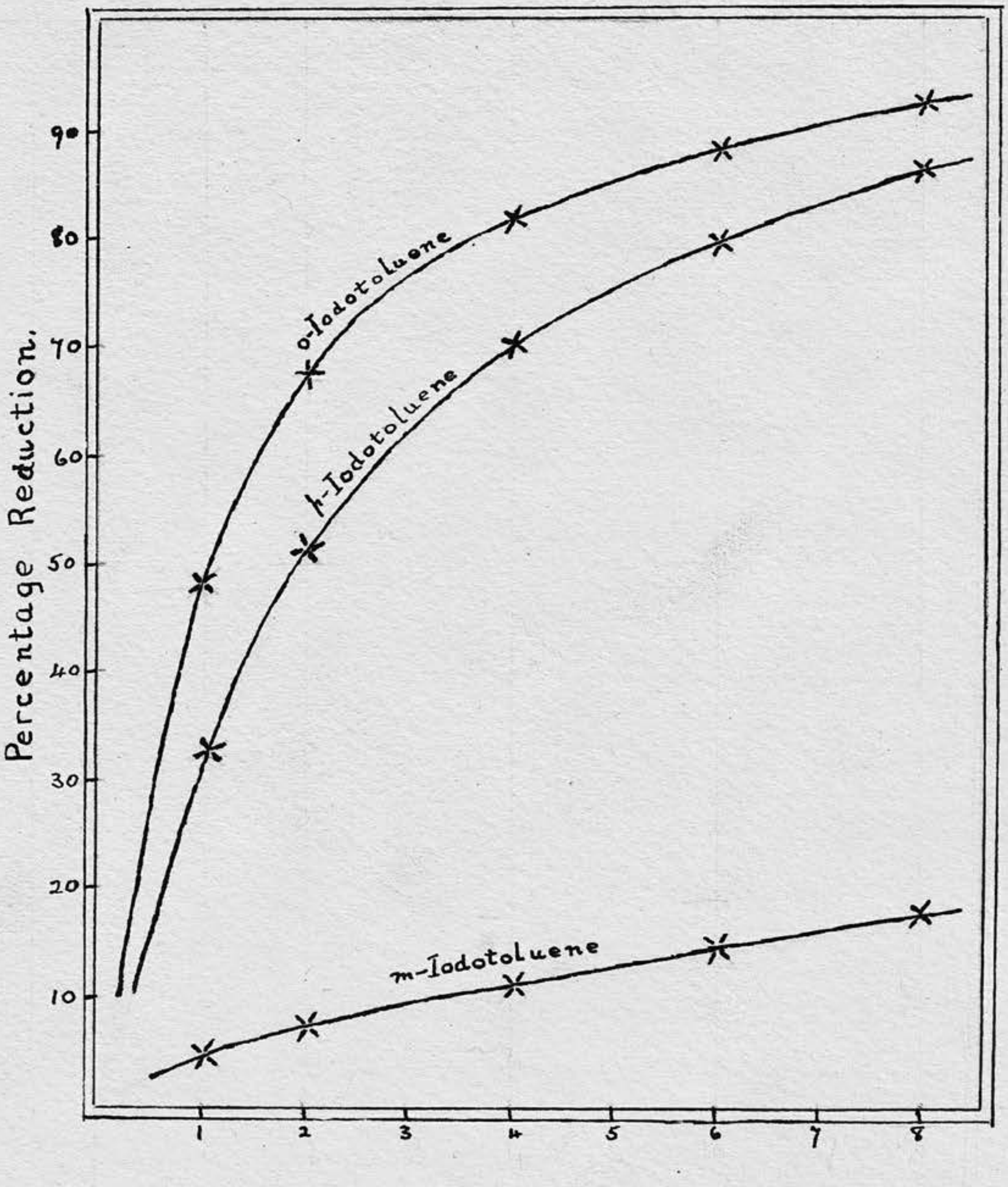
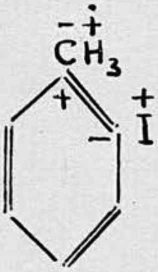
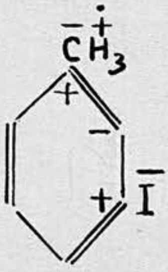
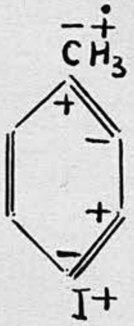


Figure II.

smaller than that of the meta- compound. This, therefore, indicates that the hydrogen atoms of the methyl group are capable of acting as positive "key-atoms", and it would be expected,on an examination of the mono-iodotoluenes,that the ortho and para-halogen atoms should be removed by hydriodic acid at a greater rate than the meta-halogen atom.





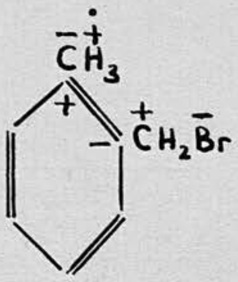


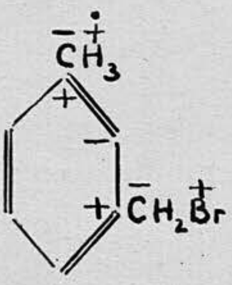
The action of hydriodic acid showed this to be true, and the order of reduction to toluene was found to be para and ortho > meta.

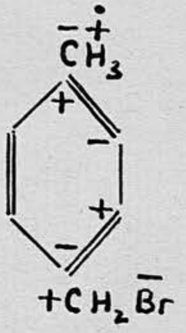
Just as in the case of the mono-halogenated phenols it was found impossible to remove any of the halogen atoms in the above compounds by the action of hydrolysing agents.

The great increase in halogen reactivity that is met with when one moves from a nuclear to a side-chain halogen atom is very well known. This difference may be due to the fact that in reactions which involve nuclear halogen atoms addition precedes substitution./

substitution. Substituted benzyl halides are, therefore, the most suitable type of compounds for this kind of work. The influence of the methoxyl group and of the nitro and carboxyl groups on the side-chain halogen atom have already been investigated in this connection by Lapworth and Shoesmith (loc. cit.) and by Shoesmith and Hetherington (J. Soc. Chem. Ind., 1923, <u>42</u>, 1134.) respectively. In order, therefore, to demonstrate still further the influence of the methyl group, the reactivity of the halogen atoms in the isomeric ω-bromoxylenes was examined.

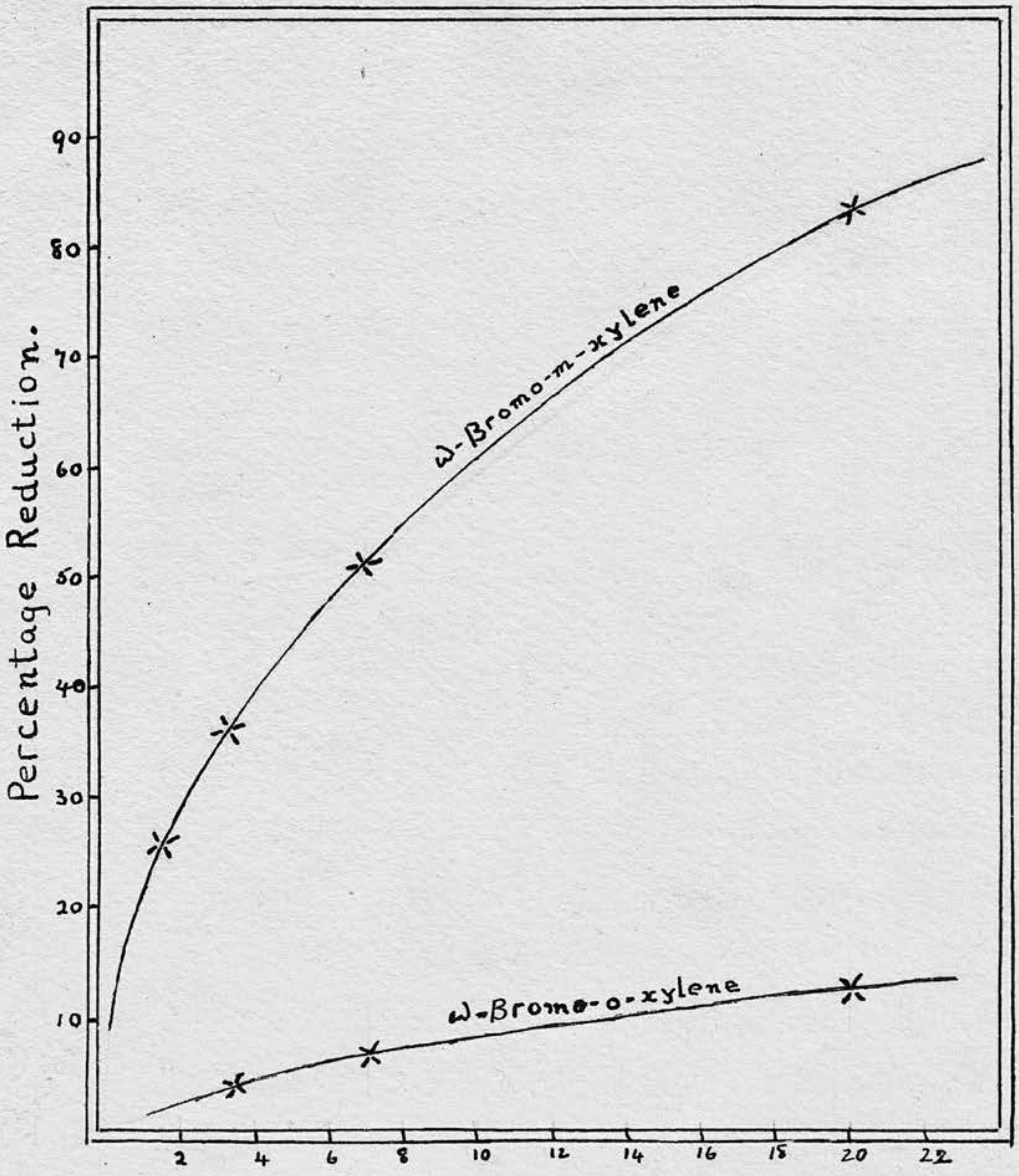






In these compounds the halogen atom has been removed one place further away from the activating hydrogen atoms of the methyl group than was the case in the mono-iodotoluenes. It would, therefore, be expected that the order of reduction by hydriodic acid would be, this time, meta > para and ortho, and the order of hydrolysis para and ortho > meta; in fact the compounds should react in an order analogous to/

Reduction of the ω·bromoxylenes.



Time – in hours.

Figure III.

to that discovered in the methoxybenzyl bromides.

The action of hydriodic acid on the ω-bromoxylenes showed that the first prediction was correct; the meta reduces slowly, the ortho very slowly, and the para not at all. An examination of the reduction mixture after forty hours treatment with hydriodic acid showed that ω-bromo-m-xylene had been reduced to m-xylene and that, on the other hand, ω-bromo-p-xylene had been converted quantitatively into the corresponding iodo-compound. These results may be expressed by the equations:

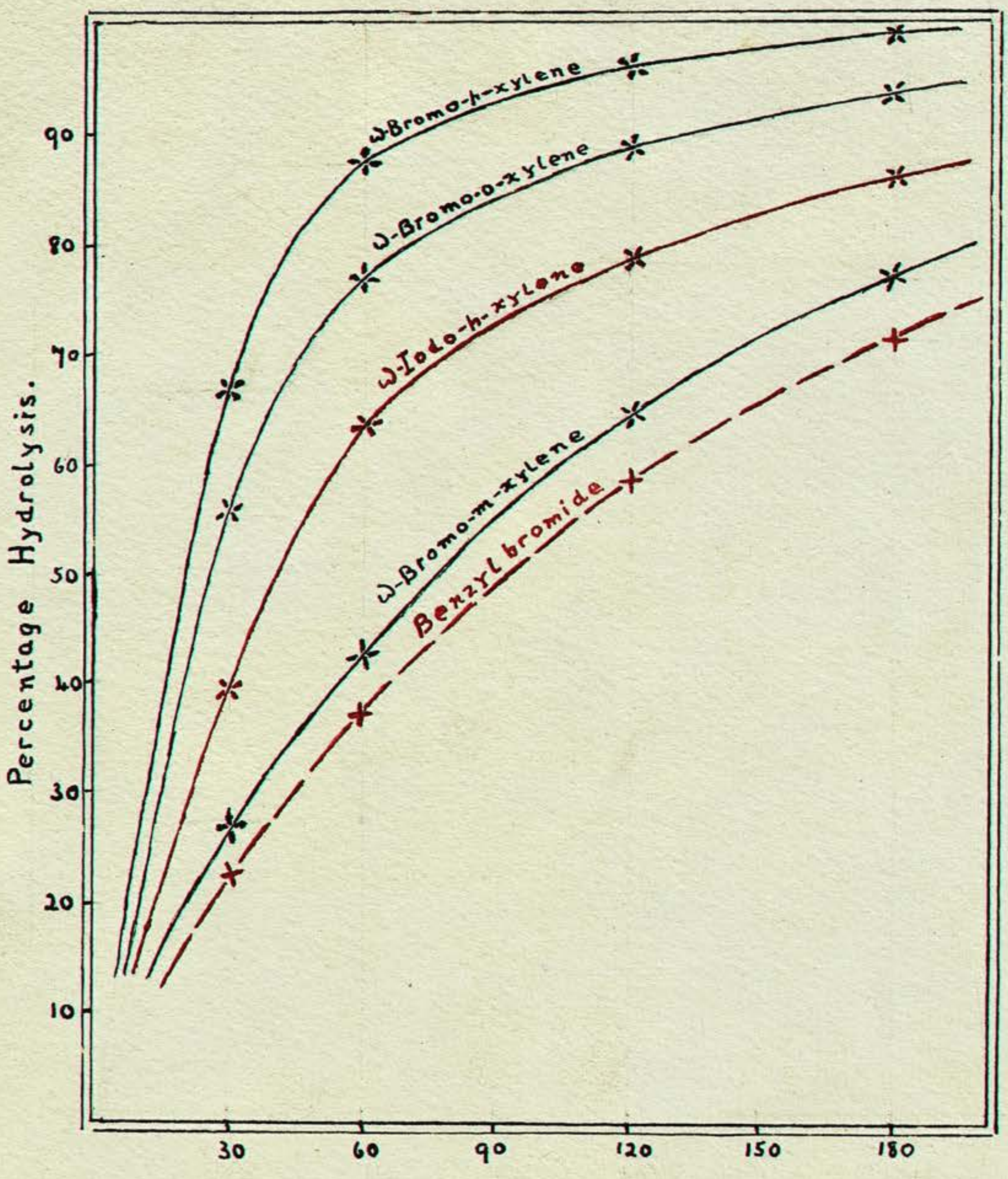
meta $CH_3C_6H_4CH_2Br + 2HI = CH_3C_6H_4CH_3 + H\,Br + I_2$

para $CH_3C_6H_4CH_2Br + HI = CH_3C_6H_4CH_2I + H\,Br$

Thus ω-bromo-m-xylene reacts with hydriodic acid in such a way that the bromine atom is removed and replaced by the hydrogen (or positive ion) of the hydriodic acid; whilst ω- bromo-p-xylene reacts in exactly the opposite manner and the bromine atom is replaced by the iodine (or negative ion) of the same acid. This difference in the mode of reactivity of the halogen atom in the two isomerides is remarkable, and yet is in perfect agreement with the principle of induced alternate polarities.

ω-Bromo-o-xylene reduces only very slowly under the same conditions, and about an eighty per cent yield of ω-iodo-o-xylene was obtained. This tendency which/

Hydrolysis of the ω-Bromoxylenes.



Time – in minutes.

Figure IV.

which the ortho-isomeride shows towards reduction with hydriodic acid must be attributed to structural influences.

The order of reactivity of the halogen atoms in the ω-bromoxylenes with respect to hydrolysis was that anticipated, that is para and ortho $>$ meta*.

This prediction of the reversal in the order of reactivity accompanied by a change in the character of the reagent used to demonstrate such effects is the remarkable feature of the principle, and could not have been foreseen by the aid of any hypothesis enunciated prior to that of induced polarities.

In the above investigations the activation produced by an atom has been examined with respect to the reactivity of a halogen atom in various positions in the molecule. Experiments were now undertaken with a view to determining whether such similar activation influenced the mode of addition of a molecule at an ethylenic side-chain. The compound used in this investigation was anethole in view of its para-methoxyl group - the group which has been shown to possess an enormous directive influence (compare Lapworth and Shoesmith, loc. cit.). As the formula of anethole clearly demonstrates,

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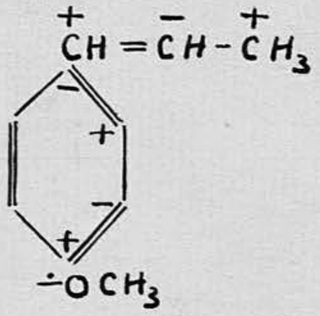
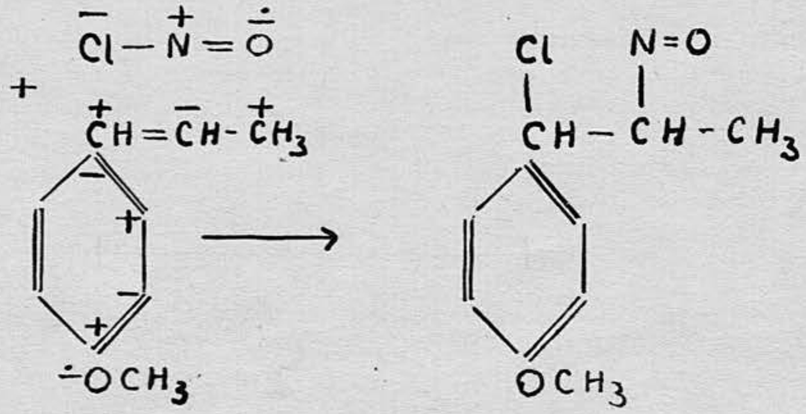
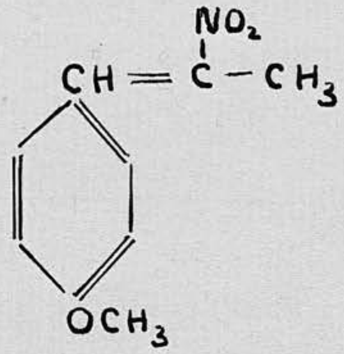
* Olivier(Rec. trav. chim., 1922, <u>41</u>, 301.) has investigated the rates of hydrolysis of the halogen atoms in various substituted benzyl chlorides, and he has obtained the same order (i.e. p and o $>$ m) on an examination of the ω-chloroxylenes.



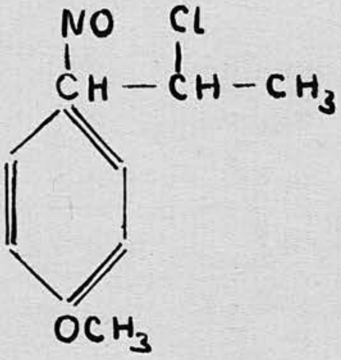
it would be expected that addition would take place at the side-chain in such a way that the negative portion of the addendum attaches itself to the positive alpha carbon atom and the positive portion to the negative beta carbon atom. The addition of hydrocyanic acid to anethole was first investigated, but it was found that no reaction takes place between these molecules under ordinary conditions. It was, therefore, decided to consider the addition of nitrosyl chloride. Nitrosyl chloride readily forms an addition-compound with anethole but the constitution of this addition-compound is not known. From the point of view of induced polarity it would be expected that addition would take place as follows:-



That is to say, the negative chlorine atom attaches itself to the positive alpha carbon atom, and the positive nitrogen atom of the nitroso-group attaches itself to the negative beta carbon atom. Evidence of the attachment of a positive nitrogen atom to this same (beta) carbon atom is to be found in the nitration of anethole by means of tetranitromethane, when the reaction product is β-nitroanethole (Schmidt and Fischer, Ber., 1920, 53, 1536; Allsop and Kenner, T., 1923, 123, 2314.).

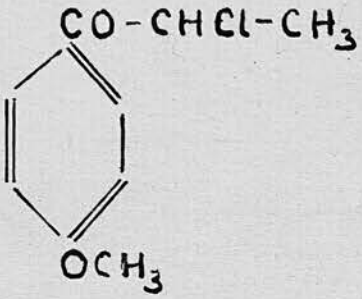


Wallach (Annalen, 1904, 332, 326.), however, for no apparent reason, formulates anethole nitrosochloride thus:-

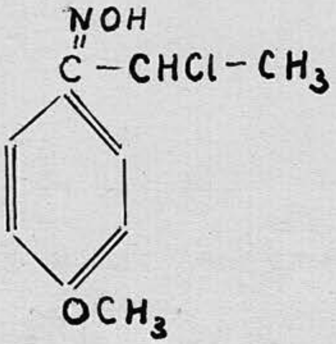


The/

The first method adopted in attempting to determine the constitution of anethole nitrosochloride was to synthesise 4-(α-chloropropionyl) - anisole



by direct Friedel Craft of anisole and α-chloropropionyl chloride; and then to convert it into the oxime by the action of hydroxylamine hydrochloride.



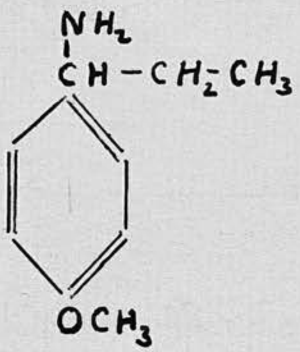
This compound is the oximino-form of anethole nitrosochloride as formulated by Wallach. This would, therefore, be a direct synthesis as Wallach states that the oximino-form is produced when the nitrosochloride is warmed with aqueous solutions. This method of synthesis was, however, not a success, and no ketone could be isolated on an examination of the products obtained by the Friedel Craft reaction.

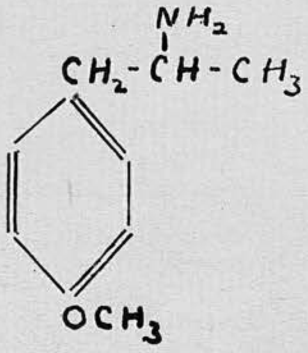
Tönnies (Ber. 1879, <u>12</u>, 169) states that anethole nitrosochloride/

nitrosochloride, on reduction, yields an amino-compound the molecular weight of which corresponds to the formula:-

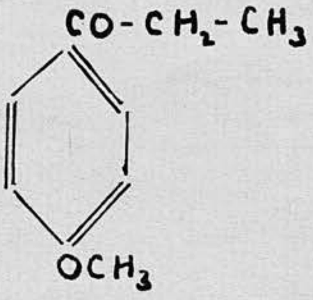
$$CH_3O - C_6H_4 - C_3H_6 - NH_2$$

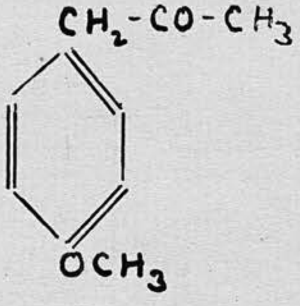
This at first sight appears to offer a method for determining the constitution of the nitrosochloride for this amino-compound must have one of the two formulae:-





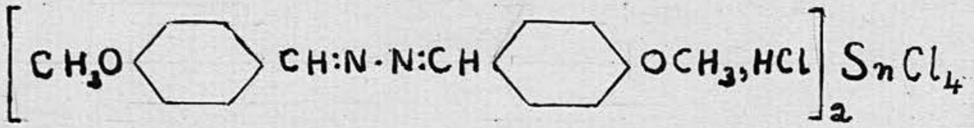
Either compound could be readily obtained by the reduction of the oximes of the ketones:-



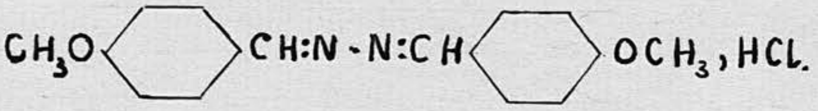


Unfortunately, however, Tönnies fails to mention his method of reduction to the amino-compound or any of the properties of that compound. Owing to the readiness/

readiness with which anethole nitrosochloride decomposes with formation of anethole and anisaldehyde, it was never found possible to obtain an amino-compound by the action of reducing agents. The most interesting compound isolated was a stannic chloride addition-compound of anisaldazine with the formula:-



when the reducing agent used was a solution of stannous chloride in concentrated hydrochloric acid. This compound, on the addition of water, rapidly decomposes with formation of anisaldazine and stannic hydroxide. Anisaldazine dissolves readily in warm dilute hydrochloric acid and forms a hydrochloride the constitution of which corresponds with the formula:-



This hydrochloride by the action of nitrous acid yields anisaldehyde.

Addition of stannic chloride to a solution of anisaldazine in concentrated hydrochloric acid re-precipitates/

reprecipitates the above stannic chloride addition-compound.

No stannic chloride addition-compound is produced by the action of stannous chloride on the oxime of anisaldehyde.

PREPARATIVE.

Preparation of the mono-chlorophenols.

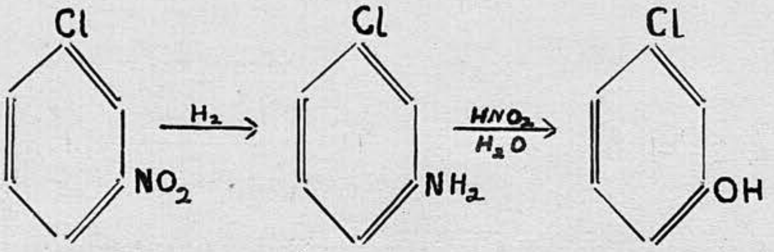
o-Chlorophenol. No account of the preparation of this compound from the corresponding aminophenol, by means of the Sandmeyer reaction, is given in the literature. It was, however, found that the following gave a very satisfactory result both from the point of view of purity and yield.

25 grams of o-aminophenol were carefully ground up with a mixture of 60 cc. of concentrated hydrochloric acid and 40 cc. of water. Diazotisation was effected by the gradual addition of 20 grams of sodium nitrite dissolved in 25 cc. of water. The temperature of the mixture was not allowed to rise above 0°. During the diazotisation a brown solid separated out, which when filtered off was found to be the solid diazo-chloride ($HO.C_6H_4N_2Cl$); it was dissolved in a little water and added to the filtrate. The diazo-solution was then slowly added to a slight excess of freshly prepared cuprous chloride dissolved in hydrochloric acid. When the first vigorous reaction was over, the mixture was warmed on the water-bath until evolution of nitrogen ceased, and the chlorophenol distilled/

distilled over in steam. It was purified by distillation; b.p. 175-176°. The yield was 22 grams.

p-Chlorophenol was prepared from p-aminophenol in exactly the same way. It distilled over at 215°, and when it had stood for a short time it solidified; m.p. 39-40°.

m-Chlorophenol was most conveniently obtained from m-chloronitrobenzene by reduction to m-chloroaniline, and diazotisation of the latter. These reactions may be represented thus:-



m-Chloronitrobenzene was prepared by two methods (1) direct chlorination of nitrobenzene (2) from m-nitraniline by means of the Sandmeyer reaction.

The chlorination of nitrobenzene was carried out at the ordinary temperature in presence of pure ferric chloride (compare Varnholt, J. pr. Chem., 1887, 36,25). This method was not a success, and only about one third of the nitrobenzene was chlorinated in 8 hours.

The second is the better method. The nitraniline was/

was diazotised at 5°, and treated with cuprous chloride in the usual way. m-Chloronitrobenzene was purified by distillation (b.p. 234-236°) and by crystallisation from ethyl alcohol. It melted at 45°.

m-Chloronitrobenzene was reduced to m-chloroaniline by means of iron filings and hydrochloric acid (compare Morgan, T., 1900, 77, 1204.).

100 grams of m-chloronitrobenzene (at a temperature above the melting point) were allowed to drop slowly into a mechanically stirred mixture of 200 grams of iron filings, 400 cc. of water, and 15 cc. of concentrated hydrochloric acid. After a slight preliminary warming the heat of the reaction was sufficient to keep the temperature at 95°. When all the chloronitrobenzene had been added the temperature was maintained at 90° for one hour in order to complete the reduction. The whole was then neutralised by the addition of 30 grams of sodium bicarbonate, and the chloroaniline distilled over in steam. It was extracted from the distillate with ether, dried over sodium sulphate, and then purified by distillation; b.p. 227-229°. The yield was 50 grams. This method of reduction was found to be much more convenient than that which involves the use of tin and hydrochloric acid; the yield, however, by either method was found to be identical.

The conversion of m-chloroaniline to m-chlorophenol/

m-chlorophenol was carried out as described by Varnholt (loc. cit. p.27). m-Chlorophenol, in presence of acid, is very liable to resinify, and in order to prevent this as far as possible, diazotisation was carried out in presence of a large excess of water; slightly less than the required amount of sulphuric acid was used. The chlorophenol was purified by distillation; b.p. 212°. After it had stood for a short time it solidified and melted at 28-29°. The yield was 40 per cent. of the theoretical quantity.

Preparation of m-chloroanisole.

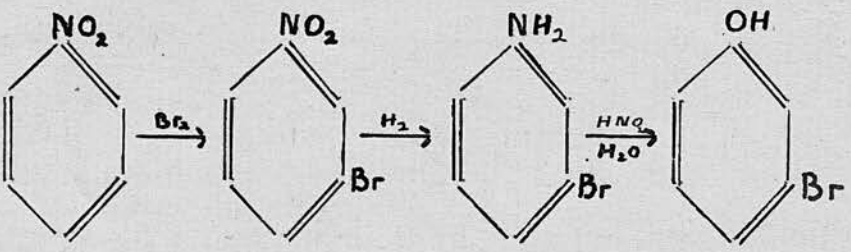
m-Chloroanisole was prepared from m-chlorophenol which was boiled with a slight excess of dimethyl sulphate in presence of a 10 per cent. solution of sodium hydroxide for 4 hours. This ensured the hydrolysis of unchanged dimethyl sulphate. The chloroanisole was extracted with ether and purified by distillation. It boiled at 192-193°.

Preparation of the mono-bromophenols.

Ortho and para bromophenol were prepared from the corresponding aminophenols by the same methods as were used in the preparation of the chloro-compounds. Cuprous bromide in hydrobromic acid solution was substituted/

substituted for cuprous chloride. o-Bromophenol was purified by distillation (b.p. 192-193°), p-bromophenol, by crystallisation from chloroform (m.p. 66°).

m-Bromophenol was most conveniently obtained from nitrobenzene by bromination to m-bromonitrobenzene, reduction to m-bromoaniline, and diazotisation of the latter.



The nitrobenzene was brominated at a temperature of 120-130° in presence of pure iron wire (compare Wheeler and McFarland, Amer. Chem. J., 1897, 19, 366). This preparation was much more successful than that of the corresponding chlorination, and the reaction went practically to completion in 6 hours. After bromination the mixture was subjected to steam-distillation. Any unchanged nitrobenzene distilled over first, and was followed by the less-volatile m-bromonitrobenzene which solidified in the receiver. It was purified by crystallisation from ethyl alcohol. It melted at 55-56°.

The/

The reduction of m-bromonitrobenzene to m-bromoaniline was effected by means of iron filings and hydrochloric acid as in the preparation of the corresponding chloro-compound. The m-bromoaniline distilled over at 247-249°.

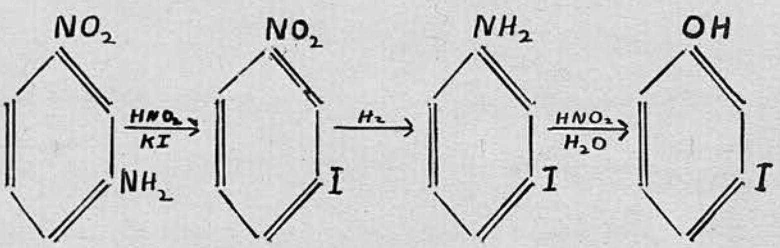
The best method for the conversion of m-bromoaniline to m-bromophenol was found to be that of Diels and Bunzl (Ber., 1905, 38, 1495). This method involves the isolation of the solid diazo-sulphate. The bromophenol, after distillation in steam, was extracted with ether and purified by distillation under reduced pressure. It boiled at 125-127° under 12 mm. pressure, and at 235-236° under atmospheric pressure. On account of resinification the yield only amounted to 20 per cent. of the theoretical quantity.

Preparation of the mono-iodophenols.

Ortho and para-iodophenol were prepared from the corresponding aminophenols by the replacement of the amino-group by iodine as described by Nölting and Stricker (Ber., 1887, 20, 3019.). The former was purified by crystallisation from ligroin (m.p. 43-44°), the latter, by crystallisation from water (m.p. 93-94°).

m-Iodophenol was obtained from m-nitraniline by/

by conversion into m-iodonitrobenzene, reduction to m-iodoaniline, and diazotisation of the latter.



m-Iodonitrobenzene was obtained in excellent yield from the nitraniline by the action of potassium iodide on a solution of the diazotised base. The iodonitrobenzene was obtained in a pure state by steam-distillation; m.p. 34-35° (compare Nölting and Stricker, loc. cit.).

The reduction of m-iodonitrobenzene to m-iodoaniline was carried out by means of iron filings and hydrochloric acid (compare the preparation of the corresponding chloroaniline p. 26.). During the steam-distillation m-iodoaniline solidified in the condenser in the form of fine white needles which melted at 27°.

m-Iodoaniline was converted into m-iodophenol by the method described by Nölting and Stricker (loc.cit.). The tendency which the meta-halogenated phenols show to/

to resinify is very pronounced in the preparation of this compound. This is probably due to the fact that a large excess of sulphuric acid must be used during the diazotisation in order to prevent the formation of complex hydroxyazo-compounds. When diazotisation was complete the mixture was allowed to stand for 12 hours, then warmed gently on the water-bath until evolution of nitrogen ceased, and steam distilled. After extraction of the distillate with ether an oil was obtained which, however, would not crystallise; and it was only after the preparation had been repeated many times that a portion was obtained which did solidify. m-Iodophenol was purified by crystallisation from petroleum ether, and was obtained from this solvent in the form of beautiful snow-white needles which melted at 39°. The yield was very poor, and did not exceed 10 per cent. of the theoretical quantity. m-Iodophenol has quite an appreciable vapour pressure at the ordinary temperature, and when placed in an evacuated desiccator, rapidly vaporises.

Preparation of 4-iodoresorcinol.

This compound was prepared by direct iodination of resorcinol in ethereal solution in presence of a large excess of litharge (vide Stenhouse, Annalen, 1874, 171, 311.). The litharge prevents the reduction of/

of the iodoresorcinol by the hydriodic acid produced in the reaction. 4-Iodoresorcinol was purified by crystallisation from water, and melted at 67-68°.

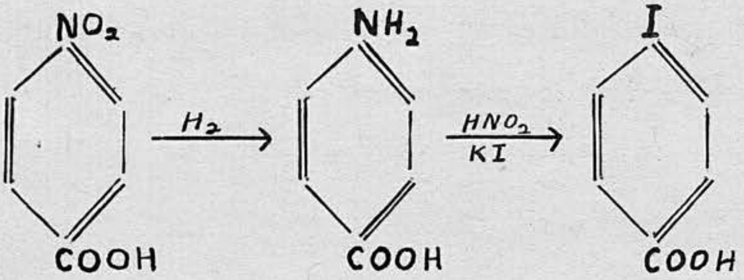
Preparation of the mono-iodobenzoic acids.

o-Iodobenzoic acid was obtained from anthranilic acid by the action of potassium iodide on its diazo-solution (Wachler, Ber., 1893, 26, 1744; Cohen and Raper, T., 1904, 85, 1272.).

20 grams of anthranilic acid were carefully ground up with 200 cc. of dilute sulphuric acid, and diazotised with a solution of 12 grams of sodium nitrite in 15 cc. of water. The temperature of the mixture during diazotisation was not allowed to rise above 5°, and when the reaction was complete the solution was filtered, and poured into a large beaker which contained 25 grams of potassium iodide dissolved in 25 cc. of water. Evolution of nitrogen took place immediately, and when this had abated somewhat, the reaction was allowed to complete itself on the water-bath. When the mixture was cooled, the iodobenzoic acid crystallised out, and after filtration, was washed with an aqueous solution of sodium bisulphite in order to remove free iodine. Obtained in this way, the acid was brown in colour due, no doubt, to the presence of adsorbed iodine, and it was decolorised very/

very slowly when it was boiled in aqueous solution with animal charcoal. To effect purification Cohen and Raper (loc. cit.) recommend conversion into the ethyl ester with subsequent hydrolysis of the latter. It was, however, found more convenient to dissolve the iodobenzoic acid in a concentrated solution of sodium hydroxide, and after passing in a current of sulphur dioxide for a short time, to reprecipitate the acid with hydrochloric acid. Thus obtained the iodobenzoic acid was perfectly white in colour, and when recrystallised from dilute acetic acid melted at 163°. The yield was 60 per cent. of the theoretical quantity.

p-Iodobenzoic acid was prepared from p-nitrobenzoic acid by reduction to the corresponding amino-acid and diazotisation of the latter.

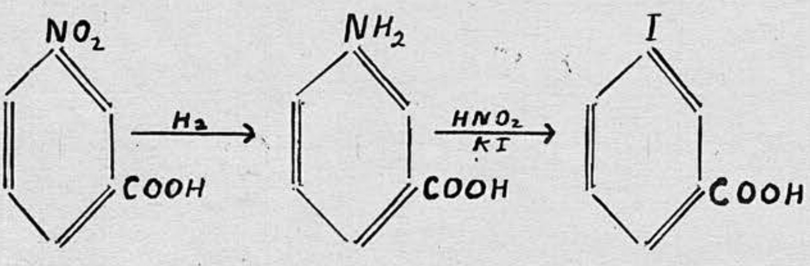


The reduction of p-nitrobenzoic acid to p-aminobenzoic acid was effected by means of tin and hydrochloric acid in the usual way (Wilbrand and Beilstein, Annalen,/

Annalen, 1863, 128, 264.). The removal of the tin salts after the reduction by precipitation with hydrogen sulphide was found to be most unsatisfactory. The method adopted was to add a solution of sodium hydroxide to the reduction mixture until it was almost neutral to litmus, and then sodium carbonate until precipitation of the tin, as the mixed hydrated oxides, was complete. Acidification of the filtrate with acetic acid precipitated the aminobenzoic acid in a pure condition. It was recrystallised from dilute acetic acid, and melted at 186°. The yield amounted to 80 per cent. of the theoretical quantity.

The conversion of p-aminobenzoic acid to p-iodobenzoic acid was carried out by the method recommended by Meyer (Monatsh., 1901, 22, 779.). p-Iodobenzoic acid was best purified by sublimation, by which process it was obtained in the form of snow-white clusters which melted at 267-268°. The yield was 60 per cent. of the theoretical quantity.

m-Iodobenzoic acid was most conveniently prepared from the corresponding nitrobenzoic acid, which was reduced to the amino-acid, and the amino-group replaced by iodine in the usual way.



m-Nitrobenzoic acid was obtained by two methods: (1) direct nitration of benzoic acid; (2) nitration of benzaldehyde, and oxidation of the resulting m-nitrobenzaldehyde.

The nitration of benzoic acid was carried out according to the specification of Hübner (Annalen, 1884, <u>222</u>, 72.). Any unchanged benzoic acid was distilled over in steam, and the m-nitrobenzoic acid purified by crystallisation from water. It melted at 140-141°. The yield was 60 per cent. of the theoretical quantity.

The nitrating agent used in the preparation of m-nitrobenzaldehyde was a saturated solution of potassium nitrate in concentrated sulphuric acid. (compare Friedländer and Henriques, Ber., 1881, <u>14</u>, 2802; Tiemann and Ludwig, ibid, 1882, <u>15</u>, 2045.). The nitrobenzaldehyde was purified by crystallisation from ethyl alcohol; m.p. 56°. The yield amounted to 70 per cent. of the theoretical quantity. The oxidation of m-nitrobenzaldehyde to m-nitrobenzoic acid was effected by gradual addition to an aqueous solution of potassium hydroxide (Cannizzaro's reaction). The m-nitrobenzyl alcohol was extracted away with ether and used in another preparation. Acidification of the remaining alkaline solution precipitated the m-nitrobenzoic acid. It was purified as above.

m-Aminobenzoic/

m-Aminobenzoic acid was obtained from m-nitrobenzoic acid by methods analogous to those used in the preparation of the para-isomeride. This amphoteric acid (m-aminobenzoic acid) is much more soluble in acid solutions than the para-compound, and, consequently, is not precipitated by the addition of hydrochloric acid to dilute solutions of its sodium salt. Purification was effected by crystallisation from water; m.p. 172-173°. The yield amounted to 75 per cent. of the theoretical quantity.

m-Aminobenzoic acid was converted into m-iodobenzoic acid in exactly the same way as in the preparation of the ortho and para-isomerides. It was purified by crystallisation from dilute acetic acid, and melted at 184-185°. The yield amounted to 50 per cent. of the theoretical quantity.

Preparation of p-chlorobenzoic acid.

p-Chlorobenzoic acid was prepared from p-chlorotoluene by oxidation with an aqueous solution of potassium permanganate as described by Ullmann (Amer. Chem. J., 1894, 16, 533.). Any unchanged chlorotoluene was distilled over in steam, and after filtration from the hydrated manganese dioxide, the chlorobenzoic acid was precipitated from the alkaline solution by the addition/

addition of hydrochloric acid. It was purified by crystallisation from ethyl alcohol, and melted at 238-239°.

Preparation of the mono-chloronitrobenzenes.

These compounds were obtained from the corresponding nitranilines by means of the Sandmeyer reaction. They were purified by crystallisation from ethyl alcohol.

o-Chloronitrobenzene	m.p. 34°
m-Chloronitrobenzene	m.p. 45°
p-Chloronitrobenzene	m.p. 83°

Preparation of the mono-halogenated toluenes.

These compounds were obtained from the corresponding toluidines by the usual methods.

o-Chlorotoluene	b.p. 158-159°
m-Chlorotoluene	b.p. 161-162°
p-Chlorotoluene	b.p. 161-162°
o-Bromotoluene	b.p. 180-181°
m-Bromotoluene	b.p. 182-183°
p-Bromotoluene	b.p. 184-185°; m.p. 29°.
o-Iodotoluene	b.p. 204-205°
m-Iodotoluene	b.p. 207-208°
p-Iodotoluene	b.p. 209-211°; m.p. 35°.

Preparation of the ω-bromoxylenes.

These compounds may be readily obtained from the corresponding xylenes by direct bromination (compare Radziszewski and Wispek, Ber., 1882, 15, 1743; 1885, 18, 1281; Schramm, ibid, 1885, 18, 1278.). This method of preparation has, however, several disadvantages of which may be mentioned the difficulty of obtaining the unsubstituted xylenes perfectly pure, and of preventing further side-chain as well as nuclear bromination during the preparation. Under these circumstances it was decided to prepare the ω-bromoxylenes from the pure toluidines by the series of reactions summarised below. The toluidines were first converted into the tolylnitriles, reduced to the tolylmethylamines, and the tolylcarbinols* obtained from the amines by means of nitrous acid. The synthesis was completed by the action of dry hydrogen bromide on the carbinol in benzene solution.

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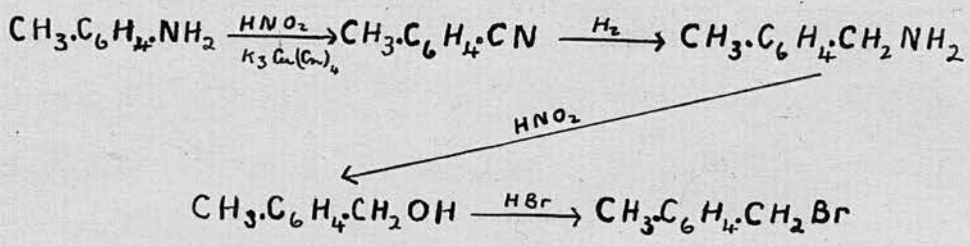
* Attempts were made to prepare the tolylcarbinols from the toluic acids by electrolytic reduction in presence of ethyl alcohol and sulphuric acid as described by Mettler (Ber., 1905, 38, 1748; 1906, 39, 2937.). This method of preparation was, however, not a success, and the products isolated were the ethyl ester of the acid, and its reduction product the ethyl ether of the carbinol.



ω-Bromo-p-xylene. p-Toluidine was converted into p-tolylnitrile by the usual Sandmeyer method. It was found advantageous to add the diazotised base to the practically boiling potassium cuprocyanide solution. The nitrile, after distillation in steam, was extracted with ether, and, in order to remove any cresol, the ethereal solution was extracted thrice with a 10 per cent. solution of sodium hydroxide. p-Tolylnitrile was purified by distillation; b.p. 215-217°; m.p. 29°. The yield was 80 per cent. of the theoretical quantity.

The reduction of the nitrile to p-tolylmethylamine was carried out by means of sodium and alcohol (compare Kröber, Ber., 1890, 23, 1026; Sommer, ibid, 1900, 33, 1073.).

30 grams of p-tolylnitrile were dissolved in one litre of dry ethyl alcohol. The solution was heated to the boiling point, and 100 grams of sodium added as rapidly as possible through an upright condenser. The addition of the sodium was completed in about half/

half an hour, and, when it had all dissolved, the reduction mixture was diluted with water, and acidified with hydrochloric acid. The ethyl alcohol was then distilled over in steam. The residual acid solution was made alkaline with sodium hydroxide, and the tolylmethylamine distilled over in the same way. It was extracted from the distillate with ether, and was purified by distillation; b.p. 194-196°. The yield was 17 grams. p-Tolylmethylamine rapidly absorbs carbon dioxide from the atmosphere, and the carbonate formed melts at 110-111°. The hydrochloride melts at 236°.

The conversion of p-tolylmethylamine to p-tolylcarbinol was effected by the addition of one and a half times the required amount of sodium nitrite to the solution of the base in excess of dilute hydrochloric acid. Evolution of nitrogen took place readily in the cold, and, after the mixture had been allowed to stand over-night, the reaction was carried to completion on the water-bath. The tolylcarbinol was extracted with ether, and the latter evaporated away. The crude carbinol obtained in this way was purified by steam-distillation. The distillate was then extracted, and after evaporation of the ether, the carbinol was obtained as an oil which immediately solidified when exposed to the atmosphere. It was further purified by crystallisation from water, and was/

was obtained from this solvent in the form of long colorless needles which melted at 60°. Owing to resinification during the steam distillation, the yield did not exceed 50 per cent. of the theoretical quantity.

ω-Bromo-p-xylene was obtained from the tolylcarbinol when a rapid current of dry hydrogen bromide was passed into its benzene solution for half an hour (compare Lapworth and Shoesmith, loc. cit.). The water liberated during the reaction was removed by the addition of calcium chloride, and the bromoxylene purified by distillation under reduced pressure. It distilled completely at 100° under a pressure of 9 mm., and crystallised in the condenser in the form of long white needles which melted at 35.5°. Analysis showed that it was pure.

ω-Bromo-m-xylene was prepared from m-toluidine by exactly the same reactions as those by which the para-isomeride was obtained. The pure m-tolylnitrile (b.p. 210-212°) was obtained in 50 per cent. yield. The yield of m-tolylmethylamine (b.p. 198-200°) was 30 per cent. of the theoretical quantity. It is noteworthy that no tarring took place at all during the steam distillation of m-tolylcarbinol. It distilled at 108-111° under 10 mm. pressure. ω-Bromo-m-xylene distilled at 97-99° under 8 mm. pressure. Analysis showed that it was pure.

ω-Bromo-o-xylene./

ω-Bromo-o-xylene. The yield of o-tolylnitrile (b.p. 202-204°) was 60 per cent. Of the theoretical quantity. o-Tolylmethylamine (b.p. 203-205°) was obtained in 55 per cent. yield. As in the case of the para-isomeride tarring took place during the steam-distillation of o-tolylcarbinol. It distilled at 112-114° under 9 mm. pressure, and melted at 33°. ω-Bromo-o-xylene boiled at 102° under 11 mm. pressure, and when cooled in liquid air solidified, and melted at 20°. Analysis showed that it was pure.

Preparation of anethole nitrosochloride.

This compound was most conveniently obtained from anethole by a slight modification of the method adopted by Orndorf and Morton (Amer. Chem. J., 1900, 23, 181.).

100 grams of anethole and 80 grams of amyl nitrite were dissolved in 400 cc. of ether and cooled to - 10°. A current of dry hydrogen chloride was then passed into the mixture, and in about half an hour precipitation of the nitrosochloride was complete. It was then filtered off and purified by precipitation from its chloroform solution by means of petroleum ether. It melted at 124-125° with decomposition. The yield was 60 grams.

Preparation of α-chloropropionyl chloride.

This compound was obtained from propionic acid by conversion into propionyl chloride, and chlorination of the latter.

The conversion of propionic acid to propionyl chloride was effected by means of phosphorus pentachloride in the usual way. The propionyl chloride distilled at 78-80°.

The chlorination of propionyl chloride was carried out at the boiling-point in presence of iodine as a carrier (compare Markownikoff, Ber., 1908, 41, 735.). The α-chloropropionyl chloride was purified by distillation; b.p. 108-110°. The yield was 60 per cent. of the theoretical quantity.

EXPERIMENTAL.

Reduction of the mono-halogenated phenols by means of hydriodic acid.

Approximately 0.6 gram of the phenol was dissolved in sufficient glacial acetic acid to make the volume 2.5 cc. in a small glass-stoppered measuring cylinder. 2.5 cc. of glacial acetic acid which contained 0.41 gram of hydrogen iodide per cc. (vide Lapworth and Shoesmith, loc. cit., p.1399) were then added, and the whole carefully mixed, and placed in a thermostat at 25°. 1 cc. of this solution was withdrawn at definite intervals, and, after dilution with 200 cc. of water, the liberated iodine* was estimated by titration with standard sodium thiosulphate solution.

In the following tables are given, under t, the time, in minutes, which had elapsed between the initial mixing and the withdrawal of the sample of solution, and, under x, the percentage amount of halogenated phenol reduced calculated from the equation:-

$$HOC_6H_4\,Hal. + 2\,HI = C_6H_5OH + H\,Hal. + I_2$$

---

* As iodine is slowly liberated from a solution of hydriodic acid on account of atmospheric oxidation, it is necessary to carry out blank experiments and make corrections accordingly.

By this method reduction curves of p-iodophenol, o-iodophenol, and p-bromophenol were obtained (see Figure I facing page 8).

p-Iodophenol.

Weight taken = 0.6394 gm.

t	x
15	69.0
45	88.8
105	95.4
225	99.9

o-Iodophenol.

Weight taken = 0.6104 gm.

t	x
15	28.2
45	56.2
105	75.6
225	89.9

p-Bromophenol.

Weight taken = 0.6070 gm.

t	x
15	4.4
45	8.7
105	15.9
225	28.7

It was found impossible to obtain a satisfactory reduction curve for o-bromophenol under these conditions, but having obtained a comparison of the iodophenols and of p-bromophenol at 25°, a series of experiments carried out at 78° gave comparative curves for para and ortho-bromophenol.

The method adopted was as follows:-
A standard solution of the phenol in glacial acetic acid/

acid was prepared. 10 cc. of this solution was placed in a 25 cc. standard glass-stoppered flask, and 10 cc. of constant-boiling aqueous hydriodic acid added. The whole was then immersed in the vapour of boiling alcohol,[*] and the liberated iodine determined as above.

In the following tables t and x have the same significance as before.

p-Bromophenol.

Weight used in each experiment = 0.1719 gm.

t	x
60	40.7
120	68.4
180	83.9
240	94.2
300	99.7

o-Bromophenol.

Weight used in each experiment = 0.1730 gm.

t	x
60	18.7
120	31.7
180	39.6
240	47.6
300	53.0

p-Chlorophenol was the only one of the chloro-isomerides to show any reduction under the different conditions described here. The reduction was, however, very slight. A strong 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 quantity/

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[*] A description of this simple thermostat is given on page 57.

quantity in four hours, but reduction to completion was never accomplished.

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

4-Iodoresorcinol, under the same conditions, was reduced to completion in half an hour.

Isolation and identification of the product of hydriodic acid reduction in the case of p-iodophenol.

6.2 grams of p-iodophenol were dissolved in 25 cc. of glacial acetic acid in a small ground glass-stoppered flask. 25 cc. of glacial acetic acid which contained 0.36 gram of hydriodic acid per cc. were then added, and the whole thoroughly mixed, and placed in a thermostat at 25°. After four hours the amount of iodine liberated represented complete reduction to phenol. The contents of the flask were then poured into 500 cc. of water which contained 20 grams of sodium thiosulphate, and neutralised by the addition of sodium bicarbonate. The mixture was extracted with ether, and, after evaporation away of the solvent, the residual oil was distilled. It boiled at 180-195° and weighed 2.0 grams. It was shown to be phenol by its ferric chloride coloration, and by conversion into the tribromo-derivative which, on crystallisation from aqueous alcohol, melted at/

at 91-92°, alone, and also when mixed with an authentic specimen of tribromophenol.

The action of hydrolysing agents on the mono-halogenated phenols.

The halogen atoms in the above compounds were not removed by the action of aqueous or alcoholic potassium hydroxide at the boiling point for twenty hours.

The action of hydriodic acid on the mono-iodobenzoic acids.

On account of the slight solubility of p-iodobenzoic acid in glacial acetic acid at 25°, it was not possible to carry out reduction experiments at that temperature. Experiments were, however, undertaken at 78°. The reducing reagent used was a mixture of equal volumes of glacial acetic acid and constant-boiling aqueous hydriodic acid. Under these conditions the mono-iodobenzoic acids showed no signs of reduction.

The action of hydrolysing agents on the mono-iodobenzoic acids.

The conditions under which it was attempted to/

to remove the halogen atoms in the above compounds, by means of hydrolysing agents, were the same as those used in connection with the halogenated phenols. As in the case of the halogenated phenols no hydrolysis took place with the iodobenzoic acids or with p-chlorobenzoic acid.

Reduction of the mono-iodotoluenes by means of hydroidic acid.

Approximately 1.2 grams of the iodotoluene were dissolved in sufficient glacial acetic acid to make the volume 2.5 cc. in a small glass-stoppered cylinder. 7.5 cc. of a solution of hydroidic acid in glacial acetic acid (0.59 gm. of H I per cc.) were then added, and the whole carefully mixed and placed in a thermostat at 25°. 1 cc. of this solution was withdrawn at definite intervals, and the liberated iodine estimated as before.

In the tables given below the figures, under t, represent the time, in days, that reduction was allowed to proceed, and, under x , the percentage reduction calculated from the equation:-

$$CH_3C_6H_4I + HI = C_6H_5CH_3 + I_2$$

o-Iodotoluene.

Weight taken = 1.2150

t	x
1	48.4
2	67.9
4	82.6
6	88.1
8	92.0

p-Iodotoluene.

Weight taken = 1.2051

t	x
1	32.1
2	50.5
4	69.8
6	79.2
8	85.9

m-Iodotoluene.

Weight taken = 1.1934

t	x
1	4.1
2	7.9
4	10.9
6	13.3
8	17.4

The above results are graphically represented in Figure II facing page 14.

The mono-bromo- and mono-chlorotoluenes, under the same conditions, did not show any signs of reduction.

Isolation/

Isolation and identification of the product of hydriodic acid reduction in the case of o-iodotoluene.

7.1 grams of o-iodotoluene were dissolved in 10 cc. of glacial acetic acid in a small glass-stoppered flask. 40 cc. of the acetic acid-hydriodic acid solution were then added, and the whole well mixed, and maintained at 25°. After ten days the liberated iodine represented about 95 per cent. reduction to toluene. The contents of the flask were then poured into 300 cc. of water, and, after decolorisation with sodium thiosulphate, neutralised by the addition of sodium hydroxide. The mixture was extracted with ether, and, after evaporation away of the solvent, the residual oil was distilled. It boiled at 105-118° and weighed 1.4 grams. This liquid was free from combined halogen, and was shown to be toluene by density determination (0.876 at 18°), and by conversion into the trinitro-derivative, the melting point (81-82°) of which was not depressed when it was mixed with an authentic specimen of trinitrotoluene.

The action of hydrolysing agents on the mono-halogenated toluenes.

It was not found possible to remove any of the halogen atoms in the above compounds by the prolonged action/

action of alcoholic potassium hydroxide at the boiling-point.

Reduction of the ω-bromoxylenes by means of hydriodic acid.

Approximately 0.5 gram of the bromoxylene was dissolved in sufficient glacial acetic acid to make the volume 1 cc. in a small glass-stoppered measuring clyinder. 4 cc. of glacial acetic acid, which contained 0.71 gram of hydrogen iodide per cc., were then added, and the whole thoroughly mixed and placed in a thermostat at 25°. 1 cc. of this solution was withdrawn at definite intervals and the liberated iodine estimated as before.

In the following tables are given, under t , the time, in hours, that reduction was allowed to proceed, and, under x , the percentage reduction calculated from the equation:-

$$CH_3C_6H_4CH_2Br + 2\ HI = CH_3C_6H_4CH_3 + H\ Br - I_2$$

ω-Bromo-m-xylene.		ω-Bromo-o-xylene.	
Weight taken = 0.5537 gm.		Weight taken = 0.5862 gm.	
t	x	t	x
0.5	17.9	0.5	-
1.5	25.6	1.5	2.5
3.5	36.5	3.5	4.2
7.0	50.8	7.0	8.2
20	83.9	20	12.1

ω-Bromo-p-xylene, under the same conditions, did not show any signs of reduction whatsoever.

The above results are graphically represented in Figure III facing page 16.

Isolation and identification of the products of the reaction between the ω-bromoxylenes and hydriodic acid.

ω-Bromo-m-xylene. 5.82 grams of ω-bromo-m-xylene were dissolved in 10 cc. of glacial acetic acid in a small glass-stoppered flask. To this solution 40 cc. of the acetic acid-hydriodic acid solution were added, and the mixture placed in a thermostat at 25° for 40 hours. The amount of iodine liberated during this time represented about 90 per cent. reduction to m-xylene. The contents of the flask were then poured into 500 cc. of water (during this operation the odour of xylene was very marked), and, after decolorisation with sodium thiosulphate, neutralised by the addition of sodium hydroxide. The mixture was extracted with ether, and, after evaporation away of the solvent, the residual oil was distilled. It boiled at 135-150°, and weighed 1.6 grams. On redistillation practically the whole came over at 135-143°, and was shown to be m-xylene by density determination (0.857 at 16°), and by conversion into the trinitro-derivative which, after/

after crystallisation from toluene, melted at 181-182°, alone, and also when mixed with an authentic specimen of trinitro-m-xylene.

<u>ω-Bromo-p-xylene.</u> 4.48 grams of ω-bromo-p-xylene were treated in exactly the same way as in the case of the meta-isomeride. No liberation of iodine took place after the reduction mixture had been maintained at 25° for forty hours. When the solution was poured into water a light brown solid was precipitated. This was filtered off and dried. It weighed 5.1 grams, and melted at 46-47° both before and after crystallisation from petroleum ether. A qualitative test showed it to be free from bromine but to contain a large amount of combined iodine. The presence of the iodine, together with the fact that no reduction had taken place by the action of the hydriodic acid, at once suggested that this solid was ω-iodo-p-xylene. Its mode of formation would thus be represented by the equation:-

$$CH_3C_6H_4\ CH_2Br + H\ I = CH_3\ C_6H_4\ CH_2I + H\ Br$$

On reference to the literature it was found that ω-iodo-p-xylene had already been prepared by Pavlovskii (J. Russ. Phys. Chem. Soc., 1911, <u>43</u>, 214.) by the action of hydriodic acid on p-p′ -dimethyl-dibenzyl ether, and the melting point is given

at/

at 45-46.5°. A halogen estimation proved beyond doubt that the compound in question was ω-iodo-p-xylene (Found: I = 54.56; C_8H_9I requires I = 54.70 per cent.).

ω-Bromo-o-xylene. The iodine liberated by the action of hydriodic acid on 4.77 grams of ω-bromo-o-xylene for forty hours represented about 15 per cent. reduction to o-xylene. When the reduction mixture was poured into water 4.6 grams of ω-iodo-o-xylene* were obtained; m.p. 33-34° (Found I = 54.45; C_8H_9I requires I = 54.70 per cent.).

Hydrolysis of the ω-bromoxylenes.

The first hydrolysis experiments were carried out at 25°. The hydrolysing agent used was ethyl alcohol which contained 10 per cent. of water. At this temperature, however, hydrolysis proceeded very slowly and in four hours ω-bromo-p-xylene only showed a 13.0 per cent conversion to the carbinol. Under these circumstances the experiments were carried out at 60°. The method adopted was as follows:- Approximately 0.1 gram of the bromoxylene was accurately weighed in a 25 cc. standard flask and then dissolved in 20 cc. of absolute alcohol. To this solution/

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* ω-Iodo-o-xylene possesses very powerful lachrymatory properties.

solution 5 cc. of distilled water were added, and after the whole had been thoroughly mixed, the flask was immersed in the vapour of boiling chloroform for a definite interval of time. The contents of the flask were then washed into excess of water, and the free hydrobromic acid estimated by titration with standard sodium hydroxide solution.

In the following tables are given, under t, the time, in minutes, that hydrolysis was allowed to proceed, under w, the weight, in grams, of bromoxylene taken, and, under x, the percentage hydrolysis calculated from the equation:-

$$CH_3C_6H_4CH_2Br + HOH = CH_3C_6H_4CH_2OH + H\,Br$$

ω-Bromo-p-xylene.

t	w	x
30	0.0983	66.3
60	0.1074	87.4
120	0.1019	96.3
180	0.0997	99.5

ω-Bromo-o-xylene.

t	w	x
30	0.1060	55.1
60	0.1064	76.8
120	0.1030	89.1
180	0.1022	94.3

ω-Bromo-m-xylene.

t	w	x
30	0.0980	27.1
60	0.0996	42.0
120	0.1037	63.9
180	0.1011	76.9

Hydrolysis/

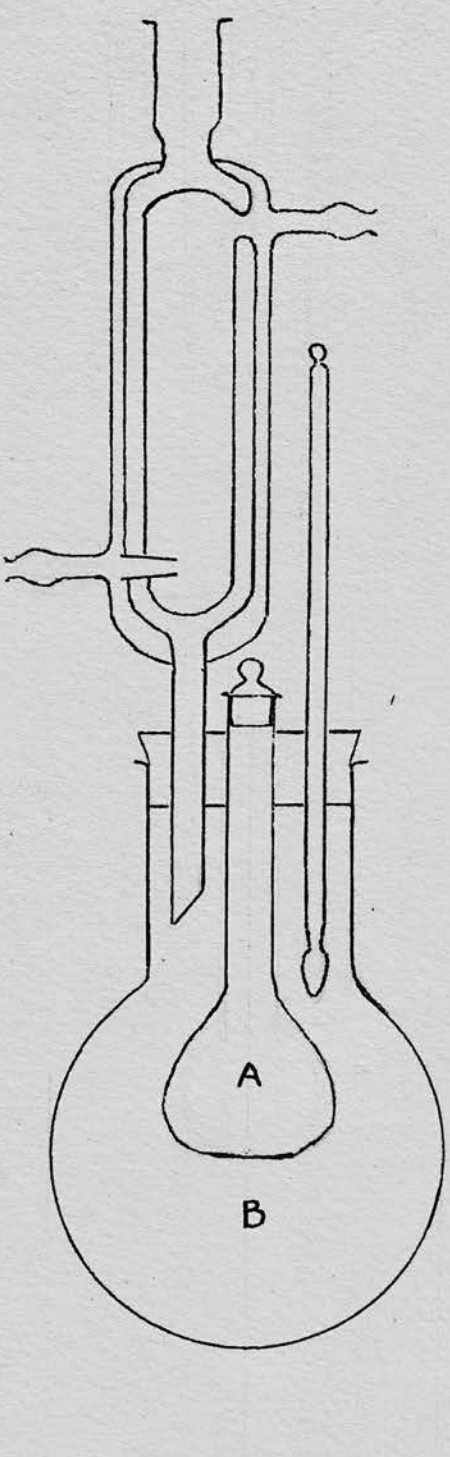


Figure V.

Hydrolysis of the unsubstituted (benzyl bromide) under the same conditions.

t	w	x
30	0.1093	22.6
60	0.1056	36.8
120	0.1100	58.6
180	0.1078	70.1

Hydrolysis of ω-iodo-p-xylene and ω-iodo-o-xylene under the same conditions,

ω-Iodo-p-xylene.			ω-Iodo-o-xylene.		
t	w	x	t	w	x
30	0.1335	38.8	30	0.1176	34.0
60	0.1146	63.1	60	0.1321	60.9
120	0.1280	78.8	120	0.1184	79.9
180	0.1291	84.7	180	0.1156	86.8

The above results are graphically represented in Figure IV facing page 17.

The boiling-vapour thermostat.

The type of apparatus which was used in this research in order to obtain a constant temperature above 25^{o} is diagrammatically represented in Figure V. The reaction mixture was placed in the 25 cc. standard glass-stoppered/

glass-stoppered flask, A, and simply immersed for a definite period of time in the vapour of the liquid which was boiling in the wide-necked flask, B. Any desirable temperature may be obtained in this way by the choice of a liquid of suitable boiling-point. Alcohol (b.p. 78°) and chloroform (b.p. 60°) were the liquids chiefly used, and over a large range of experiments, the temperature was not found to vary by more than 0.2 of a degree. This small apparatus, therefore, forms a simple and convenient thermostat, and is capable of very wide use.

Anethole and hydrocyanic acid.

The methods which were adopted in order to prepare a hydrocyanic acid addition-compound of anethole were (1) action of aqueous potassium cyanide on an alcoholic solution of anethole at the boiling-point (compare Lapworth and Higginbotham, T., 1922, 121, 51.), (2) action of liquid hydrocyanic acid on an ethereal solution of anethole at 10°. No addition-compound could be detected in either case on an examination of the reaction mixture after twenty-four hours, and the product isolated proved to be unchanged anethole.

The action of α-chloropropionyl chloride on anisole in presence of aluminium chloride (Friedel Craft).

The conditions under which it was attempted to prepare 4-(α-chloropropionyl) anisole were those specified by Klages (Ber., 1902, 35, 2262.) for the preparation of the parent compound, 4-propionyl anisole.

25 grams of α-chloropropionyl chloride were dissolved in 80 cc. of dry petroleum ether, and the solution poured on to 20 grams of powdered aluminium chloride. The whole was then cooled to -10°, and 15 grams of anisole added gradually through an upright condenser. Evolution of hydrochloric acid took place slowly, and was complete in about twelve hours. The petroleum ether was then decanted off, and the remaining solid decomposed with ice in the usual way. The aqueous mixture was extracted with ether, and after evaporation away of the latter a pale yellow oil was obtained. This oil possessed marked lachrymatory properties, and on exposure to the atmosphere, slowly turned purple in colour. It was subjected to distillation under reduced pressure. The first fraction obtained at 12 mm. distilled at 70-100°, and weighed 3 grams. It consisted chiefly of unchanged anisole. During the distillation of the remainder, decomposition/

decomposition took place with liberation of hydrochloric acid, and the whole distilled over between 100° and 170° without any indication of the presence of a definite compound. Although several fractions were taken, none of these contained a ketonic compound, and the amount of hydrolysable chlorine present was very small. Each of these fractions, though colorless when freshly distilled, slowly turned purple on exposure to the atmosphere. This reaction might repay further investigation.

The action of reducing agents on anethole nitrosochloride.

The object of these experiments was, as already pointed out, to obtain the amino-compound of the molecular formula:-

$$CH_3O.C_6H_4C_3H_6NH_2$$

described by Tönnies (loc. cit.), and in this way to determine to which of the side-chain carbon atoms in anethole nitrosochloride the nitrogen group is attached.

On account of the insolubility of anethole nitrosochloride in practically all the common organic solvents except chloroform, it is impossible to apply the usual methods for reducing a nitroso-group to an amino-group in their simplest form. Experiments were, however, carried out by emulsification of a chloroform solution/

solution of the nitrosochloride with such reduction mixtures as (1) zinc dust and glacial acetic acid (2) sodium amalgam and glacial acetic acid (3) sodium and alcohol (4) titanous chloride in hydrochloric acid. In none of these cases, however, was an amino-compound detected on an examination of the reduction mixture. The products isolated were anethole and anisaldehyde even when the experiments were carried out at as low a temperature as -10°. The tendency which anethole nitrosochloride shows to break up in this way in presence of the common organic solvents is well known (compare Wallach, loc. cit.; Orndorf and Morton, loc. cit.).

The action of stannous chloride on anethole nitrosochloride.

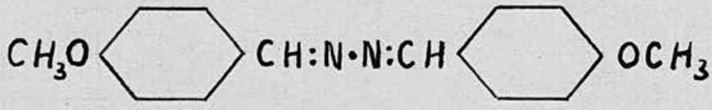
A solution of 20 grams of anethole nitrosochloride in 150 cc. of chloroform was mechanically stirred up with 150 grams of stannous chloride dissolved in 200 cc. of concentrated hydrochloric acid. The emulsion obtained in this way had a milky appearance at the commencement of the experiment. A reaction, however, soon took place, and in about half an hour the temperature of the mixture had risen to about 50°, and the emulsion was now perfectly/

perfectly transparent and bright yellow in colour. Shortly afterwards a yellow solid began to be precipitated, and the temperature fell slowly to that of the room. Precipitation of the solid appeared to be complete in about six hours, and after filtration it was dried in a vacuum over calcium chloride and potassium hydroxide. It weighed 7 grams. In order to remove any unchanged anethole nitrosochloride it was extracted with chloroform in a Soxhlett apparatus. On account of the insolubility of this yellow compound in the ordinary organic solvents it was found impossible to recrystallise it. When heated in a capillary tube it slowly darkened in colour, and melted at 259° with decomposition. On analysis it was found to contain tin, nitrogen, and hydrolysable chlorine. The percentage amounts of tin and hydrolysable chlorine present were found to be 13.11 and 24.67 respectively. On the addition of water the bright yellow colour of the compound instantly disappeared, and investigation showed that a reaction had taken place with formation of two compounds, one soluble and the other insoluble in acetone. The insoluble substance was found to be stannic oxide. The compound soluble in acetone was readily precipitated/

precipitated from that solvent by the addition of water. On recrystallisation from m-xylene it was obtained in the form of minute golden plates. This compound melted at 168° to a liquid crystal which, when further heated, was converted into the isotropic liquid at 180°. On analysis it was found to be free from tin and chlorine but to contain nitrogen to the extent of 10.82 per cent. It possessed slightly basic properties, and dissolved in warm dilute hydrochloric acid with formation of a hydrochloride. When this solution was cooled the hydrochloride crystallised out in the form of fine yellow needles which melted at 172° and decomposed at 177°. The percentage amount of chlorine present was found to be 11.72. This hydrochloride by the action of water yielded the parent compound (m.p. 168°), and by the action of nitrous acid was converted into anisaldehyde (m.p. of phenylhydrazone 120°; m.p. of semicarbazone 205°).

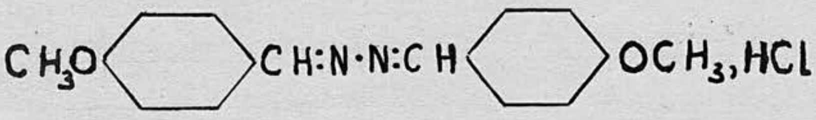
It is evident from what has been said that a reaction takes place when anethole nitrosochloride is acted upon with stannous chloride, and that there is formed a stannic chloride addition-compound of some type or other. The organic molecule in this addition-compound possesses weakly basic properties, and forms a hydrochloride. This hydrochloride is readily decomposed by the action of nitrous acid with formation of/

of anisaldehyde. The organic molecule in the stannic chloride addition-compound must, therefore, be a nitrogen derivative of anisaldehyde, and since it melts to a liquid crystal (compare Vorländer, Ber., 1906, 39, 803.) it would seem probable that its formula is of the type:-



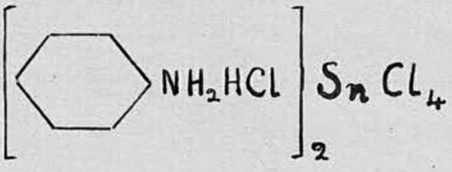
This is the formula of anisaldazine and requires 10.45 per cent. of nitrogen. Reference to the literature (Bouveault, Bull., Soc. chim., 1897, (3), 17, 944; Bredig and Schukowsky, Ber., 1904, 37, 3422.) showed that anisaldazine does possess the 168° - 180° liquid crystal phenomenon, and any doubt as to the identity of the compound described here was set at rest by determination of its melting-point when mixed with an authentic specimen of anisaldazine. The mixture again showed the 168-180° liquid crystal range.

Analysis of the hydrochloride of anisaldazine agrees with the formula:-

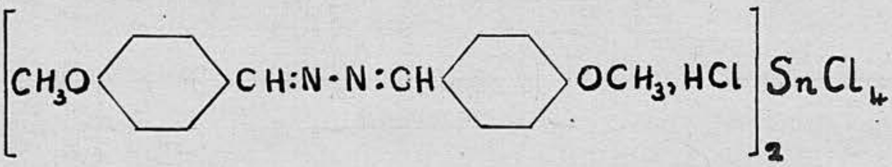


(Found: Cl = 11.72 ; $C_{16}H_{14}O_2N_2Cl$ requires Cl = 11.63 per cent.). It will be noticed that anisaldazine here acts as a mono-acid base. This is not surprising when it is remembered that hydrazine, itself, forms both a mono- and a dihydrochloride.

Just as aniline hydrochloride forms a stannic chloride addition-compound of the formula:-



so it would be expected that the stannic chloride addition compound of anisaldazine would have the formula:-

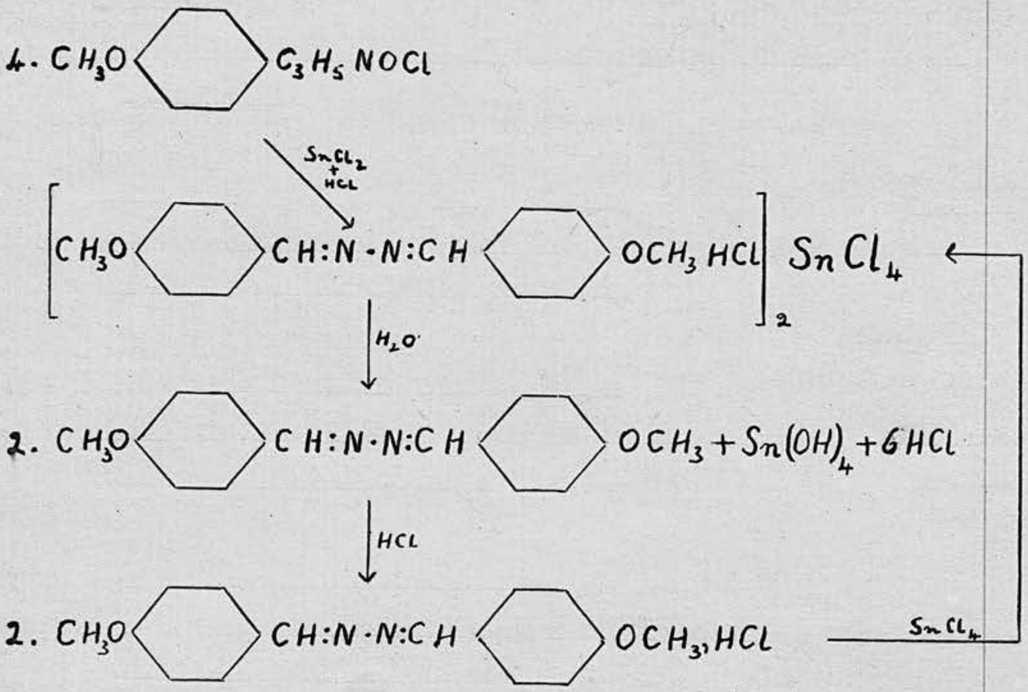


This formula agrees with the analytical results (Found: Sn = 13.11, Cl = 24.67 ; $C_{32}H_{34}O_4N_4SnCl_6$ requires Sn = 13.64, Cl = 24.45).

The above stannic chloride addition-compound of anisaldazine (m.p. 259°) is readily precipitated by the addition of stannic chloride to a solution of anisaldazine in concentrated hydrochloric acid.

The/

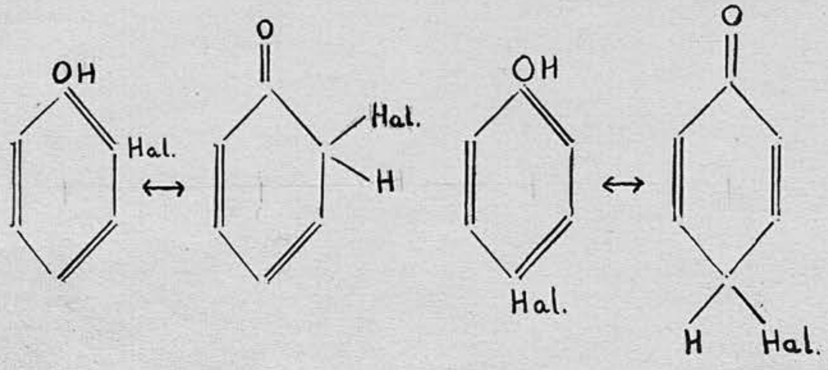
The mechanism of the above reactions may be represented thus:-



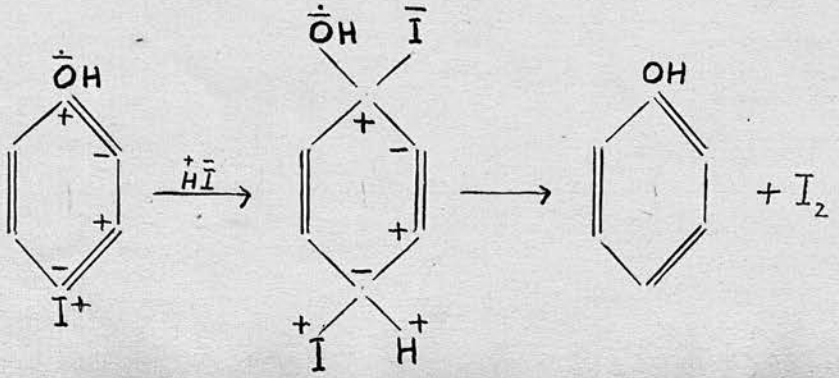
No stannic chloride addition-compound is precipitated by the action of stannous chloride on the oxime of anisaldehyde under the same conditions.

DISCUSSION OF RESULTS.

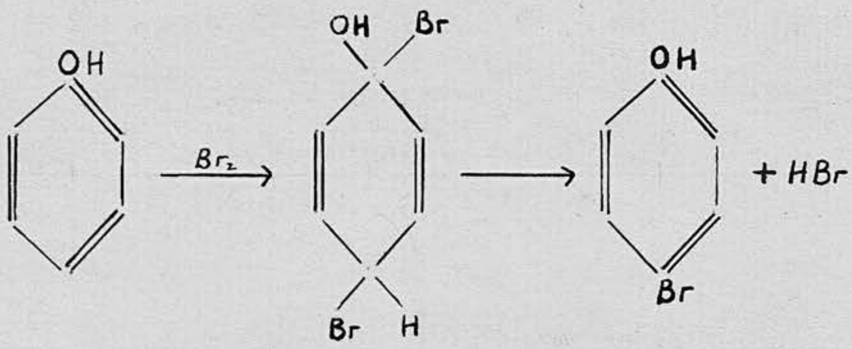
The differences in the mode of reactivity of the halogen atoms in the compounds described in this investigation were, as was pointed out, predicted by an application of the principle of induced alternate polarities. It is, however, recognised that, while no other hypothesis evolved prior to this could possibly have predicted all these results, an interpretation of some of the various phenomena might be obtained by considerations of other theories. Thus, for example, in the case of the hydriodic acid reductions of the mono-halogenated phenols, the reactivity of the halogen atoms in the ortho and para-compounds might be attributed to a tendency for these molecules to acquire a tautomeric hydrogen atom with production of an ortho or para-quinonoid structure (compare Thole and Thorpe, T., 1911, 99, 2185; Norris and Thorpe, ibid, 1921, 119, 1203; Gupta and Thorpe, ibid, 1922, 121, 1896; Robinson, Ann. Reports, 1922, 19, 102; Allsop and Kenner, loc. cit.).



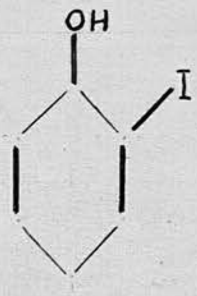
The still greater reactivity of the halogen atom in 4-iodoresorcinol would, on this assumption, be ascribed to the greater tendency which resorcinol shows to exist in a ketonic modification (compare Baeyer, Ber., 1886, <u>19</u>, 163; Perkin, T., 1895, <u>67</u>, 993; Kostanecki, Ber., 1899, <u>22</u>, 1345; Fuch and Ekner, ibid, 1920, <u>53</u>, 886; Herzig and Zeisel, ibid, 1920, <u>53</u>, 1518). These considerations, however, do not in any way detract from the value of the theory of induced polarities for the lability of such atoms is summed up by saying that they have acquired an induced positive polar character. The mechanism of the reaction is possibly more complex than might be inferred from such a statement, but this explanation has the advantage of indicating to which specific reagent the halogen atom will be reactive. The existence of the conjugated system of double bonds probably plays a large part in the reaction, and tends to diminish the resistance offered to polar induction (compare Lapworth, T., 1922, <u>121</u>, 424; Kermack and Robinson, loc. cit.; Robinson, Ann. Reports, 1922, <u>19</u>, 102.). The mode of the reaction in the case of p-iodophenol might, therefore, be represented thus:-

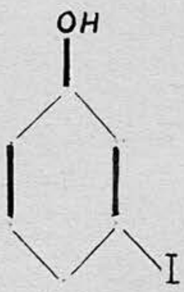


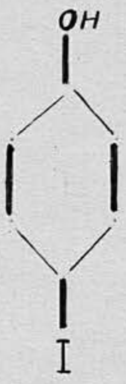
The formation of an intermediate compound of this type is in accordance with the views of Holleman ("Die direkte Einführung von Substituenten in den Benzolkern", Amsterdam, 1910, p.475.) who states, for example, that the bromination of phenol to p-bromophenol may be indicated by the reactions:-



It is interesting to note that, according to Flürscheim's nomenclature (loc. cit.) in its simplest form, of the three isomerides m-iodophenol should possess the most reactive halogen atom for in that compound the affinity between the halogen atom and the nuclear carbon atom is diminished (compare also Kenner, T., 1914, 105, 2718.).



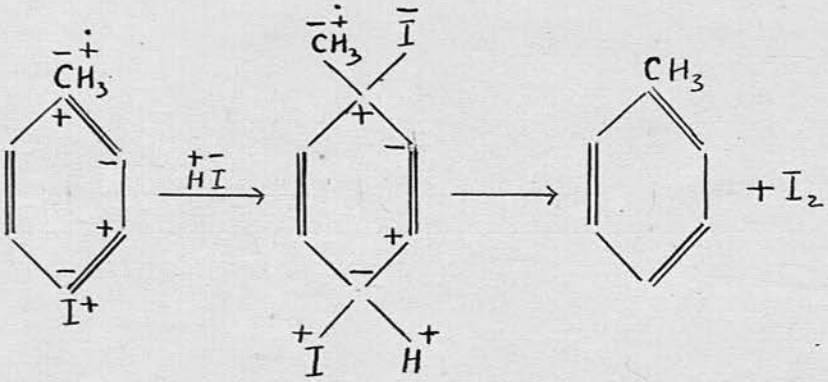




This is, of course, not in accordance with experiment.

The non-reactivity of the halogen atoms in the mono-halogenated benzoic acids is not surprising since Shoesmith and Hetherington (loc. cit.) have shown that the carboxyl group has only a slight influence on the more mobile side-chain halogen atom.

The reactivity of the ortho and para-halogens in the mono-iodotoluenes* could be explained in a similar manner to that of the halogenated phenols, conjugation enhancing the activation induced by the positive hydrogen atoms.



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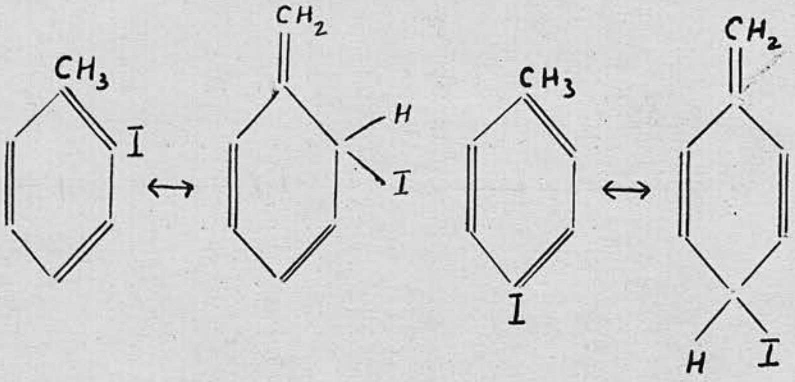
* The order of reducibility of the halogen atoms in the mono-iodotoluenes is very interesting in so far that the ortho is more easily removed than the para. In 24 hours the percentage amounts of reduction to toluene, in the three isomerides, were found to be:- ortho 48.4; para 32.1; meta 4.1. Holleman (Rec. trav. chim., 1923, <u>42</u>, 368.) has shown that, in the nitration of toluene to the mono-nitro-derivatives, o-nitrotoluene is produced in greatest quantity. The percentage amounts of the isomerides present were found to be:- ortho 58.8; para 36.8; meta 4.4. There is, obviously, a very close relationship between the replacement of a substituent (halogen) by hydrogen and the replacement of hydrogen by a substituent (nitro-group).

Here again, however, the possibility of the compounds' acquiring a tautomeric hydrogen atom must be taken into account.



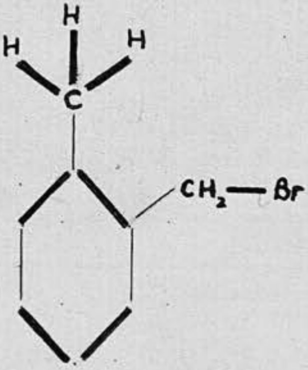
The possibility of such atomic changes' taking place is very remote although compounds of a similar type are known (compare Auwers and Ziegler, Annalen, 1921, 425, 217.).

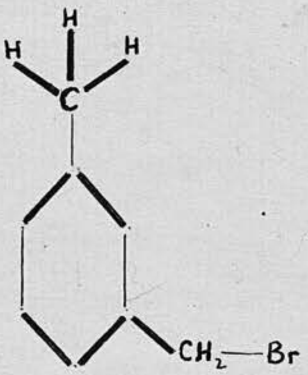
In the case of the ω-bromoxylenes, however, it is not difficult to show that the principle of induced alternate polarities is the only principle which can be successfully applied to predict halogen reactivity. Any hypothesis which depends on tautomerism cannot explain the results since no proof of the tendency for such systems to acquire a tautomeric hydrogen atom is forthcoming. The researches of Ingold and Piggott (T., 1922, 121, 2381.) appear to indicate that a system is tautomeric when it is readily alkylated. This, however,/

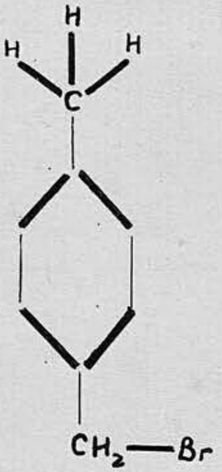
however, does not give a reason as to why the system is either easily alkylated, or tautomeric, or both. The far-reaching suggestions of Flürscheim (loc. cit.) are found to be inadequate. His theory of increased and diminished affinities can only be applied to explain the occurrence of reactive atoms in a compound when there is present in the molecule an atom or group of atoms which shows a greater affinity demand than hydrogen. The theory, therefore, cannot be applied to explain the reactivity of the halogen atoms in the mono-iodotoluenes or ω-bromoxylenes. If, however, it is assumed that the hydrogen atom is capable of co-ordination, as it is suggested to be in a few isolated cases such as in potassium hydrogen fluoride (vide Sidgwick, T., 1923, <u>123</u>, 725; Lowry and Burgess, ibid, 1923, <u>123</u>, 2111; Lowry J. Soc. Chem. Ind., 1923, <u>42</u>, 1048.),

$$K H F_2 \rightleftharpoons K^{\cdot} + F \cdot H \cdot F'$$

then an expansion of Flürscheim's hypothesis to include the hydrogen atom would explain the order of reduction of the halogen atoms in the iodotoluenes and in the ω-bromoxylenes, but not the order of hydrolysis in these latter compounds.



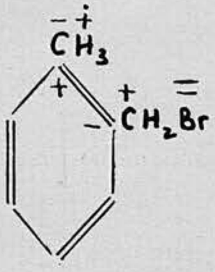


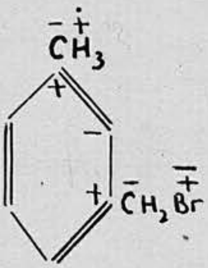


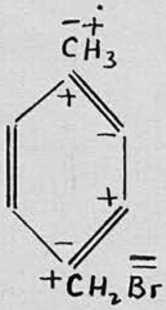
In any case, however, any tendency which the hydrogen atom may show to increase its affinity cannot be adopted to explain such halogen reactivity for then the similarity which exists between the methyl and hydroxyl groups entirely disappears. Lowry (T., 1923, <u>123</u>, 826.), in his theory of "mixed double bonds" regards the stability of a molecule as depending on whether its constituent atoms possess concordant or crossed polarities.* Derivatives, he says, which contain atoms having crossed polarities are less stable than those in which the polarities are concordant. On an examination of the formulae of the ω-bromoxylenes it would, therefore, be expected that the ortho and para-compounds would be more stable than the meta-compound for/

* Concordant and crossed polarities correspond respectively to homogeneous and heterogeneous polarities as used by Lapworth and his school.

for in the former the induced polarity of the halogen atom is concordant with its natural negative polarity whilst in the meta-compound the polarities are crossed.







From these considerations it is, therefore, possible to explain the order of reduction of the halogen atoms in the ω-bromoxylenes but impossible to explain the order of hydrolysis. Moreover, it will be observed in the above formulae that the induction of polarity is being carried along two pairs of consecutive single bonds. The induction of polarity along consecutive single bonds cannot be reconciled with Lowry's theory, and if his suggestions are to be admitted formulae for the above compounds must be devised which contain a perfectly conjugated system of double bonds. This is impossible. Allsop and Kenner (loc. cit. p. 2301.) state that "a proper understanding of the various, and often apparently contradictory, facts of organic chemistry will only be gained by referring them to and grouping them round the central principle, that the attainment/

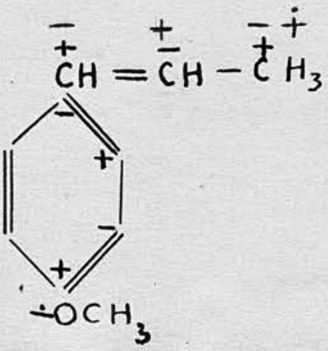
attainment of stable equilibrium of any system demands that its entropy shall become a maximum". Such a suggestion, however, in the present knowledge of entropy, does not assist. The principle of induced alternate polarities offers the only simple explanation of the different modes of reactivity of the halogen atoms in the ω-bromoxylenes.

The order of reduction of the halogen atoms in the ω-bromoxylenes is interesting in so far that the ortho shows a greater tendency to reduce than the para. This same order of reduction was observed by Lapworth and Shoesmith (loc. cit.) in their systematic examination of the methoxybenzyl bromides, and is, without doubt, closely connected with the fact that a group, which is generally called a meta-directing group, also directs to a lesser extent to the ortho-position. Thus in the nitration of benzaldehyde, m-nitrobenzaldehyde is not the sole product of the reaction, but about 19 per cent. of o-nitrobenzaldehyde is also produced (vide Brady and Harris, T., 1923, 123, 484.). Many other examples of this could be quoted. The reactions which take place during substitution in the benzene nucleus are evidently not yet perfectly understood, and much more work of this nature will have to be carried out before a definite conception is arrived at (compare Robinson, Ann. Reports, 1923, 20, 94-97.).

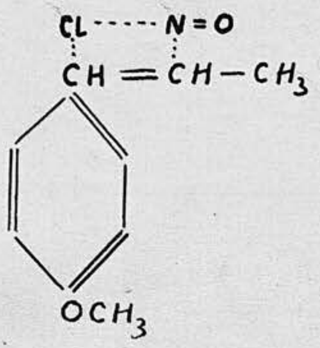
It/

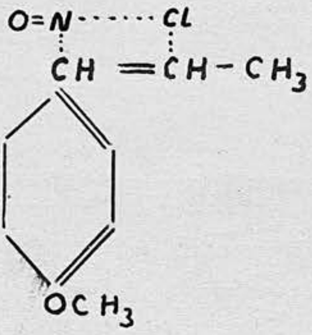
It may here also be pointed out that the halogen atoms in the ω-bromoxylenes are all removed on hydrolysis at a greater rate than that in the unsubstituted benzyl bromide (see p. 57). This is an example of the general polar effect, the substitution of the methyl group increasing the reactivity of the halogen atom as regards hydrolysis irrespective of its position in the molecule. This is to be explained as the result of the basylous nature of the methyl group, which increases the possibility of attack on the molecule as a whole by hydroxyl ions.

The experimental results obtained with anethole are rather difficult to explain, and are probably due to the combined influences of several simultaneous reactions. The fact that nitrosyl chloride shows a greater tendency to add on at the ethylenic side-chain than hydrocyanic acid may be directly attributed to the very weak bond between the nitrogen and chlorine atoms in the former compound. Again, however, the heterogeneous polarity set up by the methyl and methoxyl groups in anethole may play no small part in the reactions,

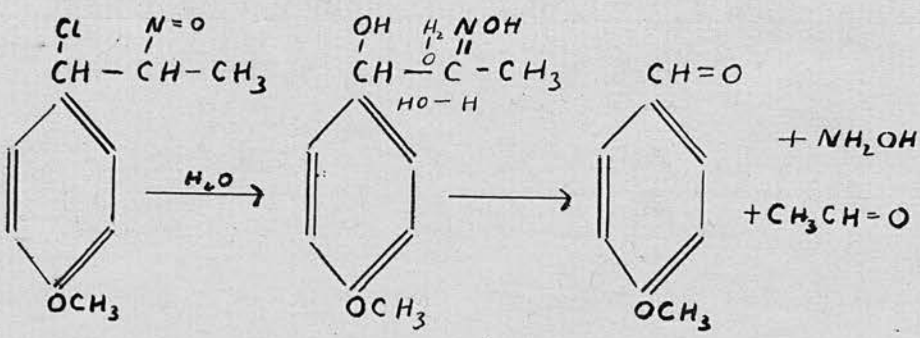


and may offer an explanation of the loose nature of the nitrosyl chloride addition,and the readiness with which it decomposes with production of anethole and anisaldehyde when warmed with the common organic solvents. This loose addition is probably best represented by a dotted line (compare Thiele, Robinson, Lapworth, and more recently, Allsop and Kenner, loca. cita.), and the two possible formulae for anethole nitrosochloride may be depicted thus:-

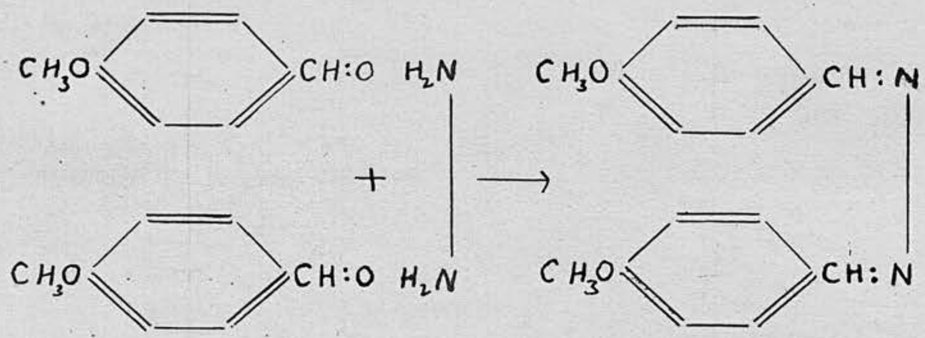




The formation of a stannic chloride addition-compound of anisaldazine, by the action of stannous chloride on anethole nitrosochloride, in no way makes it necessary to suppose that the nitrogen atom in the latter compound is directly attached to the alpha carbon atom. The non-formation of a similar derivative, by the action of stannous chloride on the oxime of anisaldehyde, is directly opposed to this suggestion. It is more probable that the first reaction that takes place is hydrolysis with production of anisaldehyde, acetaldehyde, and hydroxylamine hydrochloride.



The hydroxylamine would, as soon as it was produced, be reduced to hydrazine, and anisaldazine would make its appearance in the usual way.



The above hydrolysis could, of course, proceed just as readily if the nitroso-group were attached to the alpha carbon atom. This would, however, necessitate the addition of a negative hydroxyl group to the negative beta carbon atom, and it is doubtful if this could be accomplished.

SUMMARY.

1. The influence of the hydroxyl group on the halogen atoms in the mono-halogenated phenols is such as would have been expected by an application of the principle of induced alternate polarities. Hydriodic acid was the reagent used to demonstrate this, and the order of ease of reduction of the halogens is p-I > o-I > p-Br > o-Br > p-Cl > o-Cl. The meta-isomerides are unchanged under the same conditions. The halogen atom in 4-iodoresorcinol is very readily removed under these conditions.

2. The carboxyl group is unable to activate the halogen atoms in the mono-halogenated benzoic acids. These atoms are not removed either by hydrolysing agents or by hydriodic acid.

3. The methyl group exerts a considerable influence on nuclear as well as on side-chain halogen atoms in virtue of the positive hydrogen atoms which it contains. Thus the order of ease of reduction of the halogen atoms in the mono-iodotoluenes is p and o > m, but in the ω-bromoxylenes this order is reversed, that is m > p and o. The influencing group in these latter compounds is one place further/

further removed from the halogen atom. The order of ease of hydrolysis of the halogen atoms in the ω-bromoxylenes is the reverse of the order of reduction, that is p and o > m.

4. Anethole does not form an addition-compound with hydrocyanic acid. It was not found possible to determine the constitution of anethole nitrosochloride, and, hence, the directive influence of the methoxyl group with respect to the formation of such an addition compound, owing to the readiness with which it decomposes, under the action of reagents, with production of anethole and anisaldehyde. A stannic chloride addition-compound of anisaldazine is precipitated by the action of stannous chloride on anethole nitrosochloride. This addition-compound is readily decomposed by water into anisaldazine and stannic hydroxide. Anisaldazine forms an addition-compound with hydrochloric acid. When this hydrochloride is acted upon with stannic chloride the original stannic chloride addition-compound of anisaldazine is precipitated.
