iodide on the reaction of *iso*propyl iodide was even greater. Satisfactory constants have not as yet been obtained, but the catalyst appears to be inactivated according to the equation $HgX_2 + 2X^- = HgX_4^{--}$

Summary

1. The rates of alcoholysis and hydrolysis of propyl and *iso*propyl bromides and iodides in boiling alcohol containing definite small amounts of water have been measured.
2. The reactions considered differ from most of those which have been studied with alkyl halides in that the secondary halides show in each case a more rapid reaction than the corresponding primary halides.
3. The reactions are strongly catalyzed by the corresponding mercuric halides.

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ANOMALOUS EFFECT OF ORTHO-PARA ORIENTING GROUPS ON THE MELTING POINTS OF DIHALOGENATED BENZENE DERIVATIVES

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Introduction

The introduction of an additional substituent into the benzene nucleus usually results in the formation of a compound which has a higher melting point than the parent substance. For this reason the observation that symmetrical tribromobenzene has a somewhat higher melting point than its amino derivative led to a study of the melting points of halogenated benzenes and their derivatives. The investigation showed that the melting points of derivatives of halogenated benzene increased with the number of substituents in the nucleus, except in the case of those compounds which are formed by the entrance of a group which causes ortho-para substitution into a para halogenated benzene.

Symmetrical chloro-bromo-iodobenzene and its amino derivatives were prepared in order to show the effect of the introduction of the amino group on the melting points of the trihalogenated benzenes.

Study of the Melting Points

An examination of the melting points of the disubstituted halogen benzene derivatives showed that the amines of the ortho and meta halogen derivatives melted at a higher temperature than the corresponding dihalogenated benzene, whereas the melting points of the amino derivatives of para halogenated benzene are lower. In a similar way the melting point of a derivative of an ortho or meta dihalogenated benzene is raised when a halogen or a methyl group instead of an amino group enters the molecule while that of the para compound is lowered.

On the other hand, when a nitrile group replaces a hydrogen of a dihalogenated benzene, the melting point of the para as well as those of the ortho and meta compound is raised. The fact that the nitrile group had a different effect from the amino, halogen and methyl groups seemed to indicate that substituents which caused the formation of meta disubstituted derivatives of benzene raise the melting points of all three types of dihalogen benzene derivatives upon entering the molecule, while those groups which cause the formation of ortho and para derivatives of benzene raise the melting points of ortho and meta halogenated benzene but lower that of the para when a trisubstituted benzene derivative is formed.

A further examination of the effect of other groups which cause meta substitution showed that they had the same effect as the nitrile group.

The data are given in tabular form below.

TABLE I

EFFECT OF A THIRD SUBSTITUENT ON THE MELTING POINTS OF DIHALOGENATED BENZENES

ND—No substituted dihalogenated benzene derivative is described.
+ Melting point of the dihalogenated benzene is raised on substitution.
– Melting point of the dihalogenated benzene is lowered on substitution.

Groups present		Groups entering	Ortho deriv.	Meta deriv.	Para deriv.
Cl	Cl	I	ND	ND	–
Cl	Cl	Br	+	+	–
Cl	Cl	Cl	+	+	–
Br	Br	Cl	+	+	–
Br	Br	Br	+	+	–
Br	Br	I	ND	+	–
I	I	I	ND	+	–
Cl	Cl	OH	+	+	+
Br	Br	OH	+	+	ND
I	I	OH	+	+	–
Cl	Cl	CH_3	Liq.	Liq.	–
Br	Br	CH_3	+	+	–
I	I	CH_3	+	+	ND
Cl	Cl	NH_2	+	+	–
Br	Br	NH_2	+	+	–
I	I	NH_2	+	+	–
Cl	Br	NH_2	+	+	–
Cl	I	NH_2	+	+	ND
Br	I	NH_2	+	+	ND
Cl	Cl	CN	ND	+	+
Br	Br	CN	ND	+	+
Cl	Cl	NO_2	+	+	+
Br	Br	NO_2	+	+	–
I	I	NO_2	+	+	–
Cl	Br	NO_2	+	+	+
Cl	I	NO_2	ND	+	+
Cl	Cl	SO_3H	ND	ND	+
Br	Br	SO_3H	+	+	+
Cl	Cl	CHO	+	+	+
Cl	Cl	COOH	+	+	+
Br	Br	COOH	+	+	+
Cl	Br	COOH	+	+	+

The table shows that none of the iodo derivatives of *o*- or *m*-dichlorobenzene are described in the literature, but that the iodo derivative of *p*-dichlorobenzene has a lower melting point than that of *p*-dichlorobenzene. The + or – signifies that the melting points of all of the isomers described in the literature, which are formed by the entering group, have a higher or lower melting point, respectively, than that of the parent dihalogenated benzene.

From the table we may make the following generalizations.

1. The melting point of an ortho or meta disubstituted halogen derivative is raised by the entrance of a third group. This has been found to hold for the substitution of a chlorine, bromine or iodine atom or an hydroxyl, methyl, amino, nitrile, nitro, sulfonic acid or carboxyl group.

2. The melting point of a para disubstituted halogen derivative is raised by the entrance of a third substituent if the group entering is one which causes meta substitution.

3. The melting point of a para disubstituted halogen derivative is lowered by the entrance of a third substituent if the group entering is one which causes ortho-para substitution.

It can be seen that there is no exception to rule number 1; two exceptions to rule number 2 (1-nitro-2,5-dibromobenzene and 1-nitro-2,5-di-iodobenzene melt lower than the corresponding dihalogenated derivatives); and one to rule 3 (1-hydroxy-2,5-dichlorobenzene melts 4 degrees higher than the dihalogenated benzene). The three compounds having melting points which were exceptions to rules 2 and 3 were prepared and their melting points were found to agree with those given in the literature.

It should be noted that Holleman[1] and Francis and co-workers[2] have shown that the $—NO_2$ group has less meta directing influence than the $—SO_3H$ group, and this less than the —COOH group. Nitro compounds offer the only exception to rule 2.

The reason for the lowering of the melting points of the para dihalogenated benzenes by the entrance of certain groups is not clear. It is known that the amino group, for instance, has a strong effect on the ortho and para positions and it was thought that this lowering might be due to the influence of the entering amino group on the halogen it finds ortho or para to it. In that case, however, we should expect that any trisubstituted benzene derivative in which the amino group was ortho or para to a halogen would have a lower melting point than the corresponding dihalogen derivative; but this is not true. It is only when the halogens are para to each other that the amino or similar group has this property.

An examination of the melting points of the trisubstituted amines shows that, in, general, the melting point of the trisubstituted benzene compound is lower than that of the corresponding trisubstituted aniline with the exception of symmetrical tribromo-aniline and 3,4,5-tri-iodo-aniline. In the latter compounds the corresponding amine has a lower melting point than the trihalogenated benzene. Inasmuch as the trisubstituted aniline derivatives containing chlorine, bromine and iodine in the same molecule were not known it seemed worth while to prepare them and note the relation of their melting points to the parent trisubstituted hydrocarbon.

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[1] Holleman, *Chem. Reviews*, 1, 202 (1924).

[2] Francis, Andrews and Johnston, THIS JOURNAL, **48**, 1625 (1926).

It was found in each case that the amine melted at a higher temperature than the corresponding trihalogenated benzene.

A search for the dielectric constants and refractive indices of the compounds whose melting points have been studied was made, to see whether there was a corresponding difference in these constants for the para halogenated benzene derivatives, but sufficient data from which to draw conclusions could not be found.

Compounds which have small external fields of force should have lower melting points than similar compounds having larger fields of external force. Inasmuch as compounds having larger external fields of force should be more reactive than those having a smaller field of force, it would seem that the trisubstituted derivatives formed from ortho and meta compounds by substituting an ortho-para orienting group should be more reactive than the trisubstituted derivative formed from the para compound. This phase of the problem will be further investigated.

There are some indications that the lowering of the melting point of para disubstituted benzene derivatives by the introduction of groups causing ortho-para substitution holds for other than the halogen compounds.

Experimental

A sample of each compound whose melting point was to be determined was placed in a vacuum desiccator over concd. sulfuric acid and was allowed to remain under a pressure of 25 mm. for at least twenty minutes to remove traces of the solvent. The melting point was determined by immersing a capillary tube containing the sample in a bath of concentrated sulfuric acid about 10° below the melting point of the compound. The acid was agitated by means of a ring stirrer while the temperature was very gradually raised.

For the preparation of the three amines of symmetrical trihalogenated benzene, *p*-bromo-acetanilide, *p*-chloro-acetanilide and *o*-chloro-aniline were used. To prepare 2-chloro-4-bromo-6-iodo-aniline, *p*-bromo-acetanilide was chlorinated by means of HOCl according to the method of Chattaway and Orton,[3] producing 2-chloro-4-bromo-acetanilide. This anilide was then saponified and iodine was introduced into the benzene nucleus by using iodine monochloride. The amine was dissolved in acetic acid and the vapors of iodine monochloride were passed into the solution. The iodine monochloride was prepared according to the method of Jackson and Whitmore.[4]

The 2-bromo-4-chloro-6-iodo-aniline was prepared in a similar manner, starting with *p*-chloro-acetanilide. The bromine was introduced into the benzene ring by the method of Mannino and Di Donata.[5] In this method bromine formed by the action of nitric acid on hydrobromic acid reacts with the anilide.

In attempting to prepare 2-chloro-4-iodo-6-bromo-aniline it was found that iodine monochloride reacted with *o*-chloro-aniline to form products which had a much higher melting point than that of 2-chloro-4-iodo-aniline. This compound had been previously prepared by Dains, Vaughan and Janney[6] and was found to melt at 70–71°.

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[3] Chattaway and Orton, *Ber.*, **33**, 2398 (1900); *J. Chem. Soc.*, **79**, 274–280 (1901).

[4] Jackson and Whitmore, THIS JOURNAL, **37**, 1528 (1915).

[5] Mannino and Di Donata, *Gazz. chim. ital.*, [2] **38**, 24 (1908).

[6] Dains, Vaughan and Janney, THIS JOURNAL, **40**, 933 (1918).

The 2-chloro-4-iodo-aniline was prepared from *o*-chloro-aniline by refluxing with iodine, water and ether, according to the directions given by Dains, Vaughan and Janney[6] and was then brominated by dissolving in acetic acid and adding bromine.

The three amines were diazotized using alcohol, sodium nitrite and sulfuric acid. The same trisubstituted benzene was obtained in each case; thus proving that the amino derivatives were symmetrical trihalogen anilines.

Action of ICl on 2-Chloro-4-bromo-acetanilide

One g. of the 2-chloro-4-bromo-acetanilide, m. p. 150–151°, prepared by the general method of Chattaway and Orton,[3] was dissolved in acetic acid and ICl vapor passed into the solution. Upon the addition of water, 0.7 g. of a white precipitate was formed, which proved to be unchanged 2-chloro-4-bromo-acetanilide. The small amount remaining in the mother liquor was discarded.

Saponification of 2-Chloro-4-bromo-acetanilide

Eight and seven-tenths g. of the 2-chloro-4-bromo-acetanilide was refluxed with 6.1 g. of potassium hydroxide dissolved in 75 cc. of alcohol for about eight hours. The alcohol was distilled off on the steam-bath and water added. The amine was filtered from the cold solution, washed with cold water and crystallized from petroleum ether; b. p. 100–115°. Six and one-tenth g. of product having a melting point of 70–71° was obtained, which corresponds to an 84.6% yield.

Direct Iodination of 2-Chloro-4-bromo-aniline

The direct iodination of 2-chloro-4-bromo-aniline was carried out following the procedure of Wheeler and his co-workers.[7]

One g. of the amine gave a black tar which was subsequently discarded, and 0.3 g. of 2-chloro-4-bromo-6-iodo-acetanilide. The melting point was 97–97.5° after crystallizing from petroleum ether; yield, 18.6%. The product was identical with that obtained by the action of ICl on 2-chloro-4-bromo-aniline.

Preparation of 2-Chloro-4-bromo-6-iodo-aniline

One g. of the amine was dissolved in about 20 cc. of glacial acetic acid and sufficient water was added so that the mixed solvent was nearly saturated with the amine. One g. of ICl vapor was blown into the solution, and a light-colored, crystalline precipitate settled out. The precipitate was dissolved in the mother liquor by warming and then allowed to crystallize. One and three-tenths g. of 2-chloro-4-bromo-6-iodo-aniline was obtained, m. p. 94–95°, corresponding to a yield of 81%. On recrystallizing from petroleum ether, a product melting at 97–97.5° was obtained. Further crystallizations from alcohol by the addition of water, and from ethyl acetate by the addition of petroleum ether failed to change the melting point.

Anal. Subs., 0.5064: N_2, 21.2 cc. at 24°; 743.1 mm.(corr.) collected over 23.1% KOH. Calcd. for $C_6H_4NClBrI$: 4.21. Found: 4.59.

Preparation of 2-Bromo-4-chloro-6-iodo-aniline

2-Bromo-4-chloro-acetanilide was prepared from 4-chloro-acetanilide by the method of Mannino and Di Donata[5] and converted to the corresponding amino compound by saponification. One g. of the 2-bromo-4-chloro-aniline was dissolved in 20 cc. of acetic acid and water added until the solution became turbid. One g. of ICl vapor was then blown into the solution. One and six-tenths g. of crude 2-bromo-4-chloro-6-iodo-aniline

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[7] Wheeler and others, *Am. Chem. J.*, **42**, 441–461 (1909); **44**, 127, 493–507 (1910).

precipitated. The crude material was crystallized from petroleum ether; 1.5 g. having a melting point of 109.5–110° was obtained, corresponding to a 93.3% yield.

Anal. (semi-micro). Subs., 0.0475 g.: N_2, 1.92 cc. at 21°; 737 mm. (corr.) collected over 33% KOH. Calcd. for $C_6H_4NClBrI$: 4.21. Found: 4.48.

This analysis was carried out according to an unpublished method of Lauer and Sunde.

Preparation of 2-Chloro-4-iodo-6-bromo-aniline

Method A. By Bromination of 2-Chloro-4-iodo-aniline

Seven and seven-tenths g. of 2-chloro-4-iodo-aniline, prepared according to the directions of Dains, Vaughan and Janney[6] was dissolved in 35 cc. of glacial acetic acid and 5 g. of bromine was added. The reaction mixture warmed up and after a little while crystals began to appear. These were filtered off and water was added. Eight and five-tenths g. of crystals were obtained which had a constant melting point of 115.5–116° after 2 crystallizations from alcohol. Recrystallizing from petroleum ether failed to change the melting point. The yield was 84.2% of the calculated.

Anal. (semi-micro). Subs., 0.0223 g.: N_2, 0.77 cc. collected over 33% KOH at 26°; 759.3 mm. (corr.). Calcd. for $C_6H_4NClBrI$: 4.21. Found: 4.04.

Method B. By the Chlorination of 2-Bromo-4-iodo-acetanilide

Six g. of finely ground *p*-iodo-acetanilide was brominated according to the general method of Mannino and Di Doñata.[5] Seven and two-tenths g. of the pure anilide was obtained, melting at 140–140.5° after crystallizing from alcohol; yield, 92.3%.

Anal. (semi-micro). Subs., 0.0320 g.: N_2, 1.21 cc. at 22° and 737.2 mm. (corr.) over 33% KOH. Calcd. for C_8H_7ONBrI: 4.12. Found: 4.18.

One and eighty-five hundredths g. of 2-bromo-4-iodo-acetanilide was saponified and treated in the usual manner. One and four-tenths g. of the amine which melted at 77.5–78° after crystallizing from petroleum ether was obtained; yield, 70.4%. A small portion of the amino compound was converted to the anilide by treatment with acetyl chloride. The melting point was 139–140°, thus proving the identity of the positions before and after saponification. The picric acid addition compound melted at 125°.

The 2-bromo-4-iodo-aniline was converted to 2-bromo-4-iodo-6-chloro-aniline by dissolving in glacial acetic acid and adding the calculated amount of chlorine dissolved in glacial acetic acid. A white precipitate having a high melting point was immediately formed. On filtering and adding water, the trihalogenated aniline was obtained. It was crystallized from alcohol and from petroleum ether. A mixed melting point proved its identity with the 2-bromo-4-iodo-aniline obtained by brominating 2-chloro-4-iodo-aniline.

Preparation of *Sym.*-chloro-bromo-iodo-benzene

1. Diazotization of 2-Iodo-4-chloro-6-bromo-aniline

Forty-one hundredths g. of 2-iodo-4-chloro-6-bromo-aniline was refluxed for half an hour on a steam-bath with 1.64 cc. of ethyl alcohol, one and six-tenths cc. of concd. sulfuric acid and 1.1 g. of sodium nitrite. The mixture was then diluted and the reddish precipitate which separated was thoroughly washed and finally dried in a vacuum desiccator. Thirty-five hundredths g. of product was obtained which melted at 85.5–86° after 2 crystallizations from alcohol. The yield was 89.5%.

2. Diazotization of 2-Chloro-4-bromo-6-iodo-aniline

Six-tenths g. of this amine was refluxed for half an hour with 0.14 g. of sodium nitrite, 2.5 cc. of ethyl alcohol and 1 cc. of concd. sulfuric acid. The mixture was then diluted with water and the reddish colored oil which soon solidified was thoroughly washed with water. After drying in a vacuum desiccator 0.55 g. of product was obtained which after two crystallizations from alcohol melted at 85.5–86°. The red color was removed by boiling the alcohol solution with a little Norit. A yield of 96.2% was obtained.

3. Diazotization of 2-Chloro-4-iodo-6-bromo-aniline

To 2.15 g. of the amine was added 0.5 g. of sodium nitrite, 3.5 cc. of concd. sulfuric acid and 10 cc. of ethyl alcohol. After refluxing for half an hour and evaporating the alcohol, the residue was steam distilled. One and five-tenths g. of a white crystalline substance was obtained from the distillate on cooling. After one crystallization from alcohol, the substance melted at 85.5–86.0°. The yield was 73.2%.

Mixed melting points of the halogenated benzenes obtained from the three trisubstituted anilines showed that the products were identical. The fact that the three amines gave the same compound on diazotization proves the symmetrical arrangement of the halogens.

Summary

1. A study of the melting points of halogenated benzene derivatives shows that the melting points are raised by the introduction of additional groups except in the case of one class of compounds. Contrary to the general rule, the melting points of para dihalogenated benzene derivatives are lowered by the introduction of a group causing ortho-para substitution.

2. Symmetrical trihalogenated benzene derivatives containing iodine, bromine and chlorine in the same ring have been prepared for the first time.

3. The amino derivatives of these compounds have higher melting points than the parent hydrocarbons.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

ACTION OF THIONYL CHLORIDE ON ORGANIC ACIDS[1]

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Thionyl chloride is a reagent which has become very important for the synthesis of a large variety of organic compounds. In a recent article by Silberrad,[2] a summary of the work upon thionyl chloride is given. It is mentioned as a chlorinating and dehydrating agent, as a reagent for the removal of hydrogen from mercaptans, as a condensing agent and as a catalyst. The most frequent use of this reagent is for the conversion of an acid into its chloride, since it is easier to handle than phosphorus pentachloride. This investigation was begun some months previous to the review by Silberrad and had for its object a systematic study of the reaction of thionyl chloride on organic acids.

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[1] This paper was presented before the Division of Organic Chemistry of the American Chemical Society, Richmond, Virginia, April 11 to 16, 1927.

[2] Silberrad, *J. Soc. Chem. Ind.*, **45**, 37, 55 (1926).