A Standardization of the Sandmeyer Reaction, With Special Applications.

A Thesis

by

Irvine Walter Grote.

Presented to the Faculty

of the

Graduate School

of the

University of Cincinnati

in fulfillment of part of the requirements for

the degree of Doctor of Philosophy

Cincinnati, Ohio

June 1925.

Table of Contents.

Acknowledgement - - - - - - 2.

Introduction - - - - - - - 3.

Part A.

Historical and Theoretical - - - - - - 4.

Preparation of Diazo Compounds - - - 6.

Constitution of Diazo Compounds - - - 9.

Reactions of Diazo Compounds - - - - 14.

The Sandmeyer Reaction - - - -- 16.

Theory of the reaction - - - - 26.

Kinetics of the reaction - - - 32.

Part B.

Purpose of this Investigation - - - - 38.

Experimental - - - - - - 40.

Procedure One. Method Using Hydrochloride Salts 42.

Procedure Two. Method Using Acid Sulfate Salts 47.

Procedure Three. Standardized method Using Acetate Salts. 49.

Part C.

Table One - - - - - - 56.

Ortho Dihalogen Compounds - - - - 57.

Meta Dihalogen Compounds - - - - 58.

Table Two - - - - - - 59.

Nitrohalogen Compounds - - - - 60.

Table Three - - - - - - 62.

Cupric Salt Modification - - - - 62.

Table Four - - - - - 66.

Results without Catalyst - - - - 67.

13 Ap 25

Results Using Various Salts as Catalysts - - 67.
Conclusions - - - - - - 70.
Table Five - - - - - 72.
Summary - - - - - 77.
Bibliography - - - - - 79.

Acknowledgment.

The topic of this thesis was suggested by Dr. H. S. Fry and was carried out under his supervision. I desire to express my appreciation of the inestimable aid, constructive criticisms, and valuable suggestions given by him thruout the work.

A STANDARDIZATION OF THE SANDMEYER REACTION, WITH SPECIAL APPLICATIONS.

Introduction.

This research is an attempt to standardize the Sandmeyer reaction and to make special applications of the standardized method to certain compounds.

A thorough study of the voluminous literature relating to the Sandmeyer reaction necessarily precedes any attempt to develop a standardized method, that is, to ascertain by experiment, uniform conditions under which the reaction might be applied generally. Accordingly, this thesis naturally divides itself into three parts.

Part A is a historical and theoretical review of the Sandmeyer reaction, covering some of the more important work done in this widely studied field by several investigators.

Part B is a report on the preliminary experiments which led to a standardized method of procedure.

Part C gives the results obtained by using the standardized method and the variations resulting when other salts are substituted for the more commonly used cuprous salts.

Part A. Historical and Theoretical.

One of the most useful replacement reactions of synthetic organic chemistry is that designated by the name of Sandmeyer. (Traugott Sandmeyer, 1854-1922.) By use of this reaction, Sandmeyer discovered that the amino group of an aromatic amine may be replaced by any one of a great number of groups. Since the amino group is easily obtained by reduction of a nitro group, and the latter can be introduced into the aromatic nucleus by direct nitration, many compounds can be prepared indirectly thru use of the Sandmeyer reaction in a high state of purity very difficult to secure by any more direct means.

The first essential step in the Sandmeyer reaction is the conversion of the amino group into the diazonium group. For a proper understanding of this reaction, some of the properties and reactions of diazo and diazonium salts should therefore be understood thoroughly insofar as they are really known.

The discovery of diazo compounds is usually attributed to Johann Peter Griess , who first prepared them in 1858, although earlier work had been done.

Piria in 1849 found that amino-succinic acid was easily converted into malic acid by treatment with nitrous acid, the amino group being replaced by the hydroxyl group.

Hunt in the same year showed that aniline could similiarly be converted into phenol. In 1853 Gerland [2] prepared hydroxybenzoic acid from amino benzoic acid and observed the formation of a red intermediate product which increased in amount if cold dilute solutions were used. The red substance proved so unstable, however, that Gerland was unable to secure concordant analyses and dropped further work.

Kolbe [1] under whom Gerland had been working, suggested to Griess the further investigation of this action of nitrous acid on amines at low temperatures, Griess soon prepared many of the compounds. Analyses of the compounds showed the presence of two atoms of nitrogen which Griess considered had replaced two atoms of nuclear hydrogen. He therefore gave the name "Diazo" to the new class.

The new compounds were only stable at low temperatures, and were found highly reactive, not only in easily splitting off nitrogen, but also in reacting with various substances such as phenols, often giving rise to brilliantly colored compounds which dyed animal fabrics directly. The azo dyes were thus introduced.

Continuing his researches, Griess [3] soon found many other reactions possible. From the easily prepared nitrate salt of diazo benzene, the crystalline sulfates, platinic chlorides, aurichlorides and others were made.

By treating diazobenzene bromide in ethereal solution with bromine, the perbromide $C_6H_5N_2Br_3$ was obtained. This on addition of ammonia gave a substance containing

three atoms of nitrogen, $C_6H_5N_3$, (diazobenzeneimide). By treatment with alkalies, various metallic diazo compounds could be prepared and converted into silver, mercury and other salts.

Preparation of Diazo Compounds.

Altho many methods of preparing diazo compounds have been suggested, only two of these are used to any extent. By far the most useful of the two is the addition of sodium nitrite to a solution of the amine salt containing excess acid to liberate the nitrous acid in presence of the aniline salt. In the preparation of dry diazo compounds, almost necessarily from ethereal solution reagents, amyl nitrite is often used. In special cases barium nitrite, nitrosyl bromide or chloride, and nitrosulphonic acid have been used.

Due to (1) the great instability and explosiveness of the dry diazo salts, (2) the fact that the compound is usually only desired as an intermediate step in the preparation of another compound, and (3) the yield under proper conditions being practically quantitative, the compounds are usually prepared in solution and used directly without isolation of the unstable dry salt. Many dry diazo compounds regarded as stable may often explode after several years storage. Oddo, made investigations as to the explosion temperatures of various diazo compounds. One as low as 85°C is noteworthy, namely the case of para nitro benzene diazonium nitrate. Those containing nitro groups are in general more explosive, while the nitrate salts are more explosive than the corresponding chlorides or sulfates.

The procedure used consists therefore usually in dissolving the amine to be diazotized in several parts of water containing at least an equivalent of the acid of the salt desired, heat being used if necessary to effect solution. The solution thus obtained is then cooled to 0-5° C., an amount of ice added directly to the solution, (diazotization being an exothermic reaction,) and one to two more equivalents of acid added. A cold solution of sodium nitrite slightly in excess of the theoretical amount is then added with vigorous stirring. Sufficient nitrite should be added to give a good reaction for free nitrous acid with starch-iodide paper after the solution has been well stirred for several minutes after complete addition. In some cases there is a great tendency toward formation of diazo-amino derivitives, as in case of a-naphthylamine or para nitraniline. Here the diazo compound reacts with the unchanged amine salt as follows:

$$NO_2C_6H_4N_2Cl + NH_2C_6H_4NO_2 = NO_2C_6H_5N{=}NNHC_6H_4NO_2$$

diazotized salt amine diazoamino compound

In these cases it is well advisable to add an excess of sodium nitrite very rapidly to the solution containing a considerable excess of acid. Often the nitrite solution is previously acidified and then added all at once to the amine in order to secure very rapid diazotization and thus prevent the side reaction. The tendency toward diazo-amino formation increases if organic acids are used, eleven equivalents of acetic acid being required to secure complete diazotization.

In those cases where both the aniline salt and the diazo compound formed are insoluble, special methods must be used to secure complete diazotization. One method employed is to use a considerable excess of nitrous acid with very cold solutions under pressure to prevent escape of the nitrous acid. But if the amine salt is in a finely divided form, excess nitrous acid added slowly, and the solution stirred for a considerable length of time, complete reaction is usually secured, in spite of the theoretical danger of coating over the unchanged amine salt with insoluble diazo compound and thus rendering complete conversion impossible.

Much diffuculty is often experienced in the diazotization of substituted amines containing a number of acidic groups, a large excess of acid being needed, the use of nitrosyl chloride or sulphonic acid even may be required.

Secondary reactions may often occur when substances containing more than one amino group are treated with nitrous acid, with the production of azimino, azo and nitroso compounds. Under proper conditions however, two and even three amino groups can be diazotized in the same compounds, provided steric influences do not interfere. Usually a large excess of nitrous acid and very dilute solutions are required.

The velocity of diazotization is very great under ordinary conditions. Hantzsch and Schumann [6] by working with $N/_{1000}$ solutions, using colorimetric methods of estimating the nitrous acid, found that in presence of excess acid the

rate of diazotization of aniline, para toluidine, para brom and para nitro anilines and several others are the same under similiar conditions, the rates increasing with a temperature rise. The reaction was found to be of the second order, and constants for the equation

$$K = \frac{x}{t(a - x)}$$

were 0.036 for aniline, 0.038 for para toluidine and 0.045 for para brom aniline in $N/_{1000}$ solutions in presence of one molecule of free acid at 0°C. Schumann, by measurements of the fall of electrical conductivity during diazotization, confirmed the work of Hantzsch in concluding that all aromatic amines are diazotized at approximately the same rate.,

Constitution of Diazo Compounds.

Much controversy as to the constitution of diazo compounds has filled the literature. Endless confusion was present until a partial clearing up of the diffuculty was brot about by the separation of the true diazo salts from the diazonium compounds, but the constitution of the latter does not even yet appear to be settled satisfactorily.

Griess early assigned the formula $C_6H_5{-}N_2{-}HNO_3$ to diazonium benzene nitrate, the two atoms of nitrogen being regarded as having substituted two atoms of hydrogen in the ring.

Kekule in 1866 pointed out that the behavior of the diazonium salts was not in accordance with this formula, since in the replacement of the group a monosubstituted product was obtained. He advanced the formula $C_6H_5N{=}N{-}NO_3$ for the same

salt. This type formula held the field for over thirty years, when the discovery of the isomeric metallic diazo salts led to its replacement by Blomstrand's formula for the true diazonium salts. The Kekule formula gave the structures:

Free diazobenzene $C_6H_5N{=}NOH$

Diazobenzene sulfate $C_6H_5N{=}N{-}HSO_4$

Diazobenzene platinichloride $(C_6H_5N{=}N{-}Cl)_2PtCl_4$

Diazoaminobenzene $C_6H_5N{=}N{-}NHC_6H_5$

Diazo perbromide $C_6H_5N{=}NBr_3$

The diazo group thus was assumed to play the part of a base analogous to ammonia.

Blomstrand in 1869, and later independently Strecher [9] and Erlenmeyer [10] assigned the formula $C_6H_5\overset{NO_3}{\underset{}{N}}{\equiv}N$ to the salt, showing the analogy to the quarternary ammonium salts. Altho the formula was at first ignored, it follows easily from the amine salt without valence changes.

$$C_6H_5\overset{H_3}{\underset{}{N}}{-}NO_3 + HO\overset{3}{N}{=}O = C_6H_5\overset{5}{\underset{N}{N}}{-}O{-}NO_3 + 2H_2O$$

The Kekule formula requires a valency change in the formation reaction for which there seems no justification.

$$C_6H_5\overset{5}{\underset{H_3}{N}}{-}NO_3 + HO\overset{3}{N}{=}O = C_6H_5\overset{3}{N}{=}N{-}NO_3$$

Blomstrand further pointed out that the great instability of the salts was probably due to the unusual replacement of three atoms of hydrogen by one of nitrogen, and that the great difference in behavior of the trivalent, non-salt forming nitrogen atom of the azo compounds could be thus explained.

The chief reason for the hesitation in acceptance of the Blomstrand formula in place of the Kekule was due to the fact that it apparently could not explain the formation of phenylhydrazine by simple reduction of a diazo salt, a reaction discovered by E.Fischer in 1875.[11]

$$C_6H_5\overset{5}{\underset{3}{\overset{|}{N}}}\!-Cl \;+\; 4H \;=\; C_6H_5\overset{3}{\underset{H}{N}}\!-\overset{5}{\underset{H_3}{N}}\!-Cl$$

The formula given for phenylhydrazine having been proven correct, the Blomstrand formula by the above equation apparently requires the assumption that the pentavalent nitrogen changes to trivalent and the trivalent to pentavalent. This has been explained by Blomstrand [12] as follows:

$$C_6H_5\overset{5}{\underset{3}{\overset{|}{N}}}\!-Cl \;+\; 4H \;=\; C_6H_5\underset{{}^{+}HCl}{\overset{H}{N}}\!=NH_2 \;=\; C_6H_5\underset{H\ H_3}{N}\!-NCl$$

Bamberger,[13] aided by the work of Von Pechman and O. Fischer, drew the conclusion that diazotization involves several steps.

(1) The first product formed is a nitrosamine:

$$C_6H_5NH_2 \;+\; N_2O_3 \;=\; C_6H_5NHNO$$

(2) The ordinary diazo compound possessing the Kekule structure arises by rearrangement of this:

$$C_6H_5NHNO \;=\; C_6H_5N{=}NOH$$

Bamberger finds confirmation of this in that two sets of metallic salts exist, of which one, the "iso salts", does not couple with phenols and is transfered into the normal diazo salts by mineral acid. C_6H_5NKNO (iso-diazo) $=$ $C_6H_5N{=}NOK$ (diazo).

In 1894 Hantzsch[14] introduced the theory that the isomeric diazo compounds were analogous to the isomeric oximes, with the formulas:

C_6H_5N $\quad\quad$ C_6H_5N

X-N $\quad\quad$ N-X

Syn-diazo $\quad\quad$ Anti-diazo

The ordinary explosive and highly reactive diazo compounds were assigned the "syn" form, while the "iso" diazo compounds of Bamberger were given the "anti" form.

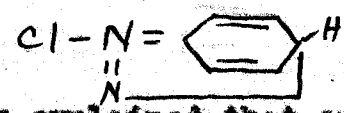
A long controversy then arose in which many compounds were prepared and many theories offered. Jacobson, Walther, Bruhl, Dobie and Tinkler, Armstrong, Robertson, as well as Bamberger, Blomstrand, Von Pechman, and Hantzsch entering into the controversy.

Even yet a complete agreement has not been reached, but a partial compromise adopted. [15]

The acid salts of diazo benzene which correspond in cryoscopic behavior and electrical conductivity with the ammonium salts, and also resembling ammonium in forming additive halogen compounds, have been assigned the formula of Blomstrand: $R-N{=}N(OH)$ with the name "diazonium" in analogy to ammonium.

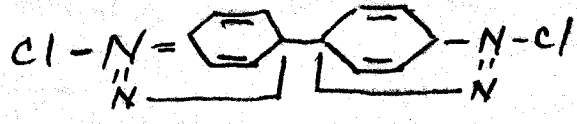
The Kekule formula has been given to the metallic salts together with the name "diazo". The isomeric forms are distinguished by the terms syn and anti, as in the above formulas given by Hantzsch.

Cain in 1907 pointed out that altho there are no other examples of singly linked nitrogen being otherwise than firmly attached to the benzene nucleus, the most striking characteristic of the diazonium compounds is the readiness with which the whole of the nitrogen is eliminated. Cain further pointed out that in the case of doubly linked nitrogen, the nitrogen is easily eliminated, as in the case of quinone chlorimide, $O{=}C_6H_4{=}N{-}Cl$, which splits off nitrogen at 100°C. By analogy to this and other examples, he assigns a quinonoid structure to the diazonium compounds, as:

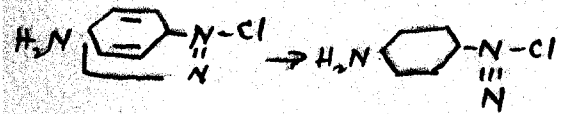


The fact is thus explained that only one amino group in such compounds as para phenylene diamine is easily diazotized, the tetrazo compound being formed with diffuculty. The structure:

having an amino group attached to a carbon atom all the affinities of which are fully satisfied would display no tendency to form a second diazo group. Benzidene however, under similiar conditions, readily gives the tetrazo form:

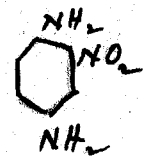


Under special conditions, the linkage between the amino carbon atom and the trivalent diazonium nitrogen atom is broken:

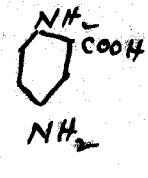


which then diazotizes to:

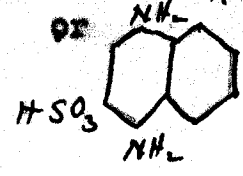
In case of



,



or



only one

group can be diazotized, because the para linkage in presence of the acidic group is too stable to be ruptured. Since not only a para, but two ortho linkages are also possible, it has been suggested that a dynamic equilibrium of para quinonoid and the two ortho quinonoid phases may exist.[16]

The Cain formula does not seem to have received the attention it deserves, but facts and opinions cited show that more work must be done on the whole subject before the structure of the diazonium compounds is fully settled.

Reactions of the Diazo Compounds.

Since the reactions of the diazo compounds are so numerous, only those which take place with the elimination of the diazonium nitrogen will be considered except such others as may take place concomitantly with the Sandmeyer reaction.

The important reaction that led Griess to the discovery of the diazo compounds has already been mentioned, namely the replacement of the N_2X group by a hydroxyl group, easily taking place on heating the diazonium salt with water, dilute sulfuric or other mineral acid:

$$ArN_2HSO_4 + H_2O = ArOH + N_2 + H_2SO_4 .$$

In the ordinary procedure, the amine is diazotized in presence of an excess of mineral acid and then heated to boiling either directly or by introduction of steam, until nitrogen evolution has ceased. In some cases the diazonium solution is added slowly to a boiling acid solution. Coupling of the unchanged diazonium compound often occurs with the phenol as

formed, producing azo dyed rather than the pure phenol. Other reactions involving an oxidation may also take place.

The action of alcohols on aromatic diazo compounds was studied by Griess, who found two reactions possible. In the case of the higher alcohols, aryl hydrocarbons are produced, the alcohol being simultaneously reduced to the aldehyde.

$$ArN_2Cl + C_3H_7OH = ArH + C_2H_5CHO + HCl + N_2$$

By variations in the temperature, and especially under the influence of certain nuclear substitients and use of lower alcohols, ether formation may take place.

$$ArN_2Cl + C_2H_5OH = ArOC_2H_5 + N_2 + HCl$$

Reducing agents such as stannous chloride produce the hydrocarbon in presence of cupric sulfate.

The observation was also made that on heating a diazonium salt with concentrated hydrochloric acid a chloro derivitive is obtained along with the phenol, but only in a small amount. The yield of the bromine compound is somewhat better with hydrobromic acid, but only in the case of the iodo derivitives is the yield at all good. In this case by adding a solution of a little more that the theoretically required amount of sodium or potassium iodide to the diazonium sulfate solution containing free acid, a good yield of the iodo derivitive is obtained.

Griess found the chlorine and bromine replacement to be more successful if the dry platinic halogen compound of the diazonium salt is heated with ten parts of sodium hydroxide.

$$(C_6H_5N_2)_2PtCl_6 + NaOH = C_6H_5Cl + Pt + Cl_2 + N_2$$

The Sandmeyer Reaction.

A much more convenient and more widely applicable procedure for the replacement of the diazonium group was discovered by Treugot Sandmeyer in 1884.[17]

In endeavoring to prepare phenylacetylene, Sandmeyer treated cuprous acetylide, (Cu_2C_2) with benzene diazonium chloride, but obtained chlorbenzene rather than the compound expected.

The result was easily proven to be due to the presence of cuprous chloride formed with the acid present rather than to the acetylide itself, since the yield of chloride was much higher on repeating the process with cuprous chloride. Several side reactions took place also, considerable benzidene sulfate, phenol and tarry matter being formed. By adding a cold diazonium solution to a boiling 10% cuprous chloride solution in hydrochloric acid, Sandmeyer found the side reactions and tar formation to be greatly reduced. Complete explaination of the reaction was not attempted by Sandmeyer, beyond stating that it was probably a catalytic one in which the cuprous salt acted similiarly to aluminium chloride, vanadium chloride etc., in other organic reactions. The action was thot to be specific to cuprous salts, since no yield could be obtained by use of either cupric or ferric chloride.

On addition to the cuprous chloride, the formation of a more or less colored intermediate product was noticed, which

almost immediately liberated nitrogen with formation of the final product. The intermediate compound contained copper but was too unstable for analysis. The following reaction was suggested as a possibility:

$$\begin{array}{l} C_6H_5 \\ N \\ \| \\ N \\ Cl \end{array} + \begin{array}{l} CuCl \\ | \\ CuCl \end{array} = \begin{array}{l} C_6H_5 \\ N\text{-}Cu\text{-}Cl \\ \| \\ N\text{-}Cu\text{-}Cl \\ Cl \end{array} = \begin{array}{l} C_6H_5 \\ | \\ Cl \end{array} + \begin{array}{l} CuCl \\ | \\ CuCl \end{array} + N_2$$

Gattermann[18] in 1890 found that the addition of very finely divided copper to the diazonium solution in hydrochloric acid gave good replacements of the group by chlorine at low temperatures

Sandmeyer[19] at first insisted that this was essentially the same reaction as his own, since the finely divided copper was undoubtedly coated with a film of cuprous oxide, which would act in the acid solution in a way similar to his cuprous salt. The action has been proven beyond reasonable doubt to be not the same, however, since Heller[20] found that in the preparation of isocyanates the transposition will take place using copper powder in strong sulfuric acid solution, under conditions in which cuprous salts could not exist. It was found also by Heller that if certain syn-diazo compounds are treated with cuprous chloride in an inert, acid free solvent, such as methyl sulfid, no reaction will take place, while the addition of copper powder will cause brisk evolution of nitrogen and the formation of the halogen compound. The copper powder works then as a pure catalyst in a manner certainly different from that of cuprous salts, with which a more or less stable intermediate product is formed.

Sandmeyer, together with several later workers, extended the method to the preparation of many derivitives, the desired cuprous salt ,(or in a few cases, the oxide) being added in presence of the acid containing the group desired. Good yields have been obtained for the introduction of bromine, iodine, nitrile, nitro, cyanate, thiocyanate, selenocyanate, sulfite, arsenite and other groups.

The procedure as most often carried out consists in slowly adding the ice cold diazonium salt, preferably a salt of the group to be introduced, to an ice cold, strongly acid solution of the desired cuprous salt in the corresponding acid. Molar equivalents of the aniline and cuprous salt are used, together with several moles of acid, varying from three to five. Excess ice should be present and the solution vigorously stirred during the addition. The cuprous solution is often prepared by boilin a cupric salt in presence of excess acid and copper strips until the colorless cuprous salt is obtained, tho very often the solid cuprous salt required is merely dissolved in the acid as needed. Upon the addition of the diazonium salt solution to the cuprous solution there is usually formed a more or less voluminous and colored "between" product, the solution usually frothing and foaming considerably due to the excess nitrous acid and nitrogen evolved. The solution after mixing and thoro stirring is then let stand at room temperature for several hours or over night. The product if volatile is then separated by steam distillation, since more or less tarry matter is usually present. If non-volatile,

it is best to heat slightly before filtering in order to complete decomposition of the intermediate product, which may not completely decompose even on standing over night.

Sandmeyer early found that good yields could be obtained not only by adding the diazotised salt to a boiling cuprous solution, but also by adding the salt of the amine itself to the cuprous solution, heating this to boiling, and diazotising the mixture by slowly adding sodium nitrite solution thru a reflux tube. ;; Later experience has shown however that this method of diazotisation of a hot solution in presence of the cuprous salt does not give good yield, very much tarry matter being formed.

Erdmann in an exhaustive study of the reaction, as particularly objects to this method of diazotisation, and states that by this method the tar and phenol may reach 80% of the theoretical yield. He recommends the use of very dilute, strongly cooled solution for diazotisation, and decomposition with the cuprous chloride or other cuprous salt at a temperature characteristic of each compound, and found empirically. These temperatures vary widely. For example they are 0, 37, and 30-40° C. in case of the cuprous chloride derivitives of diazonium benzene, ortho and para diazonium toluenes respectively. This characteristic temperature factor had been also assumed by Sandmeyer, but not investigated. If the reaction is carried out below this temperature Erdmann states that the nitrogen evolution is slow and incomplete, part of the diazonium compound being reduced to an azo compound by the excess cuprous chloride.

In summary, Erdmann gives the three following reactions as possibilities in the decomposition of the diazonium halides, using benzene diazonium chloride as an example.

I. $C_6H_5N_2Cl + H_2O = C_6H_5OH + N_2 + HCl$

II. $C_6H_5N_2Cl = C_6H_5Cl + N_2$

III. $2C_6H_5Cl + CuCl + HCl = C_6H_5N{=}NC_6H_5 + N_2 + CuCl_2$

Reaction one is caused by decomposition of the diazonium salt before the cuprous addition productcan form. This occurs not only when the amine is diazotized in presence of the cuprous salt, but also if the solutions are too concentrated, insufficiently cooled, or if the diazonium solution after preparation is added too slowly, or at the other extreme, all at once to the cuprous solution. This is particularly true if hot cuprous solution is being used.

Behrend and Nissen [22] obtained 240 grams of ortho cresol from one kilogram of ortho toluidine using the procedure recommended by Sandmeyer of pouring the diazonium solution into a boiling cuprous solution. Only a 29% yield of the chlortoluene desired was obtained.

Reaction II illustrates the normal decomposition of the diazo-cuprous compound, and goes promptly and smoothly only at temperatures slightly above the characteristic decomposition temperature peculiar to each compound.

Reaction III is favored by remaining below this characteristic temperature, since the reaction then goes so slowly that part of the compound is reduced. This reaction may in

some cases proceed to such an extent as to give a 10% yield of the azo compound, as in the case of the preparation of para azo toluene from para diazonium toluene chloride by addition of the reactants at 0°C.

Besides the reactions noted and discussed by Erdmann, several others often occur. Gattermann, as well as Ullmann found that two benzene nuclei may condense in presence of cuprous chloride to form diphenyl derivitives. By simply reversing the usual procedure and adding the cuprous solution to the diazonium solution, Ullmann and Forgan [24] obtained a yield of 66% of 2-2 dinitrodiphenyl from ortho nitroaniline and only 17% yield of o-chlor-nitro benzene. The process has been patented as a method of preparation of 2-2 diphenyl derivitives. [25]

A still further reaction has been noticed by Hollemann and Slinter.[26] In the preparation of met dibrombenzene from meta bromaniline, and in several other dihalogen derivitives from the respective halogen anilines, using the methods recommended by Erdmann, a green product was obtained. This color was at first thot due to the presence of copper as reported by several other observers. The fact that it persists thru several steam, vacuum and ordinary distillations renders this idea impossible, and also the fact that it persists after washing with strong alkalies, acids and several recrystallisations from alcohol and ether. By suspending the material in an acid solution to which zinc or tin is added, the color is removed by reduction. The green product has practical-

ly the same melting and boiling points as the colorless compounds obtained by other methods. The color is hence probably due to a trace of a nitroso or other compound formed by reaction with the excess nitrous acid present. In such a case the following reactions are possible and likely:

$$BrC_6H_4N_2Cl + HNO_2 = BrC_6H_4NO_2 + N_2$$

$$BrC_6H_4NO_2 + 2CuCl + 2HCl = BrC_6H_4NO + 2CuCl_2 + H_2O$$
(green?)

The action of nascent hydrogen is thus explained, since the nitroso compound would be reduced to a colorless, soluble aniline salt.

$$BrC_6H_4NO + 4H = BrC_6H_4NH_2 + H_2O$$

The formation of more or less tarry matter is usually found accompanying the Sandmeyer reaction, particularly when hot cuprous solutions are used. No attempt at explaination has apparently been made as to the formation reaction or composition of this tarry matter. Possibly it may result from a further polymerization reaction similiar to that of the formation of the diphenyl compounds, many nuclei thus aggregating, after which more or less decomposition takes place.

Tobias [37] pointed out that since the cuprous salt was regenerated in the reaction, a small amount should be sufficient to complete the reaction. This was tested by Votocek, [38] who found that the amount could be reduced to $1/_{24}$ or even $1/_{28}$ mole of cuprous chloride.(as Cu_2Cl_2) per mole of amine without serious diminution of yield, since with chlorbenzene the yield only fell from 66% to 63% with a change from one mole of cuprous chloride to $1/_{24}$ mole, and with meta chlor-

toluene from 78% to 73% with a change from one to 1/28th mole of cuprous chloride.

Various methods have been tried using cupric salts and then reducing these in presence of the diazonium compound, thus Votocek [28] added cupric salt and electrolyzed the solution with copper electrodes, obtaining a 64% yield of chlorbenzol. A. Angeli [29] used cupric salts and reduced these by addition of hypophosphoric acid.

A. Contardi [30] found that for the replacement with chlorine or bromine, the use of cupric salts without reduction, and with as little as 0.05 to 0.1 equivalents of cupric salt per equivalent of diazonium salt gave as good yields or better than the corresponding cuprous salts. Contardi states that the yield depends principally upon the temperature and the rate of decomposition of the double salts, and gives as general concluions the following:

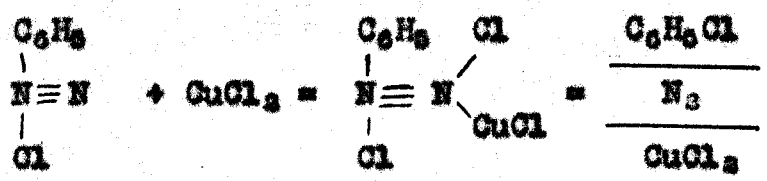
I. Mono-halogenated and nitrated aniline derivitives give almost theoretical yields using cuprous salts except in the case of meta nitraniline.

II. The amino group in a mono-halogenated mon or dinitroaniline can be replaced by preliminary diazotization only when the new nitro group is so orientated that it in turn can be replaced by heating with alcoholic ammonia.

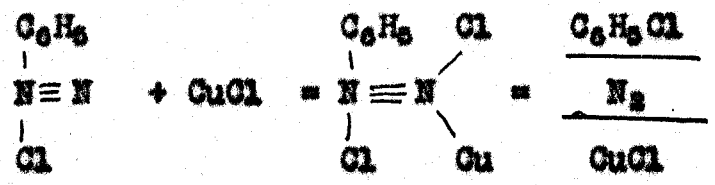
III. Halogen atoms introduced into the nucleus have usually but slight influence upon the substitution reactions of the amino group, tho in certain cases it is rendered impossible, as when halogens are present in positions 2,4,6 to the amino group.

IV. A nitro group cannot be introduced into an amine already containing three nitro groups.

No yields are given by Contardi however, but the following reaction is suggested for the cupric salt replacement, without an actual analysis:



based on that of Hantsch for cuprous:



In view of the fact that Hantzsch himself found later that two atoms of copper were present in the intermediate cuprous compound, the formula assumed by Contardi is a decidedly uncertain one.

The effect of replacing cuprous salts by those of other metals was tried by A.Koreanski [24] by use of the following procedure:

Three grams of para nitraniline were heated with three moles of hydrochloric acid and diazotized after cooling in the usual manner with sodium nitrite. The product was then poured into a solution of the metallic chloride containing one mole of the salt and enough potassium sulfocyanid to convert this and the diazonium salt to the sulfocyenid. The mixture was then let stand for twenty-four hours, the crystalline product obtained filtered off, treated with animal charcoal and recrystallized from alcohol. The purity was then tested, after weighing, by a melting point determination. In practically all cases an in-

termediate molecular product of the diazonium compound and the metallic salt was obtained, each possessing a definite and characteristic color. Metanitraniline forms intermediate compounds which are very stable in comparison with the ortho and para and hence gave lower yields due to incomplete decomposition and side reactions. The yields obtained from the para nitraniline are as follows:

Chromium -	6.6%
Manganese	10.0%
Iron	80.0%
Cobalt	53.0%
Nickel	30.0%
Copper	60.0% (by Gattermann method)
Zinc	3%
Molybdenum	0
Tin	0
Tungsten	20.0%
Uranium	20.0%

The property of transformation is thus shown best by elements of atomic weights 55-64 and diminishes above this range (Mn.Cr,Zn) finally to zero. On reaching tungsten with three times the active atomic weight, activity is again evident, while uranium with four times the weight gives practically the same results as tungsten.

The yields given above are to be accepted only as rough approximations however, since the quantities used were so small and the method of purification very crude. It is curious that Korczynski does not give the results obtained using the ordinary method with cuprous salts.

Theory of Reaction of the Sandmeyer.

The mechanism, kinetics and theory of reaction of the Sandmeyer have been studied by many workers, but with contradictory and widely divergent results.

Considerable importance with reason has been attached to the so-called "intermediate" compounds almost always formed instantly upon addition of the diazonium salt to the cuprous solution. The compounds so formed vary in color not only with the amine, but also with the acid and cuprous salt used. The color varies from almost white or cream, thru yellow, crimson, chocolate, to almost black. The compounds are very unstable and hence very hard to separate and purify. Sandmeyer originally assumed the formula to be $RN_2X \cdot Cu_2X_2$.

Hantzsch [23] made several analyses of the red bromdiazobenzene cuprous bromide compound and arrived at the formula $C_6H_5N_2Br \cdot Cu_2Br_2$. Hantzsch regarded it as a syn-diazo complex salt $\begin{matrix} C_6H_5\text{-}N \\ \| \\ Br\text{-}N \end{matrix} \cdot Cu_2Br_2$.

A similiar formula was found for the double salt of para bromdiazobenzene bromide, the chloride salt in both cases being too unstable for analysis. Hantzsch and Blagden [23] later gave the following as their conclusions.

I. The Sandmeyer is in no sense a simple catalytic reaction, but always involves a double salt formation. This double salt, both from direct analyses and also from analyses of the more stable mercury salts, is most probably a syn-diazo compound of the formula just given.

II. In the decomposition of the double salt, the halogen or radical remaining attached to the nucleus is that originally attached to the cuprous salt rather than that attached to the diazo nitrogen. This is shown by the fact that a diazonium salt of one halogen acid when treated with a second cuprous halide, the reaction being carried out in an inert solvent such as methyl sulfide and in the absence of acid, gives by far the greater amount of a compound containig the halogen originally attached to the cuprous salt. Only a small amount of the compound containing halogen linked originally to nitrogen is formed. The reaction conforms to the equation:

$$RN_2X + CuY = RY + CuX + N_2$$

The behavior of iodides could not be investigated due to the great insolubility of cuprous iodide in methyl sulfide.

III. Normal diazonium cyanide compounds act with cuprous halides exactly as the halogen salts, but with syn-diazo cyanides no reaction is obtained in concentrated alcoholic solution in which the normal diazonium compounds will react briskly. The syn-diazo salt on similiar treatment with copper powder gives a vigorous reaction, showing that the Sandmeyer and Gattermann reactions are essentially different; the latter being strictly a catalytic one, while the former involves the formation of a labile copper double salt. With normal diazonium compounds, however, the cuprous salt may tend to have a slight catalytic effect, as shown by the fact that a small percentage of nitrogen linked halide becomes united with the aromatic nucleus when mixed halides are used.

Walter, [34] using diazonium benzene chloride as an example, believes that the diazonium salt is first reduced by the cuprous salt to a phenylhydrazine, cupric chloride being formed simultaneously. The phenylhydrazine is then oxidized by the cupric salt thus formed to chlorbenzene, regenerating the cuprous salt. The fact is thus explained that no cuprous salt is needed in the preparation of iodo derivitives, since the hydriodic acid present in this case acts as the reducing agent. But in view of the fact that no phenylhydrazine can be detected during the reaction, the explaination does not seem very feasible, especially since good yields apparently can be obtained by use of cupric salts alone, with no reducing agent present, as shown by the work of Contardi.

G.Heller [35] made an extensive quantitative investigation of the Sandmeyer reaction and came to the following conclusions:

That it is clear from the work of Erdmann and Hantzsch that the diazonium compounds are able to yield two different series of metallic double salts. One series, containing the mercury double salt is colorless, stable and with the properties more like the potassium diazo compounds than than those of normal diazonium compounds, but may be decomposed in aqueous solutions under certain conditions to give a phenol, or in presence of copper powder, to give halogen or other substitution products. This series cannot take part in the Sand-

meyer reaction. The second series of salts, the so called unstable "between products" of the normal Sandmeyer, are, from the point of view of Hantzsch, syndiazo derivitives, colored and decomposable directly with formation of substituted benzenes. Erdmann and Hantzsch found this series to contain two atoms of copper, with the formula $RN_2XCu_2Y_2$. The amount of this product separating has been found to increase with higher acid concentrations.

It is suggested then by Heller that the double copper salt may also form in two ways, one in which the cuprous salt acts as a complex acid, (as $HCuCl_2$), and the other as the normal salt. The two series are readily distinguished by their solubility, the highly insoluble series giving but poor yields. This series may be regarded as analogous to the mercury diazo salts. The other series is more readily soluble, but may be isolated by use of concentrated acid solutions, in which it is less soluble. These soluble double salts are formed in the ordinary smooth running reaction, and therefore are desired. Further investigation on this subject is needed, but according to Heller, it is atleast clear that for the best yields, such concentrations should be taken that there will be but little separation of the insoluble complex upon mixing the diazonium and cuprous solutions and that gas evolution should not start for a moment and then gradually become more brisk. If this condition is secured, the "decomposition temperatures" of Erdmann are of little importance, since for example, a 93% yield of ortho chlortoluene was obtained at 30°

while Erdmann obtained 97% at his decomposition temperature of 5°C. In some cases where the acid concentration is high, considerable intermediate product may separate, but of the "soluble" form and hence decomposes rapidly to the product desired. Heller gives some comparative yields as follows:

	Sandmeyer	Gattermann	Ullmann	Heller
Chlorbenzene	70%	65%	74%	Quantitative
Para chlor-toluene	63%	76%	81%	Quantitative
Ortho chlor-toluene	31%	66%	70%	97%

The effect of variations in concentration are shown in the following table given by Heller[38]:

Cuprous Solution				o-Toluidine-HCl solution			Yield		Temperature of addition of solns.
Mole Cu_2Cl_2	Mole HCl	Total Volume	% Cu_2Cl_2	HCl mole	Volume	%o-tol.	% crude	% pure	
1/4	3.3	1020	4	1.3	423	12.6	96	79	5°
1/4	3.3	1020	4	1.0	600	8.9	93	83	5
1/4	2.4	710	7	1.0	700	7.6	97	90	5
1/4	3.2	710	7	1.0	700	7.6	92	87	20
1/4	2.4	710	7	1.0	800	6.7	93	83	3
1/4	2.4	710	7	1.0	900	5.9	90	82	3
3/10	1.8	532	7	1.0	700	7.6	90	84	3
1/8	1.2	355	7	1.0	700	7.6	86	79	3

1/2 mole of ortho toluidine and 37 grams of sodium nitrate in 80 c.c. of water were used in each case.

The yields given in the table were obtained by adding the diazonium solution in a thin stream (15 minutes) to the Cu_2Cl_2 solution kept at the temperature noted durng the addition. After standing several hours, the solution was steam distilled and dried, This is the crude yield. Redistillation gave a fraction boiling within 2-3 degrees of that given for the pure compound. This is given as the pure yield in the table.

Kinetics of the Sandmeyer Reaction.

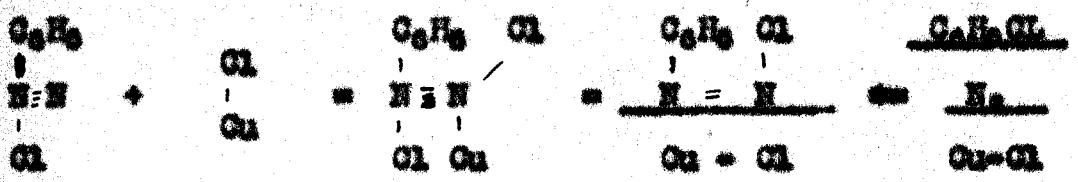
The course of the Sandmeyer reaction was studied by measuring the rate of nitrogen evolution upon addition of the diazonium salt to a cuprous chloride-hydrochloric acid solution. as Aniline, ortho and para toluidine were tried by Heller and Tichner in this way. Assuming that the diazo compound is formed instantly, and decomposes at a measureable velocity, the reaction is a unimolecular one. Plotting the volume of gas evolved against time, Heller and Tischer obtained very poor constants, showing that other factors were involved. Variations were found to be obtained nd only with a change in the amine, but by a change in concentration of any sort, particularly by slight changes in acid concentration. The following conclusions were drawn by the above workers:

I. The velocity of decomposition of the readily soluble cuprous chloride complex salt is increased catalytically by presence of free nitrous acid.

II. The velocity of decomposition of the phenyl diazonium cuprous chloride complex salt decreases with time, but the converse is true with the salts of ortho and para toluidine. The

course of decomposition thus depends upon the parent amine, and relatively small changes in the structure of this affect the course of the reaction markedly. and Blagden

Waentig and Thomas [37] point out that altho Hantzsch [38] found the formula of a cuprous bromide complex salt to be $C_6H_5N_2Br \cdot Cu_2Br_2$, in a later article [39] they ignore this formula in their suggestion as to the course of reaction for the Sandmeyer, using a single copper chloride molecule, the following reaction equation being suggested by them:



Waentig and Thomas hence made another determination of the copper content. A concentrated solution of benzene diazonium chloride at a temperature of -17° C. was added without stirring to a saturated solution of cuprous chloride in 36% hydrochloric acid at -60° C. A red voluminous precipitate formed instantly, was filtered rapidly and washed with very cold ether, (free from alcohol and water.) The residue consisted of red prismatic crystals which decomposed rapidly at room temperature or if treated with alcohol or water. The para toluene proved the most stable of several salts tried, and analyses were attempted on this salt. Exact determinations were impossible, due to the instability of even this salt, but five copper and chlorine determinations, and three nitrogen determinations warrant the assignment of the formula: $C_6H_5N_2Cl \cdot Cu_2Cl_2$ to the benzene diazonium compound. This

formula is thus in agreement with that of Hantzsch. Lieberman and Remy [40] in an analysis of the double salt of cuprous bromide and beta naphyldiazonium bromide also found two atoms of copper per molecule.

Waentig and Thomas state however that it is impossible to state absolutely that the product formed in the ordinary Sandmeyer is the same as that isolated at the low temperatures used, nor is it possible to determine the molecular weight from freezing point or conductivity methods due to the large amount of acid necessarily present in the ordinary reaction. Assuming it to be the same, and that it forms instantly and decomposes with measureable velocity, into phenyl chloride, nitrogen and cuprous chloride, the reaction will be of the first order, provided it goes to completion without side reactions and that enough cuprous salt is present originally to convert all the diazonium compound into the labile intermediate compound. Then the reaction $C_6H_5N_2Cl\text{-}Cu_2Cl_2 = C_6H_5Cl + N_2 + Cu_2Cl_2$ should follow the equation $\frac{dx}{dt} = K$.

Waentig and Thomas found the reaction not so simple. An apparatus was devised that permitted there stirring, exclusion of oxygen and collection of the nitrogen evolved in gas burettes at constant temperature.

When equal molar amounts of diazonium salt and cuprous salt were used, constants were obtained varying within but a slight range, K x .4343 for Benzene diazonium chloride being 123-140 and for para toluene diazonium chloride 83-90,

using concentrations of $1/_{112}$ M. phenyldiazonium chloride with .295 M. hydrochloric acid and $1/_{28}$ M. para toluene diazonium chloride with .314 M. hydrochloric , together with one equivalent of cuprous chloride in each case. But little side reactions were noticed.

The greater the initial concentrations of diazonium salt and cuprous chloride, the greater the value for the constant, but with an approximate proportionality between the two, constants for $1/_{14}$.$1/_{42}$.$1/_{56}$.$1/_{72}$ and $1/_{112}$ phenyldiazonium chloride with constant amounts of acid and cuprous chloride were 2068,695,288,204, and 136 respectively. Since no catalytic activity by the normal reaction products or traces of secondary products could be established, the increase in the values of the constants must be due to the relative increase in concentration of cuprous chloride rather than the simultaneous increase in concentration of the diazonium salt. this can be made clear by regarding the reaction I:

$RN_2Cl + Cu_2Cl_2 = RN_2Cl\text{-}Cu_2Cl_2$, as slow, while the reaction II:

$RN_2Cl\text{-}Cu_2Cl_2 = RCl + N_2 + Cu_2Cl_2$, as fast or instantaneous, The value of the constant then really depends upon the rate of the first reaction, but may be still regarded as of the first order, since the amount of cuprous chloride is practically a constant, being regenerated essentially as rapidly as consumed. Hence $\frac{dn}{dt} = K\,(RN_2Cl).(Cu_2Cl_2)$ is really dependent largely upon the initial concentration of

cuprous chloride since this concentration remains practically unchanged thruout the reaction, but increases in relative concentration therefore as the diazonium salt is increased. Constants for the same concentrations are hence possible to obtain, but will vary with any change in concentration even tho the ratio of equimolecular amounts of cuprous and diazonium salts be maintained. With less than an equimolecular amount of cuprous salt to diazonium salt, no concordant results could be obtained, phenols and azo compounds being formed and the reaction ceasing before the calculated amount of nitrogen is evolved, but roughly, the reaction velocity increases with increase in the cuprous salt ratio.

The reaction is further complicated by the fact that relatively small increases in the concentration of the hydrochloric acid decrease the reaction velocity tremendously, although K remains constant for any one concentration. Thus 1/10 molar phenyldiazonium chloride with 1/200, 1/225, 1/250, 1/285 and 1/324 Normal hydrochloric acid gave constants of 32.68, 133, 154 and 316 respectively, with similiar changes holding for the toluidine salt. Contrary to the statement of Heller however, Waentig and Thomas found free nitrous acid to be without catalytic effect. Temperature influences are very noticeable, a drop from 0° to -18°C. causing a change in the constant from 136 down to 39.

The work of Waentig and Thomas and others thus seems to show that due to the numerous factors influencing the course of the reaction, and the numerous assumtions required to cover deviations from any one course, the mechanism of the Sandmeyer

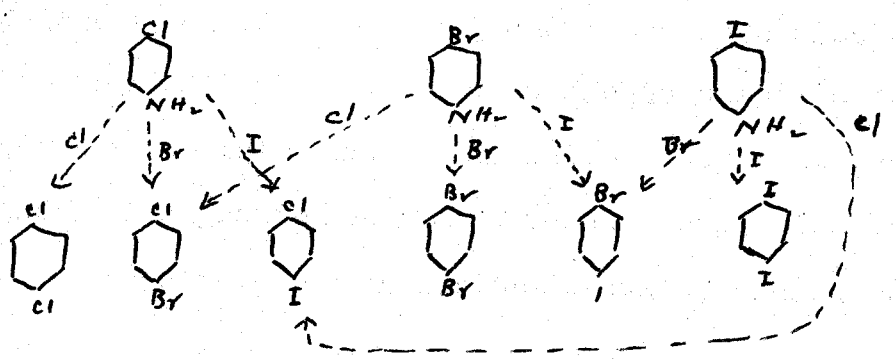
reaction is very complicated, the final result being most probably due to several concurrent reactions as pointed out by Hantzsch. Any arbitrary statement as to the course of the reaction is there fore very uncertain and should be accepted with caution unless far more convincing explanations and proofs are offered than any advanced up to the present time.

Purpose of This Investigation.

The preceding survey of the literature shows that although the Sandmeyer reaction has been very largely studied from many angles, very little attempt has been made to study the percentage yields obtained when various groups are introduced under such standardized conditions of concentration and temperature as will permit legitimate comparisons. After first developing a standardized method of procedure for introducing chlorine, bromine or iodine into practically any amine, the following investigations were undertaken:

I. Determination of the relative percentage yields of dihalogen substituted derivitives of benzene when chlorine, bromine and iodine are introduced under like conditions into a para halogen substituted amine.

II. Determination of the relative influence of a halogen atom already attached to the nucleus upon the yield of a compound resulting from the introduction of a second molecule of halogen thru use of the Sandmeyer reaction. The following graphic scheme of substitutions effected under the standardized conditions, starting with the para monohalogenated amines and obtaining the para dihalogen derivitives, indicates the plan of research undertaken:



Comparison within each set of replacements on a single amine allows the relative percentage yields for the introduction of the three halogens to be determined under identical conditions in three different cases, while the influence of nuclear halogen upon the same can be seen by cross comparisons. Thus the influence of nuclear chlorine upon the entrance of chlorine as compared to the influence of nuclear bromine and iodine can be seen by comparing the yields of para dichlor, para brom-chlor and para iodo-chlor-benzenes, the entering group in each case being named second. Similiar cross comparisons can be obtained for bromine and iodine substitutions.

III. Steric influences may be ascertained by comparison of the above yields of para substituted products with those of the ortho and meta compounds under like conditions.

IV. The effect of nitro groups present in the nucleus can be similiarly obtained by comparing the yields obtained above with those obtained under identical conditions from para, ortho and meta nitranilines.

V. By conducting the replacement in one series at 0°C. and in another series at 100°C., but otherwise identically, the influence of temperature upon the reaction can be determined. A further test as to the conclusions to be drawn in I, II, LII, and IV is thus also afforded by the duplication at the two temperatures, since comparisons are possible within each series. Consistent results in both cases can then be attributed to molecular influences with more certainty than

if only one series of runs were made, since in any single case solubility and other local influences may cause the variation.

VI. Substitution of equivalent amounts of cupric, ferric or other salts in place of the cuprous salt without further change in the procedure of the standardized method may not only throw some light upon the mechanism of the reaction, but also afford further comparisons.

Further advantage is gained in selecting the compounds above as starting materials since the products formed in all cases are volatile with steam and are therefore easily separated by steam distillation from any side products and tar formed. Any phenol carried over may be easily removed by washing with alkalies.

PART B. EXPERIMENTAL.

Preliminary Work and Development of the Standardized Procedure.

Since the primary idea of this research on the Standardization of the Sandmeyer reaction was the securing of strictly comparable, rather than highest possible yields, conditions were sought which would afford a simple method applicable without change for the introduction of the three halogens into any amine desired. For this reason the yields are in some cases naturally below those given in the literature, the standardized method desired for comparisons could hardly be as satisfactory in each particular case as a method adapted to the

behavior of a particular amine or replacement. The results obtained are therefore to be regarded rather from the viewpoint of comparability than as a method to obtain high percentage yields, the general conditions that would give good yields were adopted as far as possible.

The majority of the procedures given in the literature use the amine hydrochloride salt as starting material forthe introduction of chlorine and the hydrobromide for bromine. Little information as to the iodine replacement can be found. It is most generally done without use of the Sandmeyer, i.e., without a cuprous salt. It was decided therefore to try the use of the above, altho it was realized that diazotisation would be difficult in presence of the excess hydroiodic acid present in the case of the iodine replacement.

The amount of acid per mole of amine varies widely, but in the majority of casesthe procedures given in the literature from two to three moles of acid per mole of amine are used.

Even more wide variations are found in the amount of cuprous salt used, ranging from as little as 1/28th up to one mole of cuprous salt per mole of amine, but in very few cases is the double cuprous molecule, (Cu_2X_2), theoretically required by analyses of the intermediate compound used, probably since the relatively small solubility of cuprous salts would necessitate the use of inconveniently large volumes of cuprous solutions in comparison with those of the amine. Clarke,[44]

states that the use of larger amounts than one mole of the single molecular formula of cuprous salt per mole of amine gives no increase in yield. Hence one mole of cuprous salt,(as CuX,) per mole of amine seems a requisite amount.

To avoid any possible varying catalytic effect and concentration changes, the addition of a certain identical amount of sodium nitrite slightly in excess of the theoretical amount seems preferable in each case, tho the solution was tested in each case with starch-iodide paper.

The size of the sample to be used was set at one-eighth mole of amine, since this in no case gives theoretical yields below fifteen grams, unavoidable losses and errors being thus not overwhelmingly large and still allowing the use of easily handled volumes and a reasonable length of time for steam distillation. The following procedure was first tried.

Procedure I. Preparation of Para-Dichlor-Benzene from Para-Chloraniline using the Hydrochloride Salt.

One eighth mole of para chloraniline, (16 grams of Kahlbaum's,m.p. 70°,) reduced to a fine powder, weighed on a trip scale accurate to .05 gram,and added to a solution of 300 c.c. of hydrochloric acid (12 N.=3/8 mole) in 100 c.c. of water, heated to boiling, gave, on cooling, the white hydrochloride salt crystallizing out as a fine powder. The solution, then further cooled to zero degrees by means of an ice bath, and 50 grams of ice added directly, is

stirred rapidly and diazotized by addition of 64 c.c. of a 15% sodium nitrite solution, (15 grams $NaNO_2$ per 100c.c.) introduced in a thin stream thru a dropping funnel extending to the bottom of the solution. The temperature remains under 5°C. and the yellow diazonium salt appears as a flocculent precipitate.

The cuprous solution is prepared by addition of 12.5 grams ($1/_8$ mole) of cuprous chloride to a solution of 75c.c. of 12N. hydrochloric acid and 50c.c. of water. The cuprous solution contained in a two liter beaker is cooled to 0°C. by an ice bath and 50 grams of ice then directly added. The cold diazonium solution prepared as discribed is immediately added during rapid stirring thru a wide funnel tube reaching to the bottom of the solution, the rate of addition being regulated by the amount of frothing. Immediate reaction takes place , nitrogen and nitric oxides are evolved and a light yellow intermediate compound is formed, the reaction being accompanied by considerable foaming which will entirely fill the beaker if the addition is made too rapidly. After all the diazonium salt has been added, the solution is stirred one-half hour and let stand at room temperature. The fluffy, light yellow-brown intermediate product soon rises to the top, nitrogen being evolved very slowly. The beaker is covered and let stand over night, whereby the upper layer shrinks considerably. The entire volume of solution is then steam distilled from a two liter flask. On warming, the light brown product shrinks tremendously with but little

nitrogen evolution and then melts to an oil. The product comes over rapidly in long, pure white needles which solidify in the condenser if kept too cold. The distillation is continued until no more solid comes over, (2-3 hours.) The para dichlorbenzene is filtered off, washed with 3% sodium hydroxide and water after being powdered finely to prevent inclosure of phenol or water, dried on filter paper and let stand in a dessicator overnight. Theoretical yield is 18.4 grams; actual yield, 12.0 grams or 65%. m.p. 51°C.

Para dichlorbenzene, as well as the other dihalogen benzenes prepared, is extremely volatile even at low temperatures, and hence should be kept well closed in a dark place while drying, the compound subliming rapidly in long needles in ordinary sunlight.

After the above steam distillation, about two grams of a black, sticky tar remained in the flask. The dichlorbenzene obtained was redistiled using a direct flame. Very little tar or residue remained in the flask, the product distilling within a narrow range of 172.0°C. to give a yield of 11.0 grams. The product on crystallisation from alcohol-ether (1-2) gave huge platelike crystals of dichlorbenzene with a melting point of 53°C.

Second and third runs using the same procedure, but with more precautions to prevent loss by volatilisation gave yields of 13.1 and 13.9 grams respectively, of the steam distilled, caustic washed product. (13.9g.=75.8%theor.) In both runs about 2-3 grams of tar remained in the flask.

Preparation of Para chlor-brom-benzene from P-chloraniline.

The procedure is repeated as before except 16 grams of p-chloraniline (1/8 mole) is heated with 3/8 mole of hydrobromic acid,(44c.c. of Kahlbaums s.g.1.49=48.5% HBr calc.) and 86c.c. of water, cooled, ice added, and the solution diazotized as before, a very similiar yellow diazonium salt separating. This is then added as previously to a cold solution containing 1/8 mole cuprous bromide , (18 grams,) in 57c.c. of hydrobromic acid(1/2 mole) and water to make 125c.c.

The intermediate compound formed is of a beautiful crimson color, changing to a light chocolate-brown on standing over night. Foaming during the addition is not as troublesome as in case of the chloride replacement.

On steam distillation, the para chlor-brom-benzene comes over at first a pale green, then white and the last traces a light yellow. About 3-4 hours are required for the distillation. The product is filtered, powdered, washed with 3% sodium hydroxide and water and then dried over-night as before. Yield of the pale green product is 20.2 grams,(theoretical is 23.9 grams)or an actual yield of 85%. m.p. 66.0°C. The product on direct distillation gave a yield of 18.4 grams, and on recrystallization as before gave huge light green flat plates or monoclinic needles. m.p.67.0° b.p. 195.0°C.

Preparation of Iodo-chlor-benzene from P-chloraniline.

The hydroiodide salt of para chloraniline proved so highly insoluble, and the addition of sodium nitrite to the solution liberated so much free iodine, that diazotization was practically impossible. Since no test for complete diazotization is possible in presence of the free iodine, diazotization was attempted by the addition of a large excess of sodium nitrite over the amount theoretically required.

Variation was also necessary in the preparation of the cuprous iodide solution, 250c.c. of hydriodid acid of S.G.1.5 (1.5 mole) being required to dissolve 1/6 mole (23grams) of cuprous iodide. On addition of the diazonium solution, nitrogen is evolved, the solution becomes pasty, and a mixture of intermediate product and free iodine separates, mixed with considerable cuprous iodide. After standing over night the solution was steam distilled, a large amount of free iodine removed by sodium hydroxide solution and the light brown product powdered, dried and weighed. Theoretical yield = 39.8 grams, actual =10.6 grams or 38% theoretical.

Since the insolubility of the salt and of the diazonium compound produced from it made diazotization difficult in all cases, and practically impossible in case of the hydroiodide, procedure I starting with th halide acid salt was therefore abandoned. Formation of the acid sulfate salt was tried as the next method of procedure.

Procedure II.

Para Chlor-iodo-benzene from Para Chloraniline Sulfate.

Sixteen grams of finely powdered para chloraniline were heated with 100c.c. of water containing 3/8 mole of sulfuric acid, cooled to 0°C., 50 grams of ice added directly and diazotized with 64c.c. of cold 15% sodium nitrite solution, the temperature remaining below 5°C. After complete addition of the nitrite and stirring for ten minutes, the solution is added thru a wide funnel tube to 250c.c. of solution containing 1/8 mole of cuprous iodide (23g.) and 1 1/2 moles of hydriodic acid, together with 50 grams of ice. Free iodine is liberated by the slight amount of free nitrous acid present, and a light brown intermediate product seperates but without a great amount of frothing. After standing over night, on steam distillation the chloriodo-benzene came over mixed with much free iodine, which was removed by a warm 3% sodium hydroxide solution. The final product remained a light brownish violet. Yield 23.1 gram or 77.5% theoretical. On redistillation and crystallization from alcohol-ether, the para chlor-iodo-benzene melted at 55°C. B.P. 222°.

Para Dichlorbenzene.

Procedure II. above was repeated twice but the diazonium salt being added to 250c.c. of a cuprous solution containing 1/8 mole cuprous chloride and 1 1/2 mole hydrochloric acid. Considerable frothing took place, and a light yellow-brown intermediate product formed resembling that of the first procedure. On steam distillation the dichlor-benzene came over a deep green. The yields are given in table I., page 56.

The dihalogen benzene after steam distillation and washing with sodium hydroxide is essentially pur for purposes of comparison, especially since the yields are only weighed to an accuracy of 0.1 gram. The loss on redistillation is largely due to mechanical loss and hence is practically a fixed weight in each case if the distillation is conducted in the same manner. For this reason the yields after steam distillation, washing with alkali and thoro drying are more comparable than the pure yields, the unavoidable losses in purification being much larger in % for the lighter chlorine substitution products than for those of bromine or iodine.

Para Brom-chlor-benzene from Para Bromaniline Sulfate.

1/8 mole of para bromaniline(m.p.66.0°) was treated as above and added to a cuprous chloride solution. A yellow-brown intermediate product separated, and on steam distillation gave para brom-chlor benzene of a deep green color. The yield was 17.0 grams or 71% of the theoretical yield of 23.9g. (see also table I.)

The acid sulfate salt of para iodoaniline proved so insoluble that complete conversion was diffucult, and as the diazonium salt is also insoluble the acid sulfate procedure was discarded.

Since acetates in general are very soluble and acetic acid itself in higher concentrations a good organic solvent, formation of the aniline acetate salt was next tried, 50% acetic acid being used as the solvent. As para iodo-aniline apparently is the most insolble of the three anilines, the amount necessary to dissolve 1/8 mole of this in the cold

was determined, 350c.c. of 50% acetic acid giving a clear solution even when cooled to 0°. The following procedure was therefore finally found a satisfactory one as a general method.

Procedure III. Standardised Method. (Cold)

1/8th mole of the amine is dissolved in 200c.c. of 50% acetic acid without warming if possible. The solution is cooled to 0° by an ice bath, 50 grams of ice added directly, the solution stirred rapidly and 70c.c. of 15% sodium nitrite solution added thru a thistle tube in a thin stream, the temperature remaining under 5°. With the halogen amines, a yellow curdy diazonium salt separates out on complete addition of the nitrite solution, a colloidal solution at first forming but coagulating on further addition of nitrite.

After stirring for ten minutes, (or in case of the nitranilines for 1/2 hour) the diazonium solution is added slowly thru a wide funnel tube reaching to the bottom of the cuprous solution contained in a two liter beaker, about 15-25 minutes being usually required, the time depending on the amount of foaming. The cuprous solution, which contains 1/2 mole of cuprous salt (as CuX) and 1 1/2 moles of the corresponding halogen acid in 250c.c. of solution, is cooled to 0° by means of an ice bath, 50 grams of ice added directly and then the diazonium solution is immediately added. The temperature

remains under 5°C. and rapid mechanical stirring is maintained throuout the addition. After complete addition of the diazonium solution, stirring is continued for one-half hour, the beaker then removed from the ice bath and let stand well covered overnight. The entire solution is then transfered to a two liter round bottom flask and steam distilled until no more solid or oil comes over, a small flame being kept under the flask to assist in agitation and to prevent steam condensation. Varying with the product, from two to twelve hours are required for distillation. The product, if solid, is filtered off, shaken with 3% sodium hydroxide solution, dried on filter paper after being finely powdered and let stand in a dessicator overnight. The use of porous plates which causes ready absorbtion of the volatile product is thus avoided. The weight of the product thus obtained is used for comparisons, doubtful cases being dried for a longer time to see if there is a further appreciable loss of weight. The dihalogen products will lose noticeable amounts by volatilization however even if let stand for several days in a medium sized dessicator. Vacuum dessicators cannot be used therefore with the dihalogen benzenes.

Partial neutralization by addition of 250 c.c. of 20% sodium hydroxide solution before allowing to stand overnight was not successful. Much frothing is encountered on steam distillation and considerably more tar and phenol is formed. The yield of para iod-chlor benzene was reduced by such treatment to 57% as compared to 68% without the caustic addition.

The following amounts of the aniline and of the cuprous salt were used:

1/8 mole p-chloraniline= 16 grams. 1/8 mole CuCl= 12.5g.
" p-bromaniline = 21.6 " " CuBr= 18 g.
" p-iodoaniline = 27.4 " " CuI = 23.8g.

Considerably less frothing is observed in the method using acetic acid than those using the stronger mineral acids, probably since the intermediate compound is formed or decomposed more slowly. The intermediate compound in case of the bromine replacement is not entirely decomposed on standing overnight, while the iodine compound is even less so, considerable nitrogen being evolved when the solution is heated preparatory to steam distillation. The compounds produced in each case show more or less green color except in case of the iodine replacements where no trace of green is noticed, probably since any excess nitrous acid is instantly destroyed on addition to the cuprous iodide-hydriodic acid solution and thus the formation is prevented of the trace of nitroso or other compound to which the green color is due. Absolutely white iodine products may be obtained by redistilling the crude product, dissolving this in ether and shaking with dilute aqueous sodium hydroxide until the color is removed, adding to the ether layer separated after washing free from alkalie one half the volume of alcohol and allowing the alcohol-ether mixture to very slowly evaporate in the dark. Huge pure white monoclinic plates or needles of the dihalogen product are formed which darken very slowly upon exposure to light.

Each replacement was repeated until two yields were ob-

tained agreeing within 3%, great care being taken that the product is dry when weighed.

The intermediate products in case of the chlorine replacements are more or less yellow-brown in color, fading to a lighter shade overnight. The bromine intermediates are at first more or less a dark crimson color, quickly fading to chocolate which overnight becomes a light brown. The color is partly masked by the intense permanganate color of the solution, which is due to small amounts of cupric bromide formed by oxidation. This color is so intense that even freshly precipitated cuprous bromide gives a test on dissolving in hydrobromic acid, Mellor [42] states that .0015 milligram of copper can be detected in a drop of solution, provided the hydrobromic acid used is concentrated, the color being due to the formation of a hydrogen-cupric bromide complex acid.

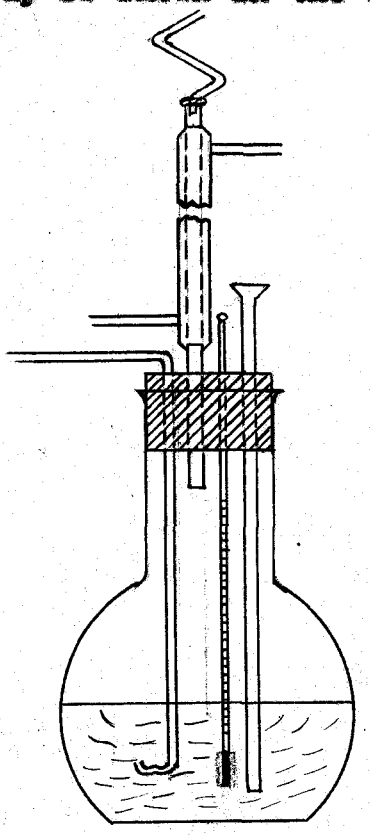
The iodine intermediates were not only more slowly decomposed than the chlorine or bromine products, but were also much heavier, a large portion settling to the bottom of the solution on standing overnight in contrast to the chlorine and bromine intermediates which form a floating layer.

As noted in the plan of the investigation, (page 39) it seems desirable to compare the yields obtained under identical conditions, but obtained by conducting the reaction at 100° to those at 0°C., a further set of internal comparisons being thus afforded as a check on the conclusions to be drawn from the results obtained with the cold procedure, as well as establishing the influence of temper-

ature. The complete series of nine replacements noted in the chart, (page 38) was then duplicated except that the diazonium solution was added to a boiling cuprous solution.

IV. Standardised Method Using Hot Cuprous Solutions.

A two liter round bottom short neck flask is fitted with a four holed rubber stopper carrying the following: 1.) a one meter reflux condenser with an additional zigzag bent tube at the upper end; 2.) a wide bore funnel tube reaching to the bottom of the flask thru which the diazonium solution is added; 3.) a thermometer with bulb immersed in the cuprous solution; 4.) a steam inlet tube curved at the bottom so that the incoming steam not only assists in keeping the temperature at 100° during the addition of the ice cold diazonium salt, but also serves as a method of agitation. The complete setup is shown in the drawing below.



The diazo solution prepared as in procedure III is slowly added thru the wide funnel tube, (which allows any solid to be pushed thru if clogged,) to the boiling cuprous solution prepared as in the same procedure. The cuprous solution is kept above 100° during the reaction both by a brisk current of steam and a direct flame beneath the flask. The boiling point of the cuprous solution is above 105° in each case due to the high acid concentration, falling off as diluted with the diazonium solution. A very brisk evolution of nitrogen takes place and a large amount of the volatile dihalogen product is carried over by the nitrogen stream far up the condenser, neccessitating the use of the long one meter condenser and the bent tube at the top. A small beaker placed over the end of the tube allows the detection of any trace of product escaping by condensation on the inside.

The diazo solution is added as rapidly as possible without the temperature falling below 100°, the last traces being washed thru with cold water. About 10-15 minutes are required for the complete addition. Boiling is continued for ten minutes after complete addition with the reflux condenser drained of water, the solid previously condensed being thereby melted and drained back into the flask, care being taken that no vapor escapes. The last remaining traces of solid are washed down the condenser by hot water. After cooling, the stopper is removed, any solid adhering to the stopper and tubes washed off and the flask fitted with a stopper carrying a steam inlet and outlet as used in pre-

vious steam distillation and immediately steam distilled. Transference of the solution, very diffucult to do without loss due to the tarry matter present, is thus avoided. After steam distillation the product is treated as previously noted. Results are given in Table I.

The green color previously noticed was entirely absent in the compounds produced by this hot method, probably since the nitrous acid excess is instantly volatilized on striking the hot solution and thus prevented from reacting. The tar and phenol formation in case of the para compounds is not noticeably greater than in the cold runs, the product being equal in purity to that from the cold runs and entirely lacking in the green color. Some decomposition was noticed in the compounds produced from para iodoaniline, free iodine being produced, but not enough to make the runs fall noticeably lower than those given by the cold method except in the case of para iodo-brom-benzene from iodoaniline, the yield being 10% lower than that of the cold method.

A voluminous but very light product appeared floating in the watery layer during the last of the steam distillation of the para chlor-brom and para dibrombenzene runs. This was separated by decantation, filtered and dried. Less than 0.1 gram could be collected. The product in both cases contained halogen, was readily soluble in benzene, alcohol and ether, the melting point in both cases was over 200° but was not sharp. The material was probably a diphenyl derivitive but was not further investigated due to the small amount present.

Table One.

Percentage Yields of Para Dihalogen Benzene form the Mono Halogen Amine.

Group Introduced.	Compound obtained	Yield using acid sulfate salt.	Yield using corresponding halogen salt as starting material.	"STANDARDIZED METHOD" using acetate salts. Cold Method Cuprous soln below 0°	Hot Method Cuprous soln. above 100°
Cl	Cl–C$_6$H$_4$–Cl	76.1 75.5 76%	75.8%	75.0 76.0 76%	68.4 66.9 68%
Cl	Br–C$_6$H$_4$–Cl	71.1%		73.9 75.0 74%	67.8 68.6 68%
Cl	I–C$_6$H$_4$–Cl			67.8 66.6 67%	68.4 66.4 67%
Br	Br–C$_6$H$_4$–Cl		84.7%	82.5 84.5 84%	81.6 82.4 82%
Br	Br–C$_6$H$_4$–Br			80.7 79?0 80% 81.3	78.0 76.6 77%
Br	I–C$_6$H$_4$–BR			80.5 81.4 81% 82.2	72.0 73.7 73%
I	Cl–C$_6$H$_4$–I	77.5%	(35.6%)	69.5 71.5 71%	79.9 81.8 81%
I	Br–C$_6$H$_4$–I			71.5 73.4 72%	78.8 77.1 78%
I	I–C$_6$H$_4$–I			78.7 77.5 78%	78.9 77.3 78%

The melting points of the para dihalogen compounds given in the above table were found as follows.

Dichlorbenzene	54.0°
Dibrombenzene	88.0
Diiodobenzene	128.0
Chlorbrombenzene	65.0
Chloriodobenzene	55.0
Bromiodobenzene	91.5

As noted in the plan of research, an investigation seems desirable as to the influence of the position of the halogen atom already present in the nucleus when a second halogen is introduced by the Sandmeyer reaction into a mono halogen amine. The yields given when bromine and chlorine are introduced into ortho and meta chloranilines by the standardized method were next obtained therefore.

Ortho Dihalogen Compounds.

Chlorine and bromine were introduced into ortho chloraniline, (B.P.206) by procedure III using a cold cuprous solution. Immediate solution of the liquid aniline is obtained upon addition to 50% acetic acid and a yellow diazonium salt much like that of the para compound is obtained on diazotization. Nitorgen is evolved rapidly on addition of this to the cuprous solution but with very little frothing. A reddish brown and very pasty intermediate product is formed. On standing over night a heavy oily mass collects on the bottom of the solution. The product is steam distilled until no more oily drops collect in the receiver. From two to four hours are required. Very much black, viscous tar remains in the flask,(5-8 grams.)

As both ortho dichlor and chlor-brom benzenes are liquids, the previous method of purification could not be used. The entire distillate is therefore made slightly alkaline, shaken until all phenolic odor disappears and only the characteristic dihalogen benzene ordor remains. The heavy oily layer is drawn off as far as possible by means of a seperatory funnel, but considerable oil remains as fine droplets dispersed thruout the water layer. This is twice extracted with ether and the extractions added to the oil, anhydrous sodium sulfate being added to remove water, together with a small amount of potassium carbonate. After standing several hours the ethereal solution is filtered off, the residue well washed with dry ether and the washings added to the filtrate. After the ether is partially removed by distillation on an electric hot plate, the high boiling oily product is fractionated with a free flame, the ortho dichlorbenzene being collected between 173-176 and the chlor-brom benzene between 201-204. The product in both cases has a light yellow green color after this treatment. The yields are given in table II.

Meta Dihalogen Compounds.

Meta dichlor and chlorbrom benzenes are prepared as above from meta chloraniline, (B.P.228.) The oily products are separated and purified as with the ortho compounds, the meta dichlorbenzene being collected between 171-172 and the chlor-brom between 193-196. Both compounds remained a deep emerald green. The yields are given in Table II.

In order to determine the respective losses by the two methods of purification, blanks were run starting with 18.4 grams of purified dichlorbenzene, (1/8 mole) and going thru the process of steam distillation from the cuprous chloride solution as previously described. An average yield of 18.0 grams or 97% was obtained in case of the solid para compound. But with a like amount of liquid ortho dichlorbenzene put thru the method of separation and purification described above, only 17.2 grams or 93% were recovered. A corrective factor must be added then to the liquid yields to be strictly comparable, but since the loss is a mechanical one and does not vary to any extent with the yield, the correction should be made by a weight rather than a percentage addition, since the percentage loss is relatively less in case of the heavier bromine introduction. The addition of one gram to the weight of the ortho and meta product appears from the results obtained in the blank runs to cover the loss due to variations in separation and purification. In the table following, the "comparable" percentages given have been so obtained.

Table Two.

Group introduced.	Product	Ortho %true yield	Ortho %comparable yield	Meta %true yield	Meta %comparable.	Para. %yield (cold)
Cl	Cl — Cl	44.0 43% 41.8	49.5 48% 47.2	42.4 43% 44.5 43.0	47.8 49% 50.0 48.3	75.0 76% 76.0
Br	Cl — Br	49.3 50% 50.6	53.6 54% 55.0	34.6 35% 36.0	38.5 39% 40.2	82.5 84% 84.5

Nitrohalogen Compounds.

Procedure III was then used to introduce chlorine and bromine into ortho, meta and para nitranilines. Altho the acetate salts of the three amines are rather insoluble, complete solution of 1/8th mole samples takes place on warming with 250c.c. of 50% acetic and hence complete conversion is assured. On cooling to 0° however the salt precipitates out in fine needles. After adding 50 grams of ice, the nitrite soltion must be added very slowly,(one-half hour) and is followed by stirring for another half hour, which effects complete solution of the diazonium compound formed in each case. The formation of the intermediate compound on addition to the cuprous solution is accompanied by a considerable nitrogen evolution in each case, but with very little trouble as to foaming. The diazonium salts in all three cases are of a light orange color, while the cuprous chloride intermediates of the ortho and para compounds are a yellow brown, the meta compound being a deep purple brown. The corresponding brom intermediates are ortho, light yellow; para, greenish-yellow; and meta,reddish yellow.

The ortho nitrochlor benzene on steam distillationcomes over as a yellow oil, solidifying on cooling,(m.p.32°). The watery layer was colored also a deep yellow and continued to come over yellow after oil ceased to separate at the end of the steam distillation. The entire watery layer was extracted twice with ether, whereby the yellow color was entirely

extracted from the water by this treatment. Upon evaporation of the ether however, less than 0.2 gram of a reddish orange pasty material remained which apparently contained only a small amount, if any, of ortho nitro-chlor benzene. The corresponding ortho brom-nitro benzene is also yellow, the meta chlor and brom nitrobenzenes a very light yellow color, while the para compounds are pure white, all are practically insoluble in water. Beautiful needles or rhombic plates are given by all six of the compounds on crystallization from alcohol-ether (1-4.) The shape of the crystals is apparently determined by the first seed cystal separating.

Six to eight hours are required for steam distillation of para nitro-brom benzene, (m.p.128,) and considerable difficulty is encountered in preventing the condenser from clogging, the distillation having to be frequently interrupted and the solid pushed out of the condenser with a rod.

The products were purified in a similiar way as the para dihalogen compounds, by washing with dilute alkalie, water and thoroly powdering before drying. The melting and boiling points of the compounds as prepared agree with those found in the literature, and are as follows:

Ortho	nitro-	chlor	benzene	m.p.	32.5°	b.p.	242°
"	"	brom	"	"	41.0	"	261
Para	"	chlor	"	"	83.0	"	241
"	"	brom	"	"	128.0	"	255
Meta	"	chlor	"	"	44.0	"	234
"	"	brom	"	"	56.0	"	256

Table Three

Relative Yields when Halogen is introduced into corresponding Nitro and Chlor Anilines.

Group introduced.	Compound obtained	Para		Ortho (corrected)		Meta (corrected)	
Cl	Cl – NO_2	72.6 71.1	72%	74.1 71.0	73%	57.3 59.9	58%
Cl	Cl – Cl	75.0 76.0	76%	49.5 47.2	48%	47.8 50.0 48.3	49%
Br	Br – NO_2	90.9 90.0	90%	78.2 80.9	79%	73.8 76.6	74%
Br	Br – Cl	82.5 84.5	84%	53.6 55.0	54%	38.5 40.2	39%

Cupric Salt Modification.

In view of the conflicting statements in the literature as to the results obtained when cupric salts are substituted for cuprous, and as outlined in the plan of the research, this modification of the standardized procedure was next tried.

An equivalent amount of cupric chloride, (1/8 mole $CuCl_2 \cdot 2H_2O$ = 21.3 grams,) and of cupric bromide, (28 grams $CuBr_2$,) were substituted for the corresponding cuprous salts and procedure III repeated with para chlor and para brom anilines.

On addition of the yellow diazonium salt of para chloraniline to the cold cupric chloride solution, no apparent reaction takes place immediately. On standing for two hours

after removal from the ice bath, complete solution takes place and a clear green solution is obtained. The solution is immediately steam distilled, altho little variation in yield is noted if left stand over night, a small amount of tarry material merely depositing on standing. On warming, nitrogen is evolved rapidly, an oil gradually separates and the para dichlorbenzene comes over in the form of long white needles, is purified as before, powdered, dried and weighed. Considerable tar remains in the flask after steam distillation. The yields of the several products are given in Table IV.

A trial was made neutralising the clear solution before steam distillation, sodium hydroxide solution being added thru a reflux condenser to avoid loss by vaporization, nitrogen being rapidly given off and the solution becoming warm. The yields obtained varied from 7[illegible]% down, but no concordant results were easily obtained, variations of as much as 10% being obtained in successive runs. The yields, besides being inconsistent, were not strictly comparable with those in which no caustic had been added, and hence the modification was abandoned and procedure III strictly followed except for the substitution of cupric salt for cuprous.

On addition of para chlor diazonium acetate solution to the cupric bromide solution, nitrogen is slowly evolved and the yellow salt changes to a flocculent white mass on standing for two hours with frequent stirring. After letting stand for several more hours, or better over night at room

temperature, the solution is steam distilled. Little nitrogen is given off on warming in contrast to the replacement above, in which chlorine was substituted.

On purification, the product crystallizes in both cases in huge pure white needles or plates, beautifully faceted internally and often over five centimeters long.

Diazotized bromaniline on addition to cupric chloride solution reacts very slowly, but after three hours changes from the deep yellow diazonium salt to a light cream colored flocculent product. On steam distillation nitrogen is evolved rapidly as the solution is heated. The product comes over with a deep yellow color. The yellow impurity, probably an azo compound, is removed on washing with alkali, the yellow color changing to a deep red and easily dissolving in the alkaline solution. Colorless para bromchlorbenzene remains.

The red alkaline solution on evaporation to dryness and acidification with hydrochloric acid, again regains the yellow color and possesses a distinctly phenolic odor. As the amount did not exceed a few milligrams it was not further investigated.

A practically clear solution is obtained on stirring for two hours a mixture of para brom diazonium acetate and cupric bromid solutions. Nitrogen is evolved on heating as before and the para dibrombenzene steam distills as pure white needles. About four hours are required for steam distillation. Theyields are given in Table IV.

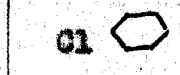
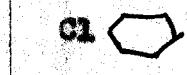
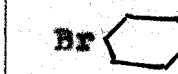
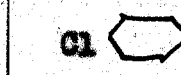
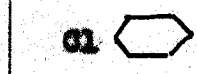
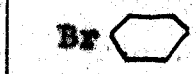
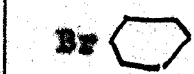
Iodine could not be introduced using cupric salts, owing to the instability or non-existence of cupric iodide.

When the procedure using hot cupric solutions was tried, considereble amounts of azo compounds were formed, the product on steam distillation coming over a deep yellow, the color being removed by washing with alkalie, turning as before a deep red on addition of the alkalie. Considereble tar is also formed and the yields fell around 10% or more in case of both the chlorine and bromine introductions.

The possibility was considered that the active agent in the cupric salt replacement might be a slight amount of cuprous salt formed by reduction by the excess nitrous acid present. An extremely dilute solution of cupric bromide in concentrated hydrobromic acid was treated with a considerable amount of solid sodium nitrite, nitrous acid was evolved but the deep purple characteristic of cupric bromide-hydrobromic acid solutions was not discharged to any visible amount. V.Thomas [43] found that cupric bromide and chloride are reduced by nitrogen dioxide and tetroxide to the cuprous form but this was by heating in a current of the gas to several hundred degrees. Under the conditions of the procedure here used however, the amount of reduction must be very little if any, particularly since acid solutions of cuprous salts usually oxidize very rapidly to the cupric form. When hot cupric solutions were used, whereby the nitrous acid is practically instantly removed before reaction can take place, a yield of 80% was nevertheless obtained in the bromine replacement.

Table Four.

Comparison of Percentage Yield Using Cupric and Cuprous Salts.

Group introduced	Para compound obtained	Copper salt used	Cold Method		Hot Method	
Cl		$CuCl_2$	57.1 58.1	58%		47%
Cl		CuCl	75.0 76.0	76%	68.4 66.9	68%
Cl		$CuCl_2$	42.3 41.0	42%		
Cl		CuCl	73.9 75.0	74%	67.8 68.6	68%
Br		$CuBr_2$	86.6 89.1	88%		80%
Br		CuBr	82.5 84.5	84%	81.6 82.4	82%
Br		$CuBr_2$	87.1 87.8	87%		
Br		CuBr	80.7 79.0 81.3	80%	78.0 76.6	77%

Results Obtained Without Use of a Catalyst.

Sixteen grams of para chloraniline were treated by procedure III, but omitting the addition of cuprous salt in order to determine the yield of halogen compound without a metallic salt present. On standing over night the diazonium compound gave a clear solution. Some little tarry matter was deposited. The solution was of a light yellow color. On heating, nitrogen was evolved, the solution turned a deep orange color and a greenish yellow distillate came over containing much chlorphenol mixed with some dichlorbenzene. The greenish color changed to a deep orange on treatment with alkali, the chlorphenol dissolved, leaving the para dichlorbenzene as a yellowish solid. On drying, the yield obtained was about two grams, or about 10-15% of theoretical.

Results Obtained With Various Salts as Catalysts.

On substitution of either nickel, manganese, ferric or cobalt chloride, ($NiCl_2$, $MnCl_2$, $FeCl_3$, $CoCl_2$,) for the cuprous salt in procedure III, no apparent action takes place on addition of the diazonium acetate solution to the metal chloride-hydrochloric acid solution, a clear solution being obtained on standing over night as when no catalyst was used. On steam distillation, much phenol and azo compounds again come over. On removal of these by the previous method, yields varying from 9-16% were obtained of the para dichlorbenzene, the same practically as those when no catalyst was used.

Substitution of ferrous chloride, ($FeCl_2$,) gave better results, the diazonium solution on addition to the ferrous

chloride-hydrochloric acid solution becomes a muddy brown, nitrogen is evolved slowly and on standing over night a clear orange colored solution is obtained which on steam distillation gives the familiar emerald green para dichlorbenzene, followed by considerable chlorphenol. On purification, the product remained a light emerald green, a yield of 8.1 grams or 43% of the theoretical being obtained.

In order to determine whether the salts noted above had any influence whatever when added to the diazonium compound, the clear solution obtained with a mixture of ferric chloride and diazonium solution on standing over night was then treated with 1/8 mole of cuprous chloride dissolved in a small amount of concentrated hydrochloric acid. On addition, nitrogen was rapidly given off, the familiar intermediate compound of cuprous chloride-diazonium compound separated, was let stand for two hours and then steam distilled. A yield of approximately 70% of para dichlorbenzene was obtained, showing that the ferric chloride present had but little or no effect on the diazonium salt even on standing over night.

When 15 grams of Gattermann's copper powder was added to a similiar solution of ferric chloride-diazonium salt and let stand stand over another night, a yield of 78% of para dichlorbenzene was obtained, approximately that obtained if a like amount of copper powder is added to a fresh solution, a further proof that the ferric chloride is without influence on the diazonium solution.

Application of the Standardized Method to Other Amines.

The standardized method of procedure III was applied in the cold to the production of ortho brom-benzoic acid from ortho amino-benzoic acid, using 1/8th molar amounts. It was found that if the non-voaltile acig product was filtered off after standing for one hour only after addition of the diazonium solution, rather than allowing to stand for four hours or overnight as recommended in the literature, the amountof tar present in the product is very greatly reduced, the tar formation being due to a slower reaction. Altho the crude yield is about 3% lower than if let stand longer before filtering off, much more than this differende is made up by the better yield on purification. The usual treatment with animal charcoal was unnecessary. The slowness of the tar formation was noted thrucut all the runs, the largest amount being formed during heating preliminary to and during the steam distillation. The tar does not interfere however in case the product is volatile with steam. Trial runs were early made filtering off the dichlorbenzene without steam distillation, but even if filtered off without allowing to stand long, the product contains considerable tar which is almost impossible to remove without direct distillation. The steam distillation is therefore disirable with volatile products except inthe case of the cyanid introduction, where the long boiling in the acid solution causes considerable of the nitrile to be

hydrolyzed to the corresponding acid, which in most cases is non-volatile. Direct filtration is hence recommended in case of a nitrle, as only a 40% yield of para chlor-benzoic nitrile could be obtained when the product was separated by steam distillation, much of the non-volatile acid remaining mixed with the tar after steam distillation.

Conclusions.

I. After several procedures were tried with a view of obtaining the best conditions for a uniform method, the use of 50% acetic acid for formation of the amine salt was found preferable to the use of mineral acids. Complete diazotisation was easily secured in most cases by this method, since not only are most acetate salts soluble, but the concentrated acetic acid itself has a considerable organic solvent power. The standardized method as recommended may be applied without concentration or condition changes to the introduction of chlorine, bromine or iodine into the amine desired.

II. The percentage yields do not differ widely using the standardized method from those using mineral acids, a 77% average yield being obtained by the standardized method against 80% for the procedure using halogen acids and 75% for that of the acid sulfate, (Table I, page 56.)

III. Chlorine, bromine or iodine introduced into the three para halogen amines by the standardized method give practically identical average yields when the diazonium salt is added to a cold cuprous solution below 5°C. or

when added to a cuprous solution at 100°C.. The average yield for nine replacements at 5° is 76% as compared with 74% if the addition is made at 100°. The various conflicting statements in the literature as to the relative merits of the hot and cold methods are thus understood in part at least, the balance of favorable yield probably varying more widely with other amines. The lower yields noticed in case of the chlorine replacements in the hot as compared to the cold, (Table I,) can probably be explained by Erdmann's decomposition "temperature" effect, the rapid decomposition of the highly unstable chlorine-copper complexes giving rise to side reactions, largely those of tar formation. The character of the tar formed during the various replacements differs widely. The plasticity varies from a hard, brittle form to a soft pasty oil which does not harden noticeably on standing for weeks. The cold method seems preferable for purposes of comparison, not onlybecause of the slightly higher yields, but because the entire range of "decomposition temperatures" is covered, since the addition is made at 0°C., the solution allowed to slowly reach room temperature and then heated to boiling when steam distilled. The actual molecular influence of the amine itself is probably thus more a factor in the cold than in the hot method, since in the latter the compound is necessarily formed and decomposed at the same high temperature.

Examination of Table I, page 56, shows that when chlorine, bromine and iodine are introduced into the same

para halogen amine in the cold, in all three sets of replacements the percentage yields are in the order Br > I > Cl. The variations between the two extremes are slight however, the largest being 14% in the case of para iodoaniline. The same replacements at 100° gives the ratio Br ≧ I > Cl, the two extremes being again 14%. The average yields in the two cases as shown by the table, (page 56,) are:

Bromine introduced 82% ±2 cold, 77% ±5 hot.
Iodine " 74% ±4 " , 79% ±2 " .
Chlorine " 71% ±5 " , 68% ±1 " .

IV. Variation of the halogen present in the nucleus apparently has but slight influence upon the yield of the group introduced in the case of the three para monohalogen amines. The slight deviations noted apparently follow no consistent order and are of too slight an amount to warrant any conclusions. The average yield for the three replacements is very uniform in all three sets, as shown by the following Table V, which embodies data from Table I.

Table Five.

Amine.	Average of Cl, Br, and I yields. Cold.		Hot.	
Para Chloranilin	Cl-Cl 76 Br-Cl 84 I-Cl 71	77%	68 82 81	77%
Para Bromaniline	Br-Cl 74 Br-Br 80 Br-I 72	75%	68 77 78	74%
Para Iodoaniline	I-Cl 67 I-Br 81 I-I 78	75%	67 73 78	73%

V. Ortho chloraniline and meta chloraniline show remarkably lower yields than the para chloraniline even when the yields are corrected for possible loss in purification. The ortho compound gives a percentage yield of brom-chlor benzene remarkably close to the ratio of Br > Cl in the para replacements, the proportion 76 (pCl-Cl) : 84 (pClBr) :: 48 (oCl-Cl) : oCl-Br requiring a yield of 55% of ortho chlor-brombenzene against 54% observed. The meta compound, altho giving a yield of meta dichlorbenzene practically the same as the ortho, gives a chlor-brombenzene yield much lower than the dichlor, 39% Cl-Br against 49% for Cl-Cl. The lower yields in case of the ortho and meta compounds cannot hence be entirely attributed to their liquid character, or to temperature factors, since in both cases the heavier bromine replacement would surely give the greater yield, while the contrary is noted in case of the meta chlor-brom-benzene, altho holding in case of the ortho compound which usually reacts more nearly like the para compounds.

VI. The use of an amine containing a positive nitro group in place of the negative halogen group, (Table III, page 62,) gives but little change in percentage yield in the para replacements, since a 72% nitro-chlorbenzene yield is obtained and a 90% nitro-brombenzene yield, the latter being slightly higher than that of the di-halogen corresponding. The ortho and meta compounds are solid in contrast to the ortho and meta dihalogen compounds, and this may partly account for the less remarkable drop

in yield, but here also the meta compound drops to a 58% yie. in the chlorine replacement. Contardi [30] states that this is probably due to the greater stability of the copper complex salt of the meta nitro-diazonium compound.

The introduction of bromine into the meta nitro compound gives a remarkably different result than the meta chloraniline, since the yield jumps up from 58% for the chlor-nitrobenzene to 74% for the bromnitro-benzene, while meta chloraniline gives a drop from 49% for the chlorine replacement to 39% for that of bromine. This effect may be attributed to some extent at least to the change in polarity, tho other factors must enter, since the order Br > Cl still holds for the ortho and para nitraniline replacements. The presence of several concurrent factors is evident thruout the whole series of replacements, since no general rule seems to hold except that in all cases the para compound gives the highest yield of the series.

VII. Table IV showing the results obtained when cupric salts are substituted for cuprous, confirms to a considerable degree the statement of A.Contardi [30] that the yield in this case is practically the same as in the ordinary Sandmeyer, and in some cases better. The introduction of chlorine into para halogen anilines by this method,however, gives yields of 20-30% lower than the corresponding cuprous salt replacement, althothe bromine replacements are from 4-6% higher.

The theories of mechanism for the Sandmeyer reaction involving the oxidation and reduction of cuprous salts must hence be abandoned as untenable in view of the above, or a different mehanism be assumed to take place in the two cases.

The substitution of nickel, ferric, cobalt or manganese chlorides in place of cuprous chloride gives approximately the same yields as when no catalyst at all is used, while ferrous chloride gave yields but little lower than the cupric salt. The difference in behavior between the salts may possibly be attributed to the greater ease of oxidation and reduction of Fe^{++} than Ni^{++} or Co^{++} even tho the latter are nearer copper in the periodic system. The non-action of ferric salts seems difficult to explain in view of the success obtained with cupric salts and further investigation should be made on this point.

The green color often noticed in compounds formed by the Sandmeyer reaction is undoubtedly due, as Holleman has stated, to nitroso or other reduced nitro compounds for the following reasons. The color is only noticed only in the presence of cuprous and ferrous solutions, which possess considerable reducing power, and is not noticed in the presence of the divalent cupric soltions, or in the presence of hydriodic acid which reacts with any free nitrous acid present. The color is also absent in all cases where the reaction is conducted hot and any nitrous acid hence instantly removed by decomposition and volatilization.

Altho the formation of more or less tar was noticed in

every preparation, the amount was very small in those runs in which no catalyst or those giving the same yields, (Co,Ni, etc.,) were used, the major product in these cases being phenols, together with azo compound. By the method of purification used, the diphenyl compounds if formed remained with the tar, and in many cases could be observed crystallising out in small crystals on the surface of the tar if spread out on filter paper,whereby most of the tarry matter is absorbed. In all cases, however, the tar formation is a much slower reaction than the desired one and hence the product sought can be largely filtered off previous to the tar separation if insoluble. The tar in such a case will then deposit slowly in the discarded filtrate. When steam distillation is used as the method of separation, the deposition of tar is hastened during the heating preliminary to and during the steam distillation, but in this case does not interfere since it is non-volatile and is left in the distillation flask. It is recommended that non-volatile compounds be filtered off more rapidly than recommended in the literature, since the tar contamination is thus greatly reduced even if the yield is slightly lower.

Since the tar formation is apparently a slower reaction, it possibly may arise from the polymerization of a second variety of complex copper or other metallic salt, similiar in form to the second variety of complex salt suggested by Heller [39]. The salt would differ from that of Heller however in that it is apparently more soluble than the easily

decomposable, normal Sandmeyer intermediate, but resembling it in being more stable. Further study is needed on this point however, before a definite statement can be made.

Summary.

A standardized method of procedure for the Sandmeyer reaction has been developed and can be applied without concentration changes for the introduction of chlorine, bromine or iodine into any amine desired.

Using this standardized procedure, a large number of runs have been made and the following general conclusions drawn:

I. The yields do not differ widely if the reaction is carried out at 0°C. or at 100°C., at least in the case of the para halogen amines.

II. The percentage yields of the disubstituted derivitives when halogen is introduced into ortho, meta and para halogen aniline or nitraniline are in the order of Br $\geqq$ I > Cl, except in the case of meta chloraniline, where Cl > Br.

III. In para halogen amines at least, the character of the halogen atom present in the nucleus shows but little difference in influence upon the entrance of a second halogen atom, irrespective of whether it be chlorine, bromine or iodine.

IV. The percentage yields when either bromine or chlorine are introduced into both monohalogen and mononitro anilines are in the order Para > Ortho > Meta.

V. Para nitro-anilines give approximately the same yields as para halogen anilines, but the ortho and meta yields are considerably higher, altho in the same order of Para > Ortho > Meta.

VI. Cupric salts may be substituted for cuprous salts with but slightly lower yields when chlorine is introduced and even higher yields than with cuprous salts when bromine is introduced in the case of para halogen amines.

VII. Substitution of Nickel, Cobalt, Ferric, or Manganese salts for Cuprous salts gives yields only of the same order as if no catalyst is used, while ferrous iron gives but slightly lower yields for the chlorine introduction than do cupric salts.

VIII. The tar formation almost universely accompanying the Sandmeyer reaction has been found to be the result of a slower reaction than the normal one. Suggested modifications have been made to prevent contamination of the pure product by removal before the tar formation takes place.

IX. From the data found, and the apparent lack of any consistent order by which it may be interpreted, the conclusions offered by Heller, Erdmann, and others seem true in that the Sandmeyer reaction cannot be regarded as that of a single reaction, but rather as the result of several concurrent or simultaneous reactionsof varied velocity and mechanism.

Bibliography.

1. Griess — Ann. — 106, 123 (1858)
2. Gerland — Ann. — 91, 185 (1854)
3. Griess — Ber. — 12, 2119 (1879)
4. Odde — Gazz. Chim. (Ital.) 25, 327 (1895)
5. Cain, Technology of the Diazo Compounds, 1920, page 15.
6. Hantzsch & Schumann — Ber. — 32, 1691 (1898)
7. Schumann — Ber. — 33, 527 (1900)
8. Griess — Phil. Trans. — 154, 667 (1864)
9. Strecher — Ber. — 4, 786 (1871)
10. Erlenmeyer — Ber. — 7, 1110 (1874)
11. E. Fischer — Ann. — 190, 67 (1877)
12. Blomstrand — J. Pr. Chim. — 53, 176 (1896)
13. Bamberger — Ber. — 27, 1948 (1894)
14. Hantzsch — Ber. — 27, 1702 (1894)
15. Cohen, Organic Chemistry, part II, page 295.
16. Transactions — 93, 617 (1908)
17. Sandmeyer — Ber. — 17, 1633, 2650, (1884), 18, 1496 (1885)
18. Gattermann — Ber. 23, 1218 (1890), 25, 1091 (1892)
19. Sandmeyer — Ber. — 23, 1880 (1890)
20. Heller — Zeit. f. Chem. Ange. — 23, 389 (1910)
21. Sandmeyer — Ber. — 17, 2650 (1890)
22. Erdmann — Ann. — 272, 1411 (1893)

23.	Behrend & Nissen	Ann.	262,	394 (1891)
24.	Ullmann & Forgen	Ber.	34,	3802 (1901)
25.	D.R.P. 126,861	Winther I		174 (1901)
26.	Holleman & Slinter	Rec.	25,	186 (1906)
27.	Tobias	Ber.	23,	1628 (1890)
28.	Votocek	Chem.Zeit.Repit.	20,	70 (1896)
29.	Angeli	Gazz.Chim.Ital.	21_2	285 (1891)

30. Contardi Chem.Abs.17,2109, 19, 827, Ann.Chim.Applicado 7, 13 (1923)

31.	Korczenski	Bull.Soc.Fr.	29,	283 (1921)
32.	Hantzsch	Ber.	28,	1752 (1895)
33.	Hantzsch & Blagden	Ber.	33,	2544 (1900)
34.		J.Pr.Chem. II	53,	427 (1896)
35.	Heller	Z.f.Ange.Che.	23,	389 (1910)
36.	Heller & Tischmer	Ber.	44,	250 (1911)
37.	Waentig & Thomos	Ber.	46,	3923 (1913)
38.	Hantsch	Ber.	28,	1734 (1895)
39.	"	Ber.	33,	2544 (1900)
40.	Llelman & Remy	Ber.	19,	810 (1886)

41. Clarke Organic Synthesis Volume III, page 54 (1923)

42. Meller Treatise on Inorganic Vol. III, page 198

43.	V. Thomas	Bull.Soc.Chim. (3)	15,	1092 (1896)