XCIII.—*Phenylacetylchloramine and its Analogues.*

By HENRY E. ARMSTRONG.

BENDER, who was the first to show that the aminic hydrogen of acetanilide can be displaced by chlorine (*Ber.*, 1886, **19**, 2272), effected the chlorination by adding a concentrated solution of bleaching powder to a concentrated aqueous solution of acetanilide mixed with an excess of acetic acid; as he refers to the interaction as one involving a slight rise of temperature, which makes it necessary to cool in warm weather, it is clear that he operated with cold solutions.

Several years ago, in the course of our experiments on the sulphonation of the chlor- and brom-anilines (Proc., 1892, **8**, 400), Mr. Briggs and I repeated Bender's experiments, but we were unsuccessful in obtaining the pure nitrogen chloride; it was always present in the product, but together with varying quantities of *p*-chloracetanilide. However, as it was easy, following Bender's directions, to convert the nitrogen chloride into its isomeride by digesting the crude product with concentrated muriatic acid, we adopted the method as being the simplest process in preparing large quantities of *p*-chloracetanilide; but we never succeeded in obtaining more than 60—70 per cent. of the amount to be expected.

Subsequently, at my request, two of my students, Messrs. Gidden and Spencer, carried out a series of experiments to discover the conditions under which Bender's compound was alone formed; and it was ascertained that almost the amount indicated by theory could be obtained by operating at an elevated temperature, but otherwise in accordance with his directions.

Five hundred grams of bleaching powder having been well stirred up with 3 litres of water, a solution of 300 grams of sodium carbonate in 1 litre of water was added, and the liquid was subsequently separated from the solid. A solution of 120 grams of acetanilide in 120 grams of glacial acetic acid having been poured into 6 litres of boiling water and the mixture well stirred, the whole of the clear solution of sodium hypochlorite, prepared as described, was at once added to the hot liquid, the temperature of which was about 80—85°. The solution immediately became turbid, and on stirring it well, the suspended matter clotted together and sank, leaving a clear, colourless liquid. An additional half-litre of hypochlorite solution was added to complete the precipitation. When the liquid was cold, the product was collected on a calico filter; in appearance, it resembled coarse sawdust, but the aggregates consisted of fine needles.

When the chlorination was effected at temperatures between about

0° and 50° in the manner described, the acetanilide being dissolved in sufficient glacial acetic acid to keep it in solution on pouring the liquid into water, the product was always a mixture of *p*-chloracetanilide with the nitrogen chloride, the proportion of the latter being less the lower the temperature. At the time, it was not easy to understand why such a paradoxical result was obtained, and especially why it was advantageous to operate at a high temperature. It should be added also that students who followed Messrs. Gidden and Spencer's directions were not always successful in imitating their results.

Slossen, in a paper published in 1895 (*Ber.*, 28, 3265), describes the preparation of phenylacetylchloramine and of the analogous formyl and benzoyl compounds by means of hypochlorous acid prepared by saturating an ice-cold 10 per cent. aqueous solution of sodium carbonate with chlorine and displacing the excess of the latter by a current of air. He succeeded in this way in completely converting acetanilide into the nitrogen chloride. Slossen's observations on the bromination of acetanilide are also noteworthy. He found that when acetic acid was used as a means of liberating hypobromous acid, only *p*-bromacetanilide was formed, but on using carbonic acid in place of acetic acid he was successful in obtaining the nitrogen bromide.

Recently, Chattaway and Orton have shown that Slossen's carbonic acid method is universally applicable, although without giving him the credit; and they do little more than mention Bender's work. Moreover, the description they give of the properties of the acetylnitrogen chloride and analogous compounds is in many respects very different from that given by Bender and Slossen; yet they make no reference to the fact that their results do not tally with those of previous observers, and in no way seek to justify their own statements.

According to Bender, phenylacetylchloramine may be recrystallised from very dilute acetic acid. When warmed with absolute alcohol, it dissolves, but after a short time the liquid boils violently and *p*-chloracetanilide begins to crystallise out. It may be boiled with water without undergoing change. Cold concentrated muriatic acid converts it into *p*-chloracetanilide, the interaction being a violent one. But according to Chattaway and Orton, although it dissolves readily in dilute acetic acid, long needles of *p*-chloracetanilide separate as the liquid cools; and in speaking of its preparation by Bender's method, they say: "The slightest excess of acetic acid causes the complete conversion of the substance into *p*-chloracetanilide," whilst in their account of the properties of the chloramines generally, they tell us that: "With alcohol the anilide is reformed." "With strong hydrochloric acid, chlorine is set free and the anilide regenerated. . . . . In some cases, however, under the influence of the acid, a portion of the compound undergoes an intramolecular transformation similar to that which takes place when it is heated."

Chattaway and Orton's statements are so entirely contrary to my own experience as well as to those of Bender and Slossen, that I have thought it to be necessary to look further into the matter, especially as this was desirable on other grounds.

Chattaway and Orton have advocated the view that when anilides are chlorinated or brominated, the nitrogen chloride or bromide is necessarily an intermediate product, and seem to claim originality for this explanation; they have forgotten to notice that in discussing the laws which govern substitution in benzenoid compounds thirteen years ago, I put forward this view, not only with reference to Bender's compound, but also in explanation of the production of ortho- and para-compounds generally, and that I have since often referred to it. In the synopsis of the discussion on laws of substitution which took place at the meeting of the British Institution at Dover in September last, which is printed in the report (pp. 683—687) after specifically referring to the conversion of phenylacetylchloramine into *p*-chloracetanilide, I said: "Moreover, bearing in mind the extreme readiness with which change takes place, for example, in the case of the formation of *p*-chloracetanilide from the compound PhNAcCl, or of sulphanilic from phenylsulphamic acid, it is difficult to believe that the formation of the one compound is not a necessary stage in the formation of the other: the readiness with which the substituted benzenoid compound is obtained is so great, that it is to be expected that both compounds would be formed together if they were independent products of the action of a single agent—just as, in fact, often happens in the case of para- and ortho-compounds." "It is very difficult to form any precise conception of the manner in which such 'isomeric changes' are brought about. Something more than a mere interchange of position of the radicles is involved in them: some agent intervenes; but the operation of the agent is easily overlooked, as only a minute quantity suffices in many cases, the action being 'fermentative' in character."

It was from this point of view, in the hope of discovering the catalyst by which the change is conditioned, that it appeared desirable to re-examine Bender's compound. I am much indebted to Messrs. P. V. Dupré and E. J. Fairhall for the assistance they have rendered me in the experiments.

From the outset, it was probable that hydrogen chloride was the active catalyst; and there is little doubt that this is the case; it is at least certain that the compound is stable so long as the conditions are such as to preclude the presence of hydrogen chloride.

When prepared by Slossen's method, being produced practically in an alkaline medium, the crude product is alkaline, and it may be purified without difficulty by recrystallisation from a neutral solvent.

The carefully purified dry substance may be preserved in the dark for months unchanged. It may be recrystallised from acetic acid of any strength. When dissolved in alcohol, sooner or later, it usually undergoes isomeric change spontaneously, but it may be recrystallised from hot alcohol in the presence of a little acid sodium carbonate, or finely divided calcium carbonate; in fact, this appears to be by far the simplest method of effecting its purification. Yet, if a drop of muriatic acid be added to the warm alcoholic solution, the temperature at once begins to rise and the chloride is converted into *p*-chloracetanilide; the same change takes place when it is added to ordinary muriatic acid. In both cases, the action is very violent, if the quantity dealt with be at all considerable.

The properties of phenylacetylbromamine appear to be very similar to those of the chloride; but it is far more sensitive to change. When it undergoes conversion into *p*-bromacetanilide in alcoholic solution, perhaps a small portion suffers reduction, but I am not satisfied that a sufficiently purified substance has been dealt with to decide this point.

p-Chlorophenylacetylchloramine, although reduced by concentrated muriatic acid in the manner indicated by Chattaway and Orton, appears to be to a large extent converted into dichloracetanilide when dissolved either in alcohol or in acetic acid and subjected to the action of a minute proportion of hydrogen chloride. It may be boiled with alkaline water without undergoing change, but if the liquid be then rendered faintly acid by adding muriatic acid and again heated, the isomeric change at once takes place.

The behaviour of dichlorophenylacetylchloramine is in accordance with Chattaway and Orton's statements, this compound being reduced both by alcohol and by muriatic acid without undergoing isomeric change.

The recognition of hydrogen chloride as being the catalytic agent which determines the isomeric change of the nitrogen chloride is of importance as defining the conditions under which compounds such as are under consideration must be prepared, and as affording an explanation of the special value of carbonic acid as the means of liberating hypochlorous acid.

In the experiments made by Messrs. Gidden and Spencer above referred to, in which the complete conversion into nitrogen chloride was secured by operating at an elevated temperature, the amount of acetic acid used was relatively small in comparison with the amount of sodium carbonate, so that probably the chlorination was effected in the presence of acid carbonate; but in the unsuccessful experiments at lower temperatures, a relatively larger proportion of acetic acid was used, in order to maintain the acetanilide in solution; consequently, acetic acid was present in excess, and doubtless led to the liberation of sufficient hydrogen chloride to induce isomeric change.

Chattaway and Orton speak of phenylacetylchloramine as being "very easily and rapidly prepared by the action of bleaching powder on acetanilide suspended in excess of potassium bicarbonate solution." According to my experience, whatever excess of hypochlorite be taken, and however long the stirring be continued, the chlorination is almost always imperfect, and eventually at most 60—70 per cent. of *p*-chloracetanilide has been obtained. The difficulty is entirely got over by heating, and apparently the operation may be carried out on any scale. For example, a kilogram of acetanilide may be completely chlorinated within a few minutes in an ordinary housemaid's enamelled iron pail mounted on a gas burner and provided with an efficient stirrer. It is desirable to use both hypochlorite and acid carbonate in considerable excess; the acetanilide is quickly added to the concentrated solution containing these, and after vigorously stirring for a short time the temperature is raised to 50—60°.

In attempting to explain the manner in which the isomeric change is effected, it appears legitimate to assume that it is dependent on the combination of the chloramine with hydrogen chloride. A condition of extreme instability is thus engendered, and probably the first consequent change is one in which an atom of chlorine attached to the nitrogen atom escapes from the molecule together with an atom of hydrogen from the nucleus; a chlorine atom then slips into the nucleus in place of the latter, whilst the atom of hydrogen introduced in the molecule of hydrogen chloride takes the place of the chlorine atom of the chloramine, the ortho- or para-derivative being formed according to the conditions prevailing at the moment of change.

In justification of the view that hydrogen is withdrawn from the nucleus, attention may be directed to E. Fischer's observation that active aminoglutaric acid is racemised on benzoylation (*Ber.*, 1899, **32**, 2464). This would seem to show that the chlorine of the benzoyl chloride is not removed in conjunction with aminic hydrogen, but in conjunction with the hydrogen atom associated with the carbon atom to which the NH_2 group is attached; opportunity being thus given to the nitrogen atom to become united momentarily by two affinities to the carbon atom, the formation of the two benzoyl derivatives of opposite activity becomes possible.

I have elsewhere (B.A. Report, 1899, p. 685) contended, in the case of the sulphamic acid formed on sulphonating acetanilide, that when the isomeric change occurs, the ortho-acid is formed from the sulphamic acid if the sulpho-group be, as it were, *let down gently*; otherwise, the para-acid is produced.*

This, perhaps, is true generally: in other words, it is only when the chlorine is "let down gently" from the chloramine that it enters into the ortho-position.

If we seek to form a picture of the manner in which the equilibrium becomes disturbed, it may be supposed that when the change takes place and an atom of hydrogen becomes separated from the ortho-position in the nucleus, the "centric mechanism" momentarily breaks down and that in consequence the molecule either lapses or is on the point of lapsing into the ethenoid condition. At such a moment, hydrogen chloride might act in one of two ways, and either a chlorine atom might be introduced into the ortho-position, or a hydrogen atom might be restored to this position; in the latter case, two atoms of chlorine would be momentarily associated with the nitrogen, and would either escape as chlorine, or one might combine with a para-atom of hydrogen whilst another atom of chlorine took the place of the hydrogen atom thus removed. The three modes in which the chloramines undergo change are thus provided for. It is obvious that the character of the change might depend on the mass of hydrogen chloride present, and that it might also be affected by the solvent.

Any alteration in the nucleus which diminishes the 'basic' properties of the nitrogen atom would necessarily exercise an influence in retarding the isomeric change, and alterations in the composition of the nucleus would also affect its stability and sensitiveness to change. It is therefore easy to understand that the behaviour of the various chloramines should be different.

Important information as to the manner in which the isomeric

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* It may be here pointed out that the acetyl group exercises an important influence on the occurrence of this isomeric change. It is doubtful whether phenylsulphamic acid can be converted into the *o*-sulphonic acid; to convert it into *p*-sulphonic acid, it is necessary to heat it at about 180°. If, however, it be acetylated by merely heating it with acetic anhydride at 100°, and the product be poured into water and the solution boiled, sulphanilic acid is at once obtained. In the case of Bamberger's experiments, in which a solution of phenylsulphamic acid in acetic acid mixed with a few drops of sulphuric acid was kept for some time at 0°, it is probable that acetylation preceded the formation of *o*-sulphonic acid. It will be desirable to study the influence of different radicles on the occurrence of this isomeric change; although I have obtained the *o*-sulphonic acid from acetanilide, I have not hitherto succeeded in preparing it from benzanilide.

change occurs will probably be obtained by determining the velocity with which change is effected under various conditions. It is proposed to undertake such experiments with chloramines when cool and dull weather sets in.

The chloramines are an inviting subject of study for other reasons—and especially on account of their stability under some conditions and their instability under others. We are too much in the habit of regarding compounds as intrinsically unstable which probably are of a comparatively high order of stability in the absence of catalysts capable of determining their alteration; and the disregard of this circumstance has led to the assumption that isodynamic changes especially are the outcome of a state of intramolecular wobble. An increasing body of evidence tends to show that in the cases in contemplation, the process of change is of a complex character and largely extramolecular—in that it involves the co-operation of several distinct molecules and their units in a conducting system.

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