CLIV.—*Metallic Derivatives and Constitution of Guanidine.*

By Hans Krall.

For some time the author has been engaged in the study of guanidine, in the hope of throwing light on its constitution (T., 1913, **103**, 1378; P., 1913, **29**, 377). Owing to circumstances, the investigation must be abandoned for the present, but as certain results, not without interest, have been obtained, it seems desirable to publish them, notwithstanding the incomplete state of the work.

When crystalline guanidine (that is, the free base) is heated, it melts, and at 160° decomposes, with brisk evolution of ammonia and formation of melamine. When heated with a molecular proportion of potassium ethoxide, a trace only of ammonia is evolved at 160°, and at 200° the change is not complete; the residue now consists of monopotassium cyanamide. When two molecular proportions of the ethoxide are used, the change is similar to the last, and the residue is essentially dipotassium cyanamide, but on being acidified has a faint odour of hydrogen cyanide.

Now cyanamide is tautomeric, having the forms $CN\cdot NH_2$ and $NH\colon C\colon NH$, and in view of the acidity of the imino-group, its alkali derivatives are probably formed from the carbodi-imide tautomeride. Since guanidine is more stable to heat in the presence of potassium ethoxide, and yields potassium cyanamide so readily, it is probable that a potassium derivative is first formed in which the hydrogen of an imino-group is replaced by the metal.

When an aqueous solution of guanidine is boiled, there is immediate evolution of ammonia and carbon dioxide, with the formation of a trace of melamine. In order to ascertain whether hydrolysis takes place according to the equation

$$CH_5N_3 + 2H_2O = CO_2 + 3NH_3,$$

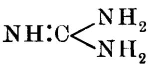
or whether urea is formed as an intermediate product according to the equation

$$CH_5N_3 + H_2O = CH_4ON_2 + NH_3,$$

a solution of guanidine was distilled until one molecular proportion of ammonia had been liberated. Carbon dioxide was evolved in such quantities as to form large crystals of ammonium carbonate in the side-tube of the flask; more than half the guanidine was recovered unchanged, and no urea could be detected. The hydrolysis therefore takes place according to the former equation. Many statements as to the supposed occurrence of urea are probably due to the fact that, like that substance, both melamine and guanidine form sparingly soluble nitrates.

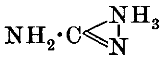
It would not be correct to argue from the formation of a trace of melamine in these experiments that dissociation to ammonia and cyanamide precedes hydrolysis, because if such were the case, since the polymerisation of cyanamide in alkaline solution is very rapid, a larger proportion of melamine would have been obtained. This dissociation is no doubt a true secondary change, and supports the view that in neutral solution (that is, in solution where the alkalinity is due only to the guanidine itself) we have an isodynamic mixture of two forms, one of which is rapidly hydrolysed, whilst the other is to a slight extent dissociated.

Three tautomeric forms of guanidine are possible:



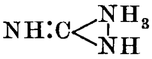
$NH{:}C{<}\begin{matrix}NH_2\\NH_2\end{matrix}$

A.



$NH_2{\cdot}C{\lessgtr}\begin{matrix}NH_3\\|\\N\end{matrix}$

B.



$NH{:}C{<}\begin{matrix}NH_3\\|\\NH\end{matrix}$

C.

The one usually written, *A*, has by no means been established, and preliminary experiments have given results opposed to the presence of two amino-groups in the molecule; thus, nitrous acid reacts slowly, and liberates nitrogen corresponding with no more than one of the three nitrogen atoms, even when excess of a strong acid is present, and all attempts to prepare a dihydrochloride, which should be obtained from so strong a base as guanidine if it had the constitution *A*, have been unsuccessful.

The forms *B* and *C* are analogous to the constitutions suggested by E. A. Werner for thiocarbamide (T., 1912, **101**, 2185) and for carbamide (T., 1913, **103**, 1013), and their tautomerism is similar to that of cyanamide. It is now suggested that guanidine in solution as the free base is a mixture of these isomerides in approximately equal proportions, that strong acids increase the proportion of *B*, whereas alkali hydroxides increase the proportion of *C*.

Thiele (*Annalen*, 1898, **302**, 334) has prepared and described a silver derivative of guanidine, to which he assigned the formula $CH_3N_3Ag_2,H_2O$, without, however, supplying any evidence of the presence of a molecular proportion of combined water in the compound; and Schenck (*Arch. Pharm.*, 1909, **247**, 466) has pointed out that, whilst the silver derivative prepared by Thiele's method always shows a deficiency of silver, it furnishes by its reaction with methyl iodide a mixture of methylguanidine and *s*-dimethylguanidine.

As the result of a large number of experiments, the author has obtained evidence of the existence of three silver derivatives of guanidine: (1) a mono-derivative, white and non-explosive; (2) a di-derivative, grey or black (when dried) and highly explosive when struck, or even rubbed; (3) a yellow and non-explosive derivative, no doubt identical with Thiele's substance, and probably a molecular compound of (1) and (2). These derivatives are probably derived from guanidine of configuration *C*.

A preliminary study of the copper derivatives of guanidine also indicates the tautomerism of the latter; thus a well-defined, stable, green, copper compound, having the composition CH_3N_3Cu, has been obtained, and, under different conditions, an unstable, deep blue, crystalline derivative, the exact nature of which has not yet been established.

The methyl derivatives of guanidine have been exhaustively studied by Schenck (*Zeitsch. physiol. Chem.*, 1912, **77**, 328; *Arch.*

Pharm., 1912, **250**, 306). Whilst one must be cautious in drawing conclusions as to the constitution of a compound from the study of its derivatives, since the entry of new groups must materially effect the distribution of forces, yet it is interesting to note that the series of methylated guanidines which Schenck was unable to obtain, namely, those containing the system $\cdot C(NH_2){:}N\cdot CH_3$, is precisely the series that is not predicted by the constitutions *B* and *C*, neither of which contains the system $\cdot C\cdot NH_2{:}NH$. Schenck's results may all be explained by the constitutions put forward above, which, however, suggest the existence of isomerides containing the group $\cdot N(CH_3)_3$. Isomerides of this type have not yet been recognised, but Schenck's experiments were not suitable for their production, and the author's experiments had to be abandoned. It is not surprising that trimethylamine does not directly unite with cyanamide, as even dimethylamine does so only with difficulty.

The author claims to have obtained evidence that guanidine is tautomeric, and the constitutions *B* and *C* are put forward as its phases. These are in strict accordance with the relation of guanidine to cyanamide, and explain its hydrolysis, and its potassium, silver, copper, and methyl derivatives. Moreover, they explain why guanidine is never a di-acidic base, and why it never behaves as a di-amino-compound towards nitrous acid.

EXPERIMENTAL.

Action of Heat on Guanidine.

A solution of the free base was prepared by the interaction of guanidine hydrochloride and potassium hydroxide in alcoholic solution, care being taken to exclude every trace of moisture.

Fifty c.c. of this solution (about *N*/4) were distilled from a glycerol bath. Almost all the alcohol passed over below 100°, and no trace of ammonia. At about 160° there was brisk evolution of ammonia from the dry, solid residue, which melted and at once resolidified. On crystallisation from water, it was found to be melamine (normal melamine; compare P., 1913, **29**, 377).

Potassium Derivatives.

Fifty c.c. of the same solution were mixed with one equivalent of potassium ethoxide in a small quantity of alcohol, and distilled as before, the distillate being passed into rather less than one equivalent of acid. At no time was brisk evolution of gas apparent, and the acid in the receiver was neutralised only when the temperature of distillation reached 245°. The residue was found to be monopotassium cyanamide.

The same experiment was repeated, using two equivalents of potassium ethoxide. Again only a trace of ammonia was liberated below 160°, but even at 200° the residue in the flask was liquid, and did not completely solidify on cooling. Without further experiment, therefore, it is not certain that guanidine forms a dipotassium derivative, although decomposition appeared to be slower than with one equivalent of alkali. The residue again dissolved in a few drops of water, and gave a copious precipitate of yellow silver cyanamide with ammonio-silver nitrate. On acidification of a portion of the residue there was no effervescence, showing the absence of carbonate, but a faint odour of hydrogen cyanide was perceived.

Hydrolysis of Guanidine.

A solution of 3 grams of guanidine in 100 c.c. of water was distilled into one equivalent of dilute acid until neutral. The residue was then neutralised with hydrochloric acid, evaporated to dryness, and extracted with absolute alcohol. Half the guanidine employed was recovered unchanged, but no urea could be detected.

A solution of 12 grams of guanidine in 100 c.c. of water was boiled under a reflux condenser. Carbon dioxide and ammonia were evolved in quantity from the start, and formed crystals of ammonium carbonate in the condenser. After six hours, the evolution of ammonium was considerably reduced. The solution was nearly neutralised with sulphuric acid, and on keeping deposited a small quantity of crystals, which were identified as melamine sulphate by their characteristic appearance, and by the picrate formed from them. The mother liquor contained no urea.

Aqueous solutions of guanidine, alone and with various proportions of alkali, were allowed to remain at the ordinary temperature. After twenty-four hours, all had an odour of ammonia, showing that hydrolysis had commenced. This series of experiments was not carried out quantitatively.

Action of Nitrous Acid on Guanidine.

A few experiments only were carried out, but they are of sufficient interest to be worthy of brief mention.

Mixtures of solutions of guanidine hydrochloride or acetate with sodium nitrite and acetic acid gave no gas.

When mineral acids were added there was slow evolution of gas, which consisted of nitrogen and nitric oxide, and sometimes also carbon dioxide. The larger the excess of mineral acid, the larger was the proportion of nitrogen. The following experiment is typical.

Two c.c. of *N*/2-guanidine nitrate with one molecular proportion of sodium nitrite and two of hydrochloric acid, mixed in the nitrometer, gave, after twenty-two hours, 2·5 c.c. NO and 14·5 c.c. N_2 (corrected).

In this connexion, it may be recalled that, according to Cordier (*Monatsh.*, 1912, **33**, 759), sodium hypobromite liberates all the nitrogen from guanidine.

Double Nitrate of Silver and Guanidine.

When concentrated solutions of guanidine and silver nitrates were mixed, colourless, needle-shaped crystals separated, which consisted of a double nitrate of the composition

$$CH_5N_3,HNO_3,2AgNO_3:$$

0·5025 required 21·5 c.c. *N*/10-KSCN. Ag = 46·2.

$CH_5N_3,HNO_3,2AgNO_3$ requires Ag = 46·7 per cent.

Silver Derivatives.

When a solution containing guanidine nitrate and silver nitrate is rendered alkaline, a precipitate is formed which may vary in colour from white through yellow to grey, according to the proportions. It is usually flocculent, and difficult to wash and dry; it is soluble in ammonium hydroxide or in nitric acid, and is not decomposed, or only very slowly, by boiling water. It is blackened slowly by light, and readily by alcohol.

In all the following experiments the precipitate was washed by decantation until the wash-water was free from alkali. The pasty precipitate was then drained, and dried in the steam-oven to a constant weight. Analyses were made by decomposing a weighed quantity with hot dilute nitric acid, and titrating with *N*/10-potassium thiocyanate. The production of a trace of silver carbonate in these experiments is difficult to avoid, as guanidine in the presence of alkalis, or even as the free base in water, is rapidly hydrolysed.

Some seventy samples have been prepared by various methods and examined, and the following experiments are typical examples of the methods found most satisfactory in each case.

Monosilver Derivatives of Guanidine.

A solution of guanidine nitrate was treated with five equivalents of sodium hydroxide, followed by one equivalent of silver nitrate.

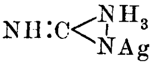
The precipitate at first formed (? silver hydroxide) changed to white on vigorous shaking; it was granular, and settled readily.

Found: Ag = 65·4.

CH_4N_3Ag requires Ag = 65·0 per cent.

This derivative is colourless, and does not explode when struck, but when heated strongly decomposes, with a mild explosion.

The constitution may be represented by the structural formula



$$NH{:}C{<}\begin{matrix}NH_3\\ |\\ NAg\end{matrix}$$

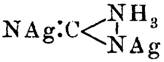
Disilver Derivatives of Guanidine.

Two equivalents of silver nitrate were added to solutions of guanidine containing excess of alkali; the precipitate formed was grey, and dried to jet-black.

Found: Ag = 77·0.

$CH_3N_3Ag_2$ requires Ag = 79·1 per cent.

This black derivative explodes violently on being rubbed or struck, or when heated to 145°. It is believed that this is essentially a disilver derivative contaminated with traces of the monoderivative. It may be represented by the structural formula



$$NAg{:}C{<}\begin{matrix}NH_3\\ |\\ NAg\end{matrix}\,.$$

The freshly-formed precipitate appears perfectly homogeneous under the microscope, and the results obtained by variations of the method are quite uniform.

When excess of alkali is avoided, the precipitate is yellow. As this is evidently the compound obtained by other workers, it was exhaustively studied.

It was hoped that neutral solutions would favour the production of an isomeride. This, however, proved true only in a limited sense.

A mixture of guanidine nitrate with one equivalent of silver nitrate in dilute solution was treated with calcium hydroxide. The precipitate was pale yellow, and gave Ag = 73 per cent.

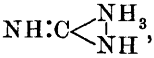
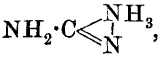
Here, as in the experiments already described, many variations were tried, but with quite a different result; for whereas in the former cases little variation in the product ensued, here the slightest alteration in the procedure resulted in considerable variations in the substance obtained. In order to test the validity of the formula, $CH_3N_3Ag_2,H_2O$, assigned to this compound by Thiele (*loc. cit.*), the yellow substance from one of these experiments, dried at 100° to constant weight, was heated at 120°; 1·777 grams lost, in successive periods of two hours each, 0·0180, 0·0175, 0·005, and 0·005 gram, and became black. The same weight of the substance, $CH_3N_3Ag_2,H_2O$, would contain 0·10 gram of water.

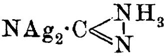
When a large number of preparations of the yellow derivative had been examined, it became apparent that it was a mixture of mono- and di-derivatives in approximately equimolecular proportions. Accordingly, solutions were mixed as required by the equations

$$3AgNO_3 + 2CH_5N_3,HNO_3 + 5NaOH = CH_3N_3Ag_2 + CH_4N_3Ag + 5NaNO_3 + 5H_2O.$$

Small variations in this method gave constant results (Found, Ag = 73·8. $CH_3N_3Ag_2 + CH_4N_3Ag$ requires Ag = 73·8 per cent.), and the precipitate was always deep yellow. Some of the washed precipitate, without drying, was decomposed by *N*/10-hydrochloric acid, the silver chloride weighed, and the excess of acid determined by titration; it was then easy to calculate the ratio of silver found to base liberated from the derivative and converted into hydrochloride; this ratio was expected to be 3 : 2, according to the simultaneous changes:

$$CH_3N_3Ag_2 + 3HCl = 2AgCl + CH_5N_3,HCl,$$
$$CH_4N_3Ag + 2HCl = AgCl + CH_5N_3,HCl.$$

The ratio, however, proved to be, not 3 : 2, but 3 : 1. Guanidine hydrochloride was isolated from the acidified product, so one at least of the substances is a true guanidine derivative; a derivative of some substance produced by the decomposition of guanidine may be present, or, as seems more probable, a derivative of a tautomeric form which decomposes as soon as it is liberated from its silver derivative by acids; the latter would be very probable in the case of derivatives of the form  $\mathrm{NH{:}C}<\begin{matrix}\mathrm{NH_3}\\ |\\ \mathrm{NH}\end{matrix}$, as this tautomeride would tend to isomerise in the presence of acids to  $\mathrm{NH_2{\cdot}C}<\begin{matrix}\mathrm{NH_3}\\ |\\ \mathrm{N}\end{matrix}$, in order to form stable salts, and it is abundantly proved that all compounds are most unstable during conditions which favour isomeric change.

The yellow precipitate in these experiments is believed to be a mixture of a di-silver derivative of *B* having the constitution  $\mathrm{NAg_2{\cdot}C}<\begin{matrix}\mathrm{NH_3}\\ |\\ \mathrm{N}\end{matrix}$ with the mono-silver derivative described already. This agrees with Schenck's observation (*loc. cit.*) that the yellow derivative yielded a mixture of mono- and di-methylguanidine.

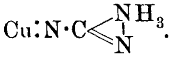
Copper Derivatives.

When a dilute solution containing guanidine and copper salts was treated with alkali, a green precipitate, soluble in ammonia, was formed. This was washed by decantation, and dried at 100°. On heating strongly, it fused and decomposed slowly, so analyses were carried out by decomposing a weighed quantity with hot nitric acid and precipitating the copper as hydroxide:

0·798 gave 0·5300 CuO. Cu = 53·0.

CH_3N_3Cu requires Cu = 52·7 per cent.

On solution in acids, this compound gave a copper and a guanidine salt, thus showing that it was a true copper derivative of guanidine. It is believed to have the constitution



$$\mathrm{Cu{:}N{\cdot}C}\left<\begin{matrix}\mathrm{NH_3}\\ |\\ \mathrm{N}\end{matrix}\right..$$

When concentrated solutions were used, and large excess of alkali, the result was very different.

A solution of 20 grams of guanidine hydrochloride in 50 c.c. of water was mixed with 25 grams of potassium hydroxide dissolved in 50 c.c. of water, and the solution, which had become warm, was cooled. After half an hour, 13 grams of cupric chloride dissolved in 100 c.c. of water were added rapidly. The liquid remained clear, but became warm, and, on cooling, crystals separated. After remaining overnight without exposure to the air, the crystals were collected, drained on porous tile, and dried in the desiccator. Thirteen grams of deep blue needles were obtained.

This compound is decomposed by water, hence the crystals were contaminated by adherent alkali, and the analytical results are only approximate.

Found: Cu = 26·9, 28·0. Cl = 15·4, 14·7.

$C_2H_9N_6ClCu$ requires Cu = 29·4; Cl = 16·5 per cent.

When decomposed by water, it gave copper hydroxide (not the copper derivative of guanidine described above, as might have been expected), and an alkaline solution containing guanidine hydrochloride. 3·60 Grams were suspended in 200 c.c. of cold water for twenty-four hours, the precipitated copper hydroxide was removed by filtration, and the filtrate made up to 250 c.c. Of this, 25 c.c. required 14·7 c.c. $N/10$-H_2SO_4, the amount theoretically required being 16·8 c.c., according to the equation:

$$C_2H_9N_6ClCu + 2H_2O = Cu(OH)_2 + CH_5N_3,HCl + CH_5N_3.$$

From the remainder of the filtrate, 1·7 grams of guanidine hydrochloride were isolated.

Analysis has shown, therefore, that for every atom of copper there are one atom of chlorine and probably two residues of guanidine in the compound. It would be futile to suggest a constitution for such a substance without making a further study of it.

The sulphates of guanidine and copper under similar conditions gave blue crystals, but they could not be separated from the alkali sulphate which crystallised out at the same time.

The author's thanks are due to Dr. E. A. Werner, to whose sympathy and encouragement this work is entirely due; also to the Research Fund Committee of the Chemical Society for a grant which has largely defrayed the expense of the work.

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