

CCXIV.—*The Preparation of Methylguanidine, and of  $\beta\beta$ -Dimethylguanidine by the Interaction of Dicyanodiamide, and Methylammonium and Dimethylammonium Chlorides Respectively.*

By EMIL ALPHONSE WERNER and JAMES BELL.

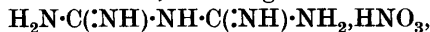
In a previous communication (T., 1920, **117**, 1133) it was shown that guanidine thiocyanate can be readily obtained, in a 90 per cent. yield, by heating a mixture of dicyanodiamide and ammonium thiocyanate at 120°, according to the equation



The reaction has now been extended to the preparation of methylguanidine,  $\text{HN}\cdot\text{C}(\text{NH}_2)\cdot\text{NH}\cdot\text{CH}_3$ , and dimethylguanidine,  $\text{HN}\cdot\text{C}(\text{NH}_2)\cdot\text{N}(\text{CH}_3)_2$ .

In the meantime, Ewan and Young (*J. Soc. Chem. Ind.*, 1921, **40**, 109r), in addition to confirming the authors' results as regards the yield of guanidine thiocyanate, have obtained excellent yields of nitrate and sulphate of guanidine, respectively, using the corresponding salts of ammonia in place of ammonium thiocyanate in the above equation (1). With ammonium chloride, however, the yield of the guanidine salt was not so good, on account of the high temperature required to effect fusion of the mixture. In the case of methylammonium and dimethylammonium chlorides, this disadvantage does not arise, and practically quantitative yields of the substituted guanidine hydrochlorides have been readily obtained.

It was suggested by the authors (*loc. cit.*), in explanation of the mechanism of reaction (1), that depolymerisation of dicyanodiamide is the first phase in the change, the guanidine salt being formed from the union of cyanamide and the ammonium salt, thus,  $\text{CN}\cdot\text{NH}_2 + \text{NH}_3\cdot\text{HSCN} \rightarrow \text{HN}\cdot\text{C}(\text{NH}_2)\cdot\text{NH}_2\cdot\text{HSCN}$ . Davis (*Amer. Chem. J.*, 1921, **43**, 2234) found that when a mixture of dicyanodiamide with two molecular proportions of ammonium nitrate was heated at 120° for six hours, some diguanide nitrate,

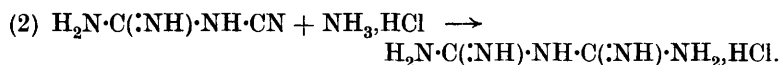


was formed, whilst a considerable proportion of the original material was unchanged. At 130°, much guanidine nitrate was formed, and at 160°, after two hours, the latter salt was produced in amount equal to 86 per cent. of the theoretical.

It was also proved that diguanide nitrate and ammonium nitrate, when fused together in molecular proportions, gave guanidine nitrate.

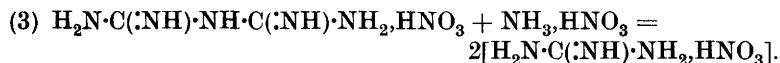
From these results, Davis concludes that "the reaction therefore is not dependent upon the depolymerisation of dicyanodiamide as Werner and Bell have supposed."

This conclusion has, we think, no foundation in fact. There is no evidence that the formation of guanidine thiocyanate is dependent on the previous formation of diguanide in the experiments described by us. If the temperature is maintained below the point ( $120^\circ$ ) at which the guanidine salt is readily formed according to equation (1), the original substances can be largely recovered unchanged. Moreover, the formation of diguanide under the conditions recorded by Davis, and the production of which was noticed also by Ewan and Young, does not prove that dicyanodiamide is not depolymerised during the progress of the reaction. Bamberger and Dieckmann (*Ber.*, 1892, 25, 545) obtained diguanide by heating a mixture of dicyanodiamide and ammonium chloride at  $195^\circ$ . Viewing the former as cyanoguanidine,\* the change was represented thus :



According to these investigators, when guanidine hydrochloride is heated at  $180$ — $185^\circ$ , it is partly decomposed, yielding diguanide hydrochloride and ammonium chloride. This observation would seem to favour the view that guanidine is a precursor of diguanide in the reactions under consideration.

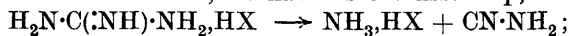
Accepting equation (2) to explain the first step in the change and assuming that diguanide there reacts with ammonia to form guanidine, Davis represents the mechanism of the final reaction, thus :



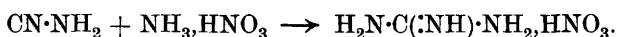
How guanidine is actually formed is not made perfectly clear by this equation.

\* The suggestion, so generally accepted, that dicyanodiamide is cyanoguanidine was originally put forward by Bamberger. The authors have very strong reasons for not accepting this view of its constitution. It is curious that no attempt has hitherto been made to prove this formula by a direct synthesis. By the action of cyanogen bromide on free guanidine, one of us (W.) has obtained evidence of the formation of the true cyanoguanidine. It is a basic substance bearing no resemblance to dicyanodiamide. It is sufficient to state here that in this reaction not a trace of dicyanodiamide was formed. Considering the stability of the latter in the static condition, it should be formed in such a reaction if it were cyanoguanidine. The theory of the mechanism of the polymerisation of cyanamide (Werner, *T.*, 1915, 107, 716) does not suggest such a formula.

As a matter of fact, the production of diguanide from a salt of guanidine, and of guanidine from a diguanide salt by the action of heat, is a reversible change dependent on the temperature. The mechanism of the reactions is strictly comparable with that of the formation of biuret from carbamide, and of carbamide from biuret as described by Werner (T., 1913, **103**, 2275). Thus when a guanidine salt is heated, we have as the first step,



diguanide being formed by the union of cyanamide with a portion of the unchanged guanidine salt. On the other hand, a diguanide salt, when heated, is decomposed into guanidine and cyanamide; if a salt of ammonia is present as shown in equation (3), then a second molecule of guanidine results from the interaction



Whilst the formation of more or less diguanide, as an intermediate product, during the fusion of dicyanodiamide with certain salts of ammonia depends on the temperature required to initiate the change, and on the rate of its progress, at no time is there much formed under the conditions which give rise to good yields of guanidine.

The authors therefore see no reason for altering their views as regards the suggestion put forward to explain the mechanism of the formation of guanidine in their previous investigation. In the preparation of the two methylated guanidines, the formation of methyl derivatives of diguanide has been recognised during the progress of the changes.

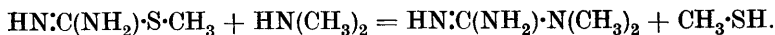
#### EXPERIMENTAL.

*Dimethylguanidine*,  $\text{H}_2\text{N}\cdot\text{C}(\text{NH})\cdot\text{N}(\text{CH}_3)_2$ .—Expt. 1. An intimate mixture of dicyanodiamide (4.2 grams) and dimethylammonium chloride (8.15 grams) was heated in a wide-mouthed test-tube partly immersed in a bath of glycerol. The tube was closed with a cork which carried a loose-fitting thermometer, which also served as a stirrer. The mixture, which commenced to melt at about  $45^\circ$ , and was completely fused at  $130^\circ$ , was heated at  $180^\circ$  for three hours. The clear viscous product, while still warm, was dissolved in 50 c.c. of pure alcohol. The cold solution, separated by filtration from a small quantity (0.14 gram) of insoluble material,\* gave, after concentration by evaporation, a viscous residue which set to a homogeneous, crystalline mass when allowed to cool in a vacuum over sulphuric acid. The absence of unchanged dimethylammonium chloride in the product was shown by the fact that it yielded nothing

\* This consisted of impurities present in the dicyanodiamide used.

to extraction with pure dry chloroform, a solvent in which this salt is very freely soluble (Found: Cl = 28.66.  $C_3H_9N_3.HCl$  requires Cl = 28.74 per cent.).

A platinichloride was prepared in orange-red, octahedral crystals, which melted and decomposed at  $210^\circ$  [Found: Pt = 33.59.  $(C_3H_9N_3)_2.H_2PtCl_6$  requires Pt = 33.42 per cent.]. Schenck (*Arch. Pharm.*, 1912, **250**, 306) gives  $225^\circ$  for the temperature of decomposition of the platinum derivative obtained from dimethylguanidine prepared from *s*-methylthiocarbamide in accordance with the change



The platinichloride prepared by us for comparison from this source was identical in appearance with that given above, and melted at the same temperature ( $210^\circ$ ). The accuracy of the thermometer used by us was tested by means of pure substances of known melting points between  $200^\circ$  and  $230^\circ$ .

A picrate prepared from the fusion product melted at  $227^\circ$ . Schenck gives  $230^\circ$  for the picrate of dimethylguanidine prepared by this method.

*Formation of Dimethyldiguanide.*—Expt. 2. Under the conditions described above, the yield of dimethylguanidine hydrochloride is practically quantitative. When the fused mixture of dicyanodiamide and dimethylammonium chloride was maintained for three and a half hours at  $120^\circ$ , a considerable residue (5.5 grams) was left after extraction of the product with alcohol as in expt. 1. By crystallisation from water, dimethyldiguanide hydrochloride was obtained in colourless, glistening prisms which melted at  $232^\circ$  (Found: Cl = 21.60.  $C_4H_{11}N_5.HCl$  requires Cl = 21.45 per cent.). The picrate, pale yellow needles from water, melted at  $219^\circ$ .

*Preparation of Methylguanidine,*  $H_2N\cdot C(:NH)\cdot NH\cdot CH_3$ .—Expt. 3. A mixture of dicyanodiamide (4.2 grams) and methylammonium chloride (6.75 grams) was dealt with as in expt. 1. The mixture, which commenced to melt at  $85^\circ$ , and was completely fused at  $125^\circ$ , was heated for three hours at  $180^\circ$  to complete the interaction. The alcoholic solution of the product, filtered to remove a trace of impurity, gave, after evaporation of the solvent, a crystalline residue of pure methylguanidine hydrochloride. The dry salt is very hygroscopic (Found: Cl = 32.48.  $C_2H_7N_3.HCl$  requires Cl = 32.41 per cent.). A platinichloride was prepared, deep orange-red, stout, rhombic prisms which melted at  $175^\circ$  [Found: Pt = 35.18.  $(C_2H_7N_3)_2.H_2PtCl_6$  requires Pt = 35.11 per cent.]. Schenck (*loc. cit.*) gives m. p.  $194$ — $195^\circ$  for the corresponding platinum salt prepared from methylguanidine obtained by the action of methylamine on *s*-methylthiocarbamide. The picrate, pale yellow, spherical

aggregates, decomposed at  $285^{\circ}$  without melting. The formation of methyldiguanide hydrochloride, as an intermediate product, in the above reaction was not considered of sufficient interest for further investigation.

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