2. Monobromo-juglone is converted into monochloro-juglone by the action of hydrochloric acid in alcoholic solution. Its benzoate was prepared.

3. Bromination of monobromo-juglone in hot glacial acetic acid solution gives a dibromo-juglone. It also gave a benzoate.

4. Dibromo-juglone becomes dichloro-juglone by the action of hydrochloric acid in alcoholic solution.

5. One bromine atom in dibromo-juglone is replaced by hydroxyl when treated with alcoholic sodium hydroxide.

CHAPEL HILL, NORTH CAROLINA

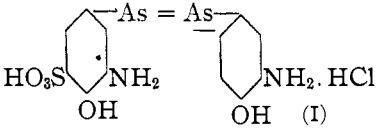
[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY, HARVARD MEDICAL SCHOOL]

THE SULFUR CONTENT OF ARSPHENAMINE AND ITS RELATION TO THE MODE OF SYNTHESIS AND TOXICITY. III[1]

BY WALTER G. CHRISTIANSEN

Received July 11, 1922

In continuing the investigation of the formation of sulfur compounds during the reduction of 3-nitro-4-hydroxy-phenylarsonic acid to arsphenamine base by sodium hydrosulfite, the action of pure hydrosulfite[2] has been examined to determine whether the presence of the sulfonic acid[3]



(I)

in arsphenamine is due to the action of the hydrosulfite or of the impurities present in commercial samples. When the reduction was carried out under the conditions favoring the formation of relatively toxic products with high sulfur content, the results were in fair agreement with those obtained using commercial hydrosulfite (Table I).

A known[4] characteristic of this type of arsphenamine is the deposition of a solid, mainly the sulfonic acid (I), when a methyl alcohol solution

[1] This is the ninth of a series of studies on the properties contributing to the toxicity of arsphenamine being made under a grant from the United States Interdepartmental Social Hygiene Board to the Harvard Medical School; the work is under the general direction of Dr. Reid Hunt, who is also responsible for the biological tests reported in this paper.

[2] Christiansen and Norton, *J. Ind. Eng. Chem.* (To be published soon.)

[3] King, *J. Chem. Soc.*, **120**, 1107, 1414 (1921), found this substance in English commercial samples of arsphenamine; it was shown later that it forms only when the nitro acid is reduced under certain conditions; THIS JOURNAL, **44**, 847 (1922).

[4] Fargher and Pyman, *J. Chem. Soc.*, **117**, 370 (1920). King, Ref. 3. Christiansen THIS JOURNAL, **44**, 854 (1922).

of the material is allowed to stand. Samples prepared by using purified or commercial hydrosulfite behave similarly in this respect. Although the average tolerated dose and sulfur content are slightly higher when purified

TABLE I

USE OF COMMERCIAL AND PURE HYDROSULFITE IN PREPARING RELATIVELY TOXIC ARSPHENAMINE[5]

Hydrosulfite		Expt.	Av. tol. dose	Limit of tol. dose	Av. S. content	Limit of S content
			Mg./kg.	Mg./kg.	%	%
Commercial.....	80–87%	7	62[a]	50–85	2.08	1.40–3.03
Purified.....	97%	8	82	50–100	2.61[b]	2.11–3.42

[a] In 13 similar expts., av. tol. dose = 62 (30–80).

[b] Only 3 samples were analyzed.

hydrosulfite is used, the development of toxicity and the formation of I during the reduction of the nitro acid to arsphenamine is not due to the presence of impurities in hydrosulfite but to the hydrosulfite itself.

In giving the directions[5] for the preparation of relatively toxic products, it was recommended that immediately after the addition of the hydrosulfite to a slowly stirred, warm (30°) solution of magnesium chloride in water the nitro solution, also at 30°, should be added rapidly. Obviously, the amount of hydrosulfite dissolved at this moment will depend partly on its coarseness. When some very coarse purified material was used in this way, the product was tolerated at 100 mg./kg., whereas by powdering this hydrosulfite and using it at once a product tolerated at 80 was obtained.

It was thought that in the reduction of the nitro acid to arsphenamine with a high sulfur content, samples of the base formed during the different periods of the reduction might have different sulfur contents and toxicities (Table II).

TABLE II

BASE FORMED AT DIFFERENT INTERVALS DURING REDUCTION

Period of formation Time after 55° was reached	S	Tol. dose
Min.	%	Mg./kg.
Start — 5	2.04	80
5–35	2.11	...
35–90	2.73	60–70

Evidently the base secured during the latter part of the reaction has a higher sulfur content than that secured at first but of approximately the same toxicity.

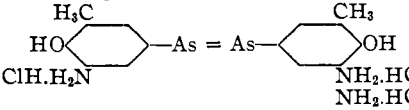
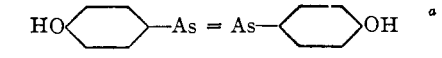
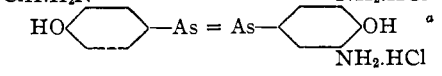
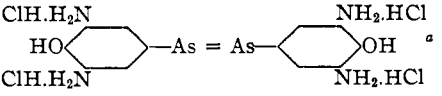
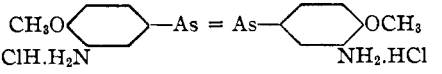
Upon investigating several arseno compounds closely related to arsphenamine it was found that the relation found between the mode of synthesis and sulfur content of arsphenamine holds true in these cases also, and that the results obtained with arsphenamine are typical for this class

[5] The preparation of this type of sample is described in THIS JOURNAL, **43**, 2208 (1921).

of arseno compounds. In Table III several arseno compounds are compared with arsphenamine; in each case the results vary in the same direction as those found for arsphenamine, and the lowest sulfur content is found when the amino acid is reduced. It appears, therefore, that from both the toxicological[4] and chemical viewpoints compounds of the arsphenamine class are best prepared from the pure amino acid.

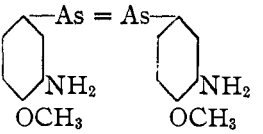
TABLE III

ARSENO COMPOUNDS OF THE ARSPHENAMINE TYPE

Substance	From amino acid %S	From nitro acid under the Most favorable conditions %S	Least favorable conditions %S
Arsphenamine	0.43	0.80	2.08
	..	0.55	1.05
 [a]	0	..	0.98
 [a]	0.39	..	1.40
 [a]	0.35	..	1.10
	0.47	..	..

[a] The preparation of these substances is discussed in THIS JOURNAL, **43**, 2209 (1921).

When the nitrohydroxy acid is dissolved in alkali prior to reduction to arsphenamine it is present mainly in the quinoid form as shown by the red color of the solutions (the solution of the monosodium salt is yellow) and by the fact that 2.2 mols. of caustic soda are used in preparing the solution. Reduction of 3-nitro-4-methoxy-phenylarsonic acid (a compound in which the hydroxyl hydrogen has been fixed by methylation) with hydrosulfite under the most favorable conditions for the production of arsphenamine from the nitrohydroxy acid instead of yielding a copious precipitate of the arseno base, as in the case of the unmethylated acid, yields a yellow, only slightly turbid solution. After cooling, the addition of sodium chloride to this solution causes the separation of a yellow arseno compound which, after washing with saturated salt solution and drying in a vacuum, can be purified and converted into its hydrochloride by precipitating with ether a solution of it in methyl alcoholic-hydrochloric acid. The final product dissolves readily in water to a clear yellow solution and

contains 3.47% S. As the compound  separates as a solid in the usual manner when the amino-methoxy acid is reduced by hydrosulfite the difficulties encountered in isolating reduction products from the nitro acid are not due to any peculiar properties of this arseno compound but to side reactions occurring during the reduction of the nitro group. To check this result, the 4-arsonic acid derivative of 2-nitro-phenoxyacetic acid, that is, 3-nitro-4-hydroxy-phenylarsonic acid with its hydroxyl hydrogen fixed by a $-CH_2CO_2H$ group, was reduced by hydrosulfite. In this case no insoluble arseno base separated during the reduction and nothing is precipitated by subsequent treatment of the yellow solution with salt. That the formation of a soluble arseno base is not due to the presence of the $-CH_2CO_2H$ group in itself but rather to its effect upon the reduction of the nitro group is evident from the fact that the 4-arsonic acid derivative of phenoxyacetic acid is readily reduced by hydrosulfite with the separation of *p*-arseno-phenoxyacetic acid as a solid.[6]

In view of these results the effect of fixation of the hydroxyl hydrogen in similar nitro arsonic acids was investigated. Above it is stated that 3-nitro-4-hydroxy-5-methyl-phenylarsonic acid is reduced by hydrosulfite to an arseno compound and the results are comparable with those obtained with 3-nitro-4-hydroxy-phenylarsonic acid. When 3-nitro-4-methoxy-5-methyl-phenylarsonic acid is reduced the reaction proceeds exactly as in the case of the methoxy compound discussed above, and the hydrochloride, prepared from the base which is salted out, contains 3.68% of S. Fargher[7] found that 3-nitro-4-hydroxy-5-methoxy-phenylarsonic acid was reduced normally by hydrosulfite to an arseno compound, but from 3-nitro-4,5-dimethoxy-phenylarsonic acid nothing could be isolated and from the 3-nitro-4-methoxy-5-hydroxy acid only a polyarsenide, formed by decomposition of some primary reduction product, was obtained.

From these results it is evident that in this class of arsonic acids those substances having a free hydroxyl group *ortho* to the nitro group, that is, those substances capable of existing in the quinoid form can be reduced easily by hydrosulfite to arseno compounds with fairly low sulfur content. However, fixation of the hydroxyl hydrogen atom causes side reactions to set in during the reduction of the nitro group, as a result of which the arseno bases are more difficult to isolate and, when isolable, have a high sulfur content. In the case of 3-nitro-4,6-dimethoxy-phenylarsonic acid the base separates unaided during the hydrosulfite reduction, but even

[6] Bertheim, "Handbuch der Organischen Arsenverbindungen," F. Enke, **1913**, p. 151.

[7] Fargher, *J. Chem. Soc.*, **118**, 866 (1920).

when prepared under the best conditions the purified hydrochloride of the arseno compound contains 1.91% of S; this is as high as that found when 3-nitro-4-hydroxy-phenylarsonic acid is reduced under the poorest conditions.

It is not improbable that the abnormalities found in reducing certain arsonic acids with hydrosulfite are closely connected with the formation of sulfamic acids[8] during the reduction of the nitro group and that the presence of a sulfonic acid group attached to the ring (demonstrated in the case of arsphenamine[3]) results from the rearrangement of a sulfamic acid. In this connection it is interesting to note that those methoxy-arseno compounds which, in this research, were found difficult to isolate contained considerable sulfur. The formation of a sulfamic acid during these reductions is in agreement with the properties of these substances. Weil and Moser[9] state that in many cases, possibly invariably, sulfamic acids are the primary products of the action of sodium bisulfite on aromatic nitro compounds. It is known that these compounds in acid solution quickly and smoothly undergo hydrolysis or rearrangement depending upon the nature of the substance and the conditions of the experiment. Bamberger[10] found that from β-phenylhydroxylamine, phenylsulfamic acid ($C_6H_5NHSO_3H$) could be obtained by the action of sulfurous acid and that this substance rearranges with the sulfonic acid group entering the ring; and Bucherer[11] states that hydroxylamines may be intermediates in the formation of sulfamic acids from nitro compounds. When hydrosulfite is used in aqueous solution considerable sulfurous acid is generated which could react with an hydroxylamine formed from the nitro group thereby producing a sulfamic acid. This substance in the warm solution, acid due to the action of water on the hydrosulfite, could rearrange to a sulfonic acid. The position taken by the sulfonic acid group would depend upon the nature of the substance in question. In the arsphenamine this group is in the 5 position, *meta* to the nitrogen atom. This is rather unexpected but is very similar to the case of 3-nitro-4-hydroxychlorobenzene which upon treatment with sodium hydrogen sulfite yields 3-amino-4-hydroxy-5-sulfochlorobenzene.[12]

Arsenic determinations in arseno compounds were made by Lehmann's method, but in the case of arsonic acids Ewin's method was used, the temperature being raised very slowly to avoid volatilization. Sulfur determinations were made by the peroxide-carbonate fusion, and toxicity determinations by intravenous injection into white rats.

[8] Ref. 7. Fargher and Pyman, *J. Chem. Soc.*, **117**, 372 (1920). Karrer, *Ber.*, **48**, 1061 (1915).

[9] Weil and Moser, *Ber.*, **55B**, 732 (1922).

[10] Bamberger, *ibid.*, **30**, 654, 2274 (1897).

[11] Bucherer, "Lehrbuch der Farbenchemie," Spamer, **1914**, p. 144.

[12] Bauer and Wieland, "Reduktion und Hydrierung organischer Verbindungen," Spamer, **1918**, p. 223.

Experimental

3-Nitro-4-methoxy-phenylarsonic Acid.—*p*-Methoxyphenylarsonic acid[13] is nitrated at 0° in sulfuric acid with 1 mol. of nitric acid diluted with an equal volume of sulfuric acid. After the nitrating acid has been added the temperature is allowed to rise to 10° before the material is diluted with 4 volumes of water; yield, 94%. Purification is readily effected by recrystallization from water.

Analyses. Calc.: As, 27.05. Found: 27.15, 27.18, 26.86.

3-Nitro-4-hydroxy-5-methyl-phenylarsonic Acid.—The monosodium 4-hydroxy-5-methyl-phenylarsonate, prepared by arsonation of *o*-cresol, is nitrated as described above. After purification by acidification of a filtered solution of the crude material in aqueous caustic soda, an 81% yield of fine yellow needles is obtained.

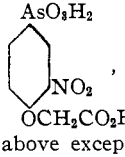
Analyses. Calc.: As, 27.06. Found: 26.73, 27.31, 27.05.

4-Methoxy-5-methyl-phenylarsonic Acid.—The monosodium 4-hydroxy-5-methyl-phenylarsonate is methylated in alkaline solution with dimethylsulfate following the method used for the *p*-hydroxy-phenylarsonate;[13] a 75% yield of crude material is secured. By recrystallization from water, white feathery needles are obtained which do not melt below 260°.

Analysis. Calc.: As, 30.52. Found: 30.10.

3-Nitro-4-methoxy-5-methyl-phenylarsonic Acid.—4-Methoxy-5-methyl-phenylarsonic acid is nitrated as above except that the temperature is permitted to rise to 15° instead of 10° after the nitrating acid has been added. After purification by acidification of a filtered alkaline solution a 70% yield of fine pale yellow needles is obtained.

Analyses. Calc.: As, 25.77. Found: 25.64, 25.61.

3-Nitro-4-carbomethoxy-phenylarsonic Acid,  , is obtained from *p*-carbomethoxy-phenylarsonic acid[14] by nitration as above except that the temperature is allowed to rise to 20° after the nitrating acid has been added. After recrystallization from water a 75% yield of coarse yellow prisms is obtained; this substance is very soluble in hot water but quite difficultly so in cold water.

Analyses. Calc. for $C_8H_8O_8NAs.H_2O$: As, 22.12; H_2O, 5.31. Found: As, 22.25, 22.08, loss at 105°, 5.39, 5.31.

2,4-Dimethoxy-phenylarsonic Acid.[15]—Resorcinolarsonic acid (25 g.) is treated in alkaline solution with an excess of dimethyl sulfate at 30–50°. By acidification with hydrochloric acid 8 g. of white solid melting at 209–217° is secured which with water and ferric chloride gives a slight red color; 2-methoxy-4-hydroxy-phenylarsonic acid melts at 209° and the parent substance gives a very deep red color with ferric chloride. Evidently only partial methylation is obtained. An alkaline solution of this partially methylated material is treated on a steam-bath with an excess of dimethyl sulfate. After 3½ hours, acidification with hydrochloric acid and cooling in the ice-box overnight yields 7.4 g. of white solid melting at 238–239° (uncorr.), giving no coloration with ferric chloride, and crystallizing from 50% acetic acid in stout white needles. Bauer gives the melting point as 242–243°.

3-Nitro-4,6-dimethoxy-phenylarsonic Acid.—The dimethoxy acid is nitrated as

[13] Bertheim, *Ber.*, **47**, 271 (1914).

[14] Ref. 6, p. 116.

[15] Bauer, *C. A.*, **9**, 1778 (1915).

previously described. The crude product is dissolved in dil. aqueous caustic soda, and the clear yellow solution—the absence of any red coloration is a further indication of complete methylation of the hydroxyl groups—is acidified with hydrochloric acid; white feathery needles with a slight tinge of greenish-yellow are obtained in 77% yield.

Analysis. Calc.: As, 24.42. Found: 24.17.

As Bauer showed[15] that upon nitration of 2,4-dihydroxy- and 2-methoxy-4-hydroxy-phenylarsonic acids the nitro group entered the ring in the 5 positions, it would be anticipated that the same would hold true for the dimethoxy compound.

3-Aceto-amino-4-methoxy-phenylarsonic Acid.—3-Aceto-amino-4-hydroxy-phenylarsonic acid (7.8 g.), obtained by acetylation of the amino acid, is dissolved in 10 cc. of water and 8.7 cc. of 10 *N* caustic soda solution, and stirred mechanically. Dimethyl sulfate (4.2 cc.) is added. After 35 minutes 4.3 cc. of aqueous caustic soda and 4.3 cc. of dimethyl sulfate are added; after 45 minutes the same amounts of alkali and dimethyl-sulfate are again added. The temperature is kept at 20–30°. At the end of $2^1/_4$ hours, 5 cc. of hydrochloric acid (sp. gr. 1.19) is added and after thorough cooling for 2 hours, the precipitate is separated by filtration; yield, 7.9 g. of gray solid.

To purify the product it is dissolved in dil. caustic soda solution containing 2 drops of hypophosphorous acid, and the brown solution is treated with a little Superfiltchar. The slightly colored filtrate from the carbon is made distinctly acid to congo red. From 2 g. of crude material 1.7 g. of white product is obtained.

Analysis. Calc.: As, 25.95. Found: 26.11.

That the hydroxyl group has been methylated can be shown by warming a suspension of the product in dil. hydrochloric acid until hydrolysis of the acetyl group is complete and then adding potassium iodide and hypophosphorous acid. The warm solution soon becomes clear yellow and when caustic soda is added a heavy yellow precipitate, insoluble in excess alkali, is obtained.

In addition, a hydrochloric acid solution of the hydrolyzed material gives an orange color when treated with *p*-dimethylamino-benzaldehyde, and with sodium nitrite gives no precipitate but a slightly yellow solution which in turn gives a very deep red color when added to an alcoholic solution of α-naphthylamine hydrochloride. These tests indicate the absence of methylation of the amino group.

3,3'-Diamino-4,4'-dimethoxy-arsenobenzene Dihydrochloride.—In preparing this substance the aceto-aminomethoxy acid described above is hydrolyzed in hydrochloric acid, and this solution, after being made alkaline, is reduced at once with sodium hydrosulfite. It was found impracticable to isolate the aminomethoxy acid.

A suspension of 4 g. of the aceto-aminomethoxy acid in 30 cc. of water and 3.5 cc. of hydrochloric acid (sp. gr. 1.19) is heated with mechanical agitation in a bath of boiling water. After 40 minutes the solid is completely dissolved; the heating is continued for 10 minutes to insure complete hydrolysis. After cooling, about 1 g. of Superfiltchar is added, and by filtration, a slightly yellow solution is secured. Conc. sodium hydroxide solution is added until the solution is only slightly acid to litmus; after evaporation to 20 cc. the solution is cooled in the ice-chest and filtered from a small amount of slimy precipitate. The filtrate is made distinctly alkaline with caustic soda, diluted to 84 cc. and added, at room temperature with vigorous mechanical agitation, to a solution of 10 g. of magnesium chloride hexahydrate in 238 cc. of water to which 46 g. of sodium hydrosulfite has been added. After filtration, the experiment is continued under the conditions used to prepare arsphenamine from the amino acid.[4] The dried, powdered arseno base had a marked tendency to be lost by mechanical agitation.

The base (1.8 g.) is dissolved in absolute methyl alcoholic hydrochloric acid and the clear yellow solution is precipitated by pouring into ether. Two g. of dihydrochloride is secured as a yellow powder which dissolves readily in water to give a yellow solution.

The product contains 30.07% of arsenic which agrees, as in the case of the other arseno compounds investigated,[15] with the value calculated for material containing 2 mols. of water, 29.82%. The sulfur content was found to be 0.47%.

An aqueous solution of the product gives a yellow insoluble precipitate with an excess of sodium hydroxide solution which dissolves to a colorless solution when oxidized with iodine. Sodium sulfate precipitates the sulfate and sodium acetate the base when added to the water solution of the hydrochloride. With *p*-dimethylamino-benzaldehyde, an orange-colored precipitate forms. A dilute solution acidified with hydrochloric acid becomes yellow when diazotized with sodium nitrite, and this solution couples in alcoholic solution with α-naphthylamine hydrochloride with the formation of a deep purple color. Ferric chloride causes the solution to become red gradually; the oxidation is slower than in the case of arsphenamine.

When 3-nitro-4-methoxy-phenylarsonic acid is reduced with hydrosulfite under the conditions found most favorable for the production of arsphenamine from the nitro acid,[4] only a very slight precipitate of the arseno base is secured. If, after the reduction, the solution is cooled to room temperature and treated with sodium chloride (35 g. per 2.1 g. of nitromethoxy acid), a yellow precipitate forms. After 1 hour in the ice-box, this is filtered off and washed with saturated sodium chloride solution. After drying in a vacuum over caustic soda the crude base is suspended in absolute methyl alcohol and treated with methyl alcoholic-hydrochloric acid. The yellow solution obtained by filtration is precipitated by ether. The product is qualitatively like that obtained from the aceto-aminomethoxy acid but contains 3.47% of sulfur. From 2.1 g. of arsonic acid 1.3 g. of arseno compound is obtained.

3,3′-Diamino-4,4′-dihydroxy-5,5′-dimethylarsenobenzene Dihydrochloride. — When 3-nitro-4-hydroxy-5-methyl-phenylarsonic acid is reduced by hydrosulfite (a) under the most favorable, or (b) under the least favorable conditions for the production of arsphenamine from the nitro acid, the reduction apparently proceeds like those by which arsphenamine is obtained. From 4.2 g. of arsonic acid, 2.6 g. of hydrochloride is obtained in (a) and 2.9 g. in (b). Again the arsenic content agrees with that calculated for a substance containing 2 mols. of water.

Analyses. Calc.: As, 29.82. Found: (a) 29.61, (b) 29.10; S, (a) 0.55, (b) 1.05.

When 3-nitro-4-methoxy-5-methyl-phenylarsonic acid is reduced with hydrosulfite the reaction proceeds exactly as in the case of the nitromethoxy acid described above. By following the procedure employed in the case of the previous methoxy compound, 2.2 g. of arsonic acid yields 1.3 g. of hydrochloride which behaves qualitatively like the previous methoxy-amino-arseno compound. It also contains 3.68% of sulfur.

3,3′-Diamino-4,4′,6,6′-tetramethoxy-arsenobenzene Dihydrochloride.—3-Nitro-4-6-dimethoxy-phenylarsonic acid is reduced with hydrosulfite under the conditions found most favorable for the reduction of the nitro acid to arsphenamine. The hydrochloride is obtained by dissolving the base in methyl alcoholic hydrochloric acid and precipitating with ether. From 2.3 g. of the nitrodimethoxy acid 1.4 g. of pale yellow arseno compound is secured.

Analyses. Calc. for the 2 H_2O salt: As, 26.64. Found: 26.09, S, 1.91.

Summary

In reducing 3-nitro-4-hydroxy-phenylarsonic acid to arsphenamine, the formation of relatively toxic products with a high sulfur content is not due to impurities in commercial sodium hydrosulfite. The arsphen-

[15] Ref. 4, p. 2207.

amine base is fairly uniform in regard to toxicity and sulfur content irrespective of the period of formation during the reduction.

Amino hydroxyarseno compounds in general contain the fewest sulfur atoms when prepared from the amino acids.

Fixation of the hydroxyl hydrogen in the nitrohydroxyarsonic acids tends to make the hydrosulfite reduction abnormal, and the products, when isolable, contain more sulfur than analogous substances prepared without fixation of this hydrogen atom. The hydroxyl hydrogen *ortho* to the nitro group seems to play an important role in the formation of arseno compounds of the type under consideration.

Probably the sulfonic acid group found in certain samples of arsphenamine enters the ring by way of the nitrogen atom with the intermediate formation of a sulfamic acid.

I wish to thank Dr. Reid Hunt for determining the toxicity of the samples involved in this work and Mr. Arthur J. Norton for his assistance in purifying the hydrosulfite and analyzing some of the substances obtained.

BOSTON, MASSACHUSETTS

[CONTRIBUTION FROM THE FIXED NITROGEN RESEARCH LABORATORY]

MECHANISM OF GUANIDINE FORMATION IN FUSED MIXTURES OF DICYANODIAMIDE AND AMMONIUM SALTS

BY J. S. BLAIR AND J. M. BRAHAM[1]

Received July 13, 1922

Introduction

In the course of an investigation on the use of calcium cyanamide as a source of nitroguanidine and other guanidine derivatives, some experiments were performed in which dicyanodiamide was fused with various ammonium salts, with the original purpose of determining the feasibility of this method for the production of guanidine salts. Their formation in this manner has been described by several investigators, but the optimum conditions for guanidine production had not at that time been ascertained. Our work along these lines was soon discontinued,[2] however, since it was learned that the method was being investigated in another laboratory.[3]

However, our preliminary experiments had led us to a conception as to the reactions occurring on fusion of dicyanodiamide with ammonium

[1] Assistance in the analytical work given in this paper was rendered by C. D. Garby and L. A. Pinck.

[2] The production of guanidine salts from calcium cyanamide by a more direct method was then studied and will form the subject of a later paper.

[3] Massachusetts Institute of Technology. See Davis, THIS JOURNAL, **43**, 2234 (1921).