CCLXXX.—The Constitution of Carbamides. Part XIV. The Decomposition of Urea by Sodium Hypobromite in Alkaline Solution, and an Improved Procedure for the Estimation of Urea by this Means.

By EMIL ALPHONSE WERNER.

WHEN urea is decomposed by 'alkaline hypobromite,' under the conditions usually adopted, it is well known that the change represented by the equation

(1)
$$\operatorname{CON}_{2}\operatorname{H}_{4} + 3\operatorname{NaBrO} + 2\operatorname{NaOH} =$$

 $\operatorname{N}_{2} + \operatorname{Na}_{2}\operatorname{CO}_{3} + 3\operatorname{NaBr} + 3\operatorname{H}_{2}\operatorname{O},$

is not quantitatively realised in practice.

A deficiency, roughly of 8 per cent., in the volume of nitrogen evolved was the first failing recognised.

Fenton (T., 1878, **33**, 300; 1879, **35**, 12) and Foster (T., 1879, **35**, 120) showed that this was due to the fixation of a portion of the nitrogen as alkali cyanate during the progress of the reaction. Fauconnier (*Bull. Soc. chim.*, 1880, [ii], **33**, 103) directed attention to the formation of a small amount of nitric acid during this decomposition of urea. Luther (*Z. physiol. Chem.*, 1889, **13**, 500) claims to have shown that from 3 to 4 per cent. of the nitrogen was oxidised to nitric acid when urea was decomposed by an excess of barium hypobromite. From the results recorded in the present paper, it is certain that this amount of nitrogen was not 'fixed' as nitrate when urea was decomposed by sodium hypobromite in alkaline solution.

Whilst Krogh (Z. physiol. Chem., 1913, 84, 379) noted the presence of carbon monoxide as a product of the reaction, Hurtley (Biochem. J., 1921, 15, 11) showed that the gas evolved from a 2 per cent. solution of urea, when attacked by 'hypobromite' of the usual

strength, contained on an average 0.7 per cent. of carbon monoxide. Since this approximately compensates for the nitrogen fixed as nitrate, it is obvious that, so far as the estimation of urea is concerned, the formation of alkali cyanate is the chief disturbing effect in the reaction.

Considering the numerous investigations which this decomposition of urea has called forth during the last forty years, it is curious that no attempt has hitherto been made to determine directly the volume of nitrogen fixed during the reaction as alkali cyanate. The fact that the formation of the latter has not received the full attention it deserves—particularly from continental investigators—is no doubt responsible for this important omission.

It is obvious that, since a cyanate is produced, neither the amount of carbonate formed nor the amount of 'hypobromite' destroyed could give a result in agreement with the requirements of the above equation (1). Dekeuwer and Lesceur (Compt. rend. Soc. Biol., 1919, 82, 445), apparently without considering this point, have confirmed the fact by direct experiments, whilst Brahm (Chem. Zentr., 1919, iv, 442) advocates the rejection of all methods for the estimation of urea which are based on its reaction with 'alkaline hypobromite.'

The author is not prepared to go so far, since the following procedure has been found to give almost theoretical results.

Two operations being necessary, a nitrometer is the most convenient form of apparatus to use.

The solution of urea is added in the usual manner to a small excess of 'alkaline hypobromite' contained in the nitrometer. After about twenty minutes the volume of gas evolved, having been carefully recorded, is expelled from the nitrometer. Sulphuric acid (1 in 5 of water) is now added to the residual liquid until the latter, after careful mixing, shows the *permanent* presence of free bromine. The carbon dioxide liberated from the solution by this treatment must not * be expelled from the apparatus. After fifteen minutes, to allow for hydrolysis of the cyanic acid set free, in accordance with the change

(2) NaOCN + H_2O + 2HX = NH_4X + NaX + CO_2 ,

sodium hydroxide solution (30 per cent.) is added in excess. Whilst this regenerates 'hypobromite' from the free bromine present, it is nevertheless advisable to add a small quantity of the reagent to the residual solution. After complete absorption of the carbon

^{*} During the process of adding the acid, and mixing the solution, reactions (2) and (3) take place to a small extent, and hence there is loss of some nitrogen if the gas is expelled.

2320 WERNER: THE CONSTITUTION OF CARBAMIDES. PART XIV.

dioxide, the volume of the gas produced, as a result of the reaction

(3) $2NH_4X + 3NaBrO + 2NaOH = N_2 + 3NaBr + 2NaX + 5H_2O$,

is added to the volume of nitrogen recorded in the first stage. In the table of results given below, the two stages are referred to as (a) and (b) respectively.

In each case 0.06 gram of urea was used, equal to 22.4 c.c. N₂ at N.T.P. TABLE I

	Urea	C.c.	of gas at N.	Percentage of total	
Expt.	per cent.	(a)	(b).	Total.	N. in urea.
1	1	20.44	1.84	$22 \cdot 28$	99.46
2	2	20.48	1.88	$22 \cdot 36$	99.82
3	3 .	20.52	1.82	$22 \cdot 34$	99.75
4	6	20.10	$2 \cdot 30$	$22 \cdot 40$	100.00

Allowing for the presence of a small quantity of carbon monoxide in the gas evolved in stage (a), it is evident from the above results that the amount of nitrogen fixed as nitrate cannot be more than about 1 per cent.

The question arises : Can the formation of cyanate be suppressed ? Duggan (J. Amer. Chem. Soc., 1882, 4, 47) obtained volumes of gas, assumed to be pure nitrogen, varying from $99 \cdot 02$ to $99 \cdot 91$ per cent. of the theoretical, by generating the 'hypobromite' in situ with urea. Le Comte (J. Pharm. Chim., 1903, [vi], **17**, 471) claims to have obtained all the nitrogen of urea by a similar procedure.

The following results were obtained when the method proposed by Duggan was completed by the addition of the second stage. In each experiment 0.06 gram of urea was dissolved in 20 per cent. sodium hydroxide solution, after which bromine was added in amount as recommended by Duggan.

TABLE II.

	Urea	C.c.	of gas at $N.T$	Percentage of total	
Expt.	per cent.	(a).	Ŭ (b).	Total.	N. in urea.
ī	0.5	21.81	0.82	22.63	101.0
2	1.0	21.54	0.89	$22 \cdot 43$	100.1
3	$2 \cdot 0$	21.63	0.95	$22 \cdot 58$	100.8
4	3.0	21.87	0.66	$22 \cdot 53$	100.5

Whilst the formation of cyanate is considerably suppressed when the 'hypobromite' is generated in the alkaline solution of urea, the reaction under such condition is extremely violent. All observers agree on the point that excess of alkali promotes the decomposition of urea by hypobromite, and Krogh and Hurtley (*loc. cit.*) showed that the volume of carbon monoxide evolved increased with the alkalinity of the reagent. The excess of gas over the theoretical value for nitrogen in the above experiments was due to this fact.

The Decomposition of Urea by Alkaline Hypobromite in the Presence of Dextrose.

Méhu (Compt. rend., 1879, 89, 175) claimed that all the nitrogen (?) of urea was evolved when the decomposition by 'alkaline hypobromite' was effected in the presence of dextrose. Supported by the fact that the sugar alone does not evolve any gas when mixed with the reagent, Méhu's procedure has been adopted in certain quarters for the estimation of urea, on the assumption that dextrose enhances the evolution of nitrogen. The following results clearly prove that it does nothing of the kind.

Pure dextrose was added to 0.06 gram of urea in 3 c.c. of water, after which an excess of alkaline * hypobromite was added, the experiments being completed by the addition of the second stage. Theoretical yield of $N_2 = 22.4$ c.c. at N.T.P.

TABLE III.

Expt. Urea Dextrose (a) (b) Total i	Percentage of total N.
	n urea.
1 0.06 nil 20.42 1.84 22.26	99.37
2 ,, 0.06 20.88 1.96 22.84	l01∙96
3 ,, 0·12 21·34 1·93 23·27	L03·88
4 ,, 0.18 21.92 1.97 23.89	l06·65
5 ,, 0.24 22.34 1.92 24.26	L08·30

It will be seen that whilst the addition of dextrose leads to a proportionate increase in the volume of gas set free in the first stage, its presence has practically no effect on the volume of gas liberated in the second stage. Therefore, since dextrose does not prevent the formation of cyanate, it cannot promote evolution of nitrogen which is fixed from this cause during the primary reaction. The gradual increase in the volumes of gas under (a) was due to carbon monoxide, the presence of which was proved by the usual tests for this gas. Whilst it is true that no carbon monoxide was evolved when alkaline hypobromite was added to dextrose alone, that is, within a reasonable lapse of time, this gas was always generated in appreciable quantity when a salt of ammonia was decomposed by the reagent in the presence of dextrose. This is an interesting point, since more or less cyanic acid is formed, as a result of the reaction

(4) $CO + NH_3 + O = NH:CO + H_2O$.

* Since oxidation of the sugar gives rise to much carbon dioxide, the absorption of this gas was ensured by adding a little extra alkali.

VOL. CXXI.

By means of the method adopted for stage (b), the amount of cyanic acid generated in this way was easily determined.

The results given below were obtained by adding an excess of alkaline hypobromite to 0.0535 gram of ammonium chloride, and the stated amounts of dextrose, dissolved in 3 c.c. of water. A control experiment with the ammonium salt alone was made for comparison, since the theoretical yield of nitrogen was not evolved, on account of the fixation of a portion as nitrate. Theoretical yield of $N_2 = 11.2$ c.c. at *N.T.P.*

TABLE IV.

						Calculated
						on percentage
			C.c.	of gas at N.	T.P.	of nitrogen in
Expt.	NH₄Cl.	Dextrose.	(a).	<i>(b)</i> .	Total.	NH₄Čl.
1	0.0535	nil	10.95	no gas	10.95	97.76
2	,,	0.03	10.58	0.80	11.38	101.60
3	,,	0.06	10.35	1.29	11.64	103.96
4	,,	0.09	10.22	1.87	12.09	107.94
5	,,	0.12	10.11	$2 \cdot 13$	12.24	109.28

When compared with the results given in Table III, it will be seen that in spite of the fact that the gas evolved in stage (a) contained carbon monoxide (except experiment 1), the volume of gas diminished as the proportion of dextrose was increased. The results of stage (b) prove that this was due to the relatively large proportion of nitrogen fixed as cyanate in accordance with equation (4). In the case of experiment 5, for example, 18.99 per cent. of the theoretical yield of cyanic acid was generated during the decomposition of the ammonium salt in the presence of the stated amount of dextrose. If the reaction under consideration is essentially an oxidation change, this result goes to show that a strong tendency must exist towards the realisation of equation (4). On the other hand, since alkaline hypobromite must act as a brominating agent as well, the formation of cyanic acid in the manner

$\rm CO + NH_2Br + NaOH \longrightarrow CO:NH + NaBr + H_2O$

must not be overlooked.

Any compound capable of yielding ammonia during its decomposition by 'alkaline hypobromite' would obviously tend to generate cyanic acid in the presence of dextrose. On comparing the values for stage (b) in experiments 1, 2, and 3 (Table I), with those in Table III, it will be seen that, all other conditions being equal, or nearly so, the proportion of nitrogen fixed as cyanate was distinctly higher when dextrose was present. Thus in this respect the sugar exerts a function the very opposite of that which it has been supposed to possess.

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WERNER: THE CONSTITUTION OF CARBAMIDES. PART XIV. 2323

Considering that any easily oxidisable carbon compound is liable to give more or less carbon monoxide by the action of 'hypobromite,' the discordant results which have been obtained in the estimation of urea in urine by this method are not surprising.

An example of the results obtained with a sample of normal urine, when stage (b) was applied, is given below.

A. Urine (3 c.c.) added to excess of 'hypobromite.'

B. Hypobromite in excess added to urine.

Vol. of gas at N.T.P.

	-	Total.	Urea per cent.
A.	(a) = 21.90 c.c. $(b) = 2.89$ c.c.	24·79 c.c.	$2 \cdot 21$
В.	(a) = 21.68 , $(b) = 2.82$,	24.50 "	$2 \cdot 18$

Comparing the results with those for a 2 per cent. solution of urea (expt. 2, Table I), it is found that whilst with urine the ratio of nitrogen fixed as cyanate to nitrogen evolved in stage (a) is 1:7.57, it is 1:10.89 in the case of the plain urea solution. Whilst this difference has been confirmed by a number of experiments, the fact is merely recorded here. Its significance will be dealt with on another occasion.

Urea and Neutral Hypobromite Solution.

Sixteen grams of bromine were added to 50 c.c. of 4N-sodium hydroxide solution cooled to 0° ; 15 c.c. of the solution were added to 0.06 gram of urea in 2 c.c. of water contained in the nitrometer. No gas was evolved after the mixture had remained for five minutes. On the addition of 2 c.c. of sodium hydroxide solution (20 per cent.). there was an immediate brisk evolution of gas equal to 12.1 c.c. at N.T.P. The yellow colour of the solution was destroyed and excess of urea remained. Had sodium hypobromite been formed in theoretical yield according to the equation 2NaOH + $Br_2 = NaBrO + NaBr + H_2O$, 1.5 c.c. of the solution, after addition of alkali, would have sufficed to decompose the whole of the urea taken. The result shows that only slightly more than 5 per cent. of the theoretical amount of 'hypobromite' was formed. The estimation of the latter by the addition of an excess of urea is a more accurate process than the reverse operation, since the only source of error is due to the small amount of carbonmonoxide evolved.

Sixteen grams of bromine were added to 50 c.c. of 8N-sodium hydroxide solution, that is, to give NaBrO:2NaOH; 2 c.c. of the solution were more than sufficient to decompose 0.06 gram of urea. The results obtained were: stage (a) = 19.9 c.c., stage (b) = 2.45 c.c., equal to 99.77 per cent. of the theoretical.

Thus whilst an excess of alkali is necessary to promote the form- $4 \ge 2$

ation of the theoretical yield of sodium hypobromite as represented in the above equation, it is also essential to initiate the decomposition of urea. Neutral 'hypobromite' does not liberate nitrogen from urea in the cyclic form. A change to the configuration $HN:C(OH)\cdot NH_2$ must precede the decomposition, which is no doubt the result of bromination, hydrolysis, and oxidation following each other with such great velocity as to be practically simultaneous.

When the reaction is slowed down, the proportion of cyanate formed is considerably increased, as shown by the following result. An excess of neutral 'hypobromite' was added to 0.06 gram of urea in 2 c.c. of water. No gas was evolved. Sodium hydroxide solution (20 per cent.) was gradually added until evolution of gas ceased.

Result: (a) = 15.74 c.c., (b) = 6.92 c.c. at N.T.P. Total = 22.66 c.c., or 101.1 per cent. of total nitrogen of urea. Approximately 30 per cent. of the nitrogen was fixed as cyanate during the decomposition of urea in stage (a) under the above conditions. The presence of carbon monoxide was responsible for the excess of gas over the theoretical.

The Mechanism of the Urea-Hypobromite Reaction.

So far as the mechanism of this reaction is concerned, whilst rapid decomposition of an unstable bromourea formed in the first instance gives rise no doubt to the products of the main change, it is evident that the tendency of urea to decompose into ammonia and cyanic acid is a prominent feature of the reaction. The change in this direction is promoted by a low concentration of alkali, whereby the velocity of the reaction is reduced.

Schestakov's discovery (J. Russ. Phys. Chem. Soc., 1905, **37**, 1) that hydrazine is formed when urea is attacked by alkaline sodium hypochlorite at about 5° has led to the suggestion that the oxidation of this substance represents the ultimate source of the nitrogen in the decomposition of urea by hypochlorites, or hypobromites in alkaline solution under the conditions usually employed. This view is not in agreement with the fact that the nitrogen fixed as cyanate is greatly increased when the velocity of the reaction is slowed down. As a matter of fact, sodium cyanate was formed in considerable amount in several repetitions of Schestakov's experiment.* The evidence is in favour of the

^{*} With respect to the large yield of hydrazine claimed by Schestakov, this has never been confirmed. Experiments made in the author's laboratory gave a very much smaller quantity than that stated. This appears to have been the experience of others (compare Fenton, Ann. Reports, 1905, 2, 96).

view that hydrazine is the product of a secondary reaction. For this reason the author is not inclined to give the attention which Hurtley (*loc. cit.*) has given to its formation in explaining the origin of carbon monoxide during the decomposition of urea by 'hypobromite.' A bromourea generated in the presence of alkali could have but an ephemeral existence. Simultaneous hydrolysis and oxidation would complete its decomposition, according to the equation

 $HN:C(OH)\cdot NHBr + O_2 + NaOH = N_2 + CO_2 + NaBr + 2H_2O.$

During the violent disruption of such a compound, it is conceivable that by-products may arise as a result of its direct decomposition in two different directions, thus :

- (1) HN:C(OH)·NHBr \rightarrow (HO·CN \rightleftharpoons HNCO) + NH₂Br.
- (2) HN:C(OH)·NHBr \rightarrow HBr + ···HN·CO·NH····.

Hydrolysis of \cdots HN·CO·NH··· at the moment of its generation would give rise to carbon dioxide and hydrazine, whilst incomplete oxidation would be represented by the change \cdots HN·CO·NH·· + $O = N_2 + CO + H_2O$. In the case of Schestakov's experiment, the formation of hydrazine from the interaction NH₃ + NH₂Cl = N₂H₄,HCl must not be overlooked. It is during a violent reaction that one would expect carbon monoxide to escape oxidation. The facts support this conclusion. Krogh (*loc. cit.*) found a greater evolution of carbon monoxide when the 'hypobromite' was very rich in alkali, and Hurtley (*loc. cit.*) showed that much less of this gas was present with the nitrogen evolved from the decomposition of urea by a hypochlorite than by a hypobromite.

UNIVERSITY CHEMICAL LABORATORY, TRINITY COLLEGE, DUBLIN.

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