

STUDIES ON THE ANALYSIS AND CHEMISTRY OF NEOARSPHENAMINE II. STUDIES ON THE CHEMISTRY OF SODIUM FORMALDEHYDESULPHOXYLATE AND THEIR RELATION TO THE STRUCTURE OF NEOARSPHENAMINE.*

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Up to the present time little has been known of the structure of neoarsphenamine other than to assume that it represents a condensation product of one or two molecules of sodium formaldehydesulphoxylate and one molecule of arsphenamine base. Previous results (1) have shown that two distinct types of "sulphoxylate" derivative might be formed in this reaction, namely, the *N* methylene substitution product and the double salt form. It is the former type with which this discussion is concerned, and in order to obtain some information regarding the nature of the linkage between the amino group of the arsphenamine nucleus and the sodium formaldehydesulphoxylate, it was necessary to obtain information concerning the structure of sodium formaldehydesulphoxylate. A number of investigators have found that neoarsphenamine is unstable in strong acid; "neoarsphenamine acid" precipitates and undergoes a decomposition whereby sulphoxylate is lost. Furthermore, the liberated sulphoxylate is decomposed simultaneously. Consequently it seemed desirable to investigate the effect of strong acid and strong alkali on sodium formaldehydesulphoxylate with the hope that evidence might be obtained bearing on its structure.

EXPERIMENTAL.

Solutions of purified sodium formaldehydesulphoxylate in oxygen-free water were maintained at 25° C. under an atmosphere of nitrogen and treated with sodium hydroxide in one case and hydrochloric acid in another. In each instance the effects of two concentrations of the reagent were studied. Aliquot portions were withdrawn from time to time and analyzed for reducing power with one-tenth normal iodine and for free alkalinity or acidity, as the case might be, using phenolphthalein as an indicator. In all experiments the solutions were neutralized to phenolphtha-

TABLE I.—EFFECT OF SODIUM HYDROXIDE ON SODIUM FORMALDEHYDESULPHOXYLATE AT 25° C.

Concentrations of alkali in moles per mole sulphoxylate.	Time in hours.	Sodium formaldehydesulphoxylate lost in %.	Sodium hydroxide used up in cc. <i>N</i> /10.
0.524	0	0.00	0.00
0.524	1/2	0.24	0.10
0.524	1	0.32	0.03
0.524	1 1/2	1.04	0.09
0.524	2	0.89	0.15
0.524	18	2.86	0.46
1.298	0	0.00	0.00
1.298	1/2	0.31	0.34
1.298	1	0.00	0.35
1.298	1 1/2	2.80	0.34
1.298	2	0.99	0.36
1.298	18	2.74	0.46

* Scientific Section, A. Ph. A., Rapid City meeting, 1929.

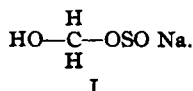
lein before determining the reducing power. The results of these experiments are recorded in Table I and II.

TABLE II.—EFFECT OF HYDROCHLORIC ACID ON SODIUM FORMALDEHYDESULPHOXYLATE AT 25° C.

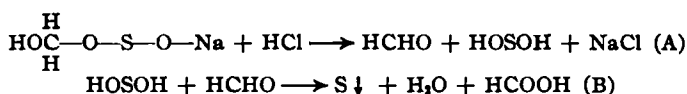
Concentration of acid in moles per mole sulphoxylate.	Time in hours.	Sodium formaldehydesulphoxylate lost in %.	Hydrochloric acid used up in cc. N/10.
0.406	0	0.00	0.00
0.406	1/2	8.95	0.12
0.406	1	10.40	0.08
0.406	1 1/2	14.78	1.23
0.406	2	20.48	1.80
0.406	18	75.20	3.36
1.014	0	0.00	0.00
1.014	1/2	5.26	0.00
1.014	1	6.47	0.33
1.014	1 1/2	9.13	0.00
1.014	2	12.12	0.37
1.014	18	68.72	1.90

The results given in Table I show that in alkaline solution sodium formaldehydesulphoxylate is quite stable; only a small quantity of the alkali originally present is neutralized by acid liberated by the sulphoxylate. Furthermore, the loss in reducing power is small and compares favorably with the loss in neutral solution; at the end of 18 hours only 2.86% of the original reducing power has been lost. It is also noteworthy that in spite of an increase of 150% in the amount of alkali present in the second set of experiments, the loss of sulphoxylate and the liberation of acid is the same as in the first instance. On the other hand, the loss of reducing power in acid solution is very strikingly shown in Table II; it increases with time and reaches 75.20% in one case and 68.72% in the other at the end of 18 hours. Also, the neutralization of the added acid by the sulphoxylate decomposition products is greater than the neutralization of alkali in the case of the alkali decomposition. However, the liberation of alkali in the acidified solutions is small as compared to the decomposition of the sulphoxylate as measured by the loss in reducing power.

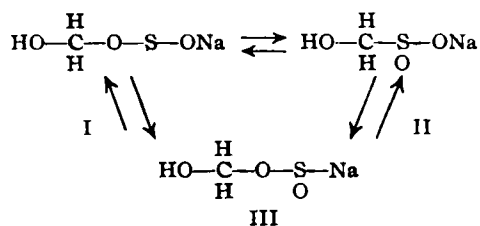
The commonly accepted structure of sodium formaldehydesulphoxylate is given by Jellinck (2) as:



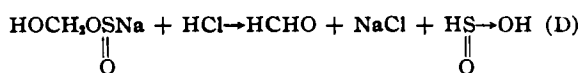
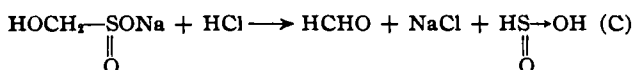
This is not the only structure which can be assigned to this substance, because the major decomposition products in acid solution are hydrogen sulphide, formic acid, and sulphur (3). Structure I permits only two decomposition products, namely, sulphur and formic acid according to the following reactions.



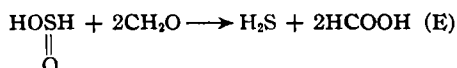
These equations do not allow for the formation of hydrogen sulphide, and in order to account for this it is necessary to assume a tautomerism of the following type.



The tautomeric form III is similar to that suggested by Orlov (4) for sodium sulphoxylate, but it could not be distinguished from tautomer II by acid hydrolysis because both would yield the same products according to the following equations.



Subsequent reduction of free sulphoxylic acid of this structure by formaldehyde readily accounts for the formation of hydrogen sulphide by the following equation.



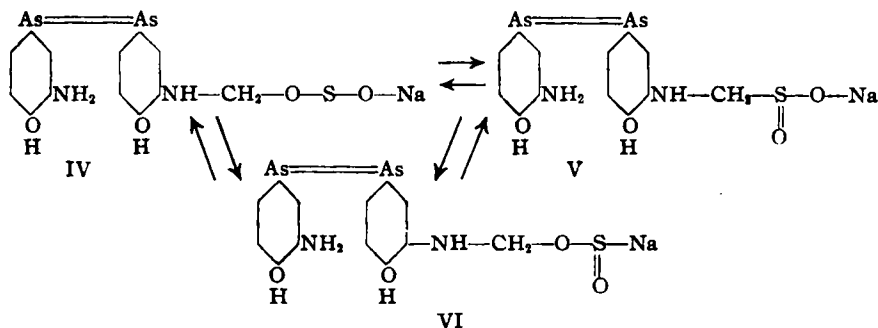
Hydrogen sulphide cannot be accounted for otherwise, because free sulphur cannot be considered as intermediate in the formation of hydrogen sulphide; it would be precipitated before it could be further reduced. Also, under the anaerobic conditions used sulphur cannot be formed by oxidation of hydrogen sulphide. Inasmuch as the hydrolysis of sodium formaldehydesulphoxylate is rapid as compared with the reduction (E), an excess of formaldehyde is constantly being supplied to meet the requirements of the reduction reaction.

On the basis of these considerations at least two, and possibly three forms of sodium formaldehydesulphoxylate appear to be necessary to account for the decomposition products. The conclusions as regards the structures of sulphoxylic acid and its salts are the opposite of those of Orlov (4) since he believes that the free acid has the structure, HOSOH, and that the monosodium salt has the structure HOSONa; the formation of hydrogen sulphide in acid solution necessitates the



existence of the form Orlov assigns to the sodium salt in acid solution. Consequently formaldehydesulphoxylic acid and sulphoxylic acid may exist in three forms corresponding to the sodium salts I, II and III. However, the existence of the tautomer III is unlikely except in very small percentages, because aqueous solutions of sodium formaldehydesulphoxylate are weakly alkaline and type III, the salt of a weak acid and a strong base, should give definitely alkaline solutions. This leaves types I and II as the two probable tautomeric forms of sodium formaldehydesulphoxylate. These conclusions are in agreement with those of Raschig (5), and Newberry and Phillips (6) who have pointed out the possible tautomeric nature of formaldehydesulphoxylates and formaldehydebisulphites.

If these conclusions are now extended to neoarsphenamine we find three possible structures for the monosubstitution product.



Of these three formulas number IV is the one usually used. However, number V, it is believed, represents a more stable structure, because the chain N—C—S should represent a more stable structure than the chain N—C—O—S. Number VI represents a type similar to that of sodium formaldehydesulphoxylate III, and since neoarsphenamine solutions are only weakly alkaline, it is thought that form VI is only present in very small amounts; type VI should be similar to III in liberating sodium ions. On the other hand the existence of the other two forms of neoarsphenamine is strongly indicated by analogy to the results obtained from the study of sodium formaldehydesulphoxylate.

On the basis of the facts presented here the existence of at least two tautomeric forms of neoarsphenamine of the types described, numbers IV and V, is strongly indicated since sodium formaldehydesulphoxylate must exist in at least two tautomeric forms to account for the decomposition products obtained in acid solution. It is possible that one of these types is present in greater amount than the others in alkaline solution and vice versa in acid solution but no evidence on this point is available.

SUMMARY.

1. Some information concerning the effect of strong acid and strong alkali on sodium formaldehydesulphoxylate is given and the results obtained are used to demonstrate the probable existence of at least two tautomeric forms.
2. The existence of two or three tautomeric forms of sodium formaldehydesulphoxylate indicates the existence of a corresponding number of tautomeric forms of neoarsphenamine.

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