A COMPARISON OF THE p_H OF NEOARSPHENAMINE AND SULPHARSPHENAMINE IN RELATION TO DIFFERENCES IN THEIR STRUCTURE.*

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In a previous publication (1) the p_H of neoarsphenamine was reported to vary from 5.8 to 8.7 and now some results of p_H determinations on sulpharsphenamine will be given showing a variation from 2.4 to 4.4 in market samples. The wide differences in the p_H ranges of these two arsenicals is of great significance in considering their structures; it has been found that neoarsphenamine is not stable in the p_H range of sulpharsphenamine and that the latter is less stable in the p_H range of neoarsphenamine than in the p_H range 2.2 to 4.4.

The p_H of sulpharsphenamine was determined in the shaking electrode vessel described by Clark (2) using a platinum wire electrode, first gold plated and then paladinized, and 10% solutions of the arsenical. As in the case of neoarsphenamine the highest voltage registered was taken as the final reading, and, except for occasional cases of electrode poisoning, a constant voltage was usually obtained for a sufficiently long period of time to give reliable results. The following table gives the results of the examination of some market and experimental samples. The pure sulpharsphenamine acid was obtained by precipitating the acid from a concentrated aqueous solution of sulpharsphenamine with an excess of glacial acetic acid. The finely divided precipitate was collected on a Büchner funnel, washed free of acetic acid with alcohol, then washed with ether and dried *in vacuo* over P_2O_5. The acid is quite stable and does not decompose as readily as does the so-called neoarsphenamine acid.

TABLE I.—RESULTS OF p_H DETERMINATIONS ON SULPHARSPHENAMINES.

Number.	Nature of sample.	p_H of 10% solution.	Number.	Nature of sample.	p_H of 10% solution.
1	Market	2.44	6	Experimental	2.38
2	Market	2.52	7	Experimental	2.64
3	Market	2.52	8	Experimental	3.45
4	Market	3.49	9	Experimental	3.57
5	Market	4.36	10	Sulpharsphenamine acid	2.15

The results show a p_H range of 2.15 for the acid to a p_H of 4.36 for one market sample. These results indicate that sulpharsphenamine contains a certain amount of free acid which is not the case in neoarsphenamine. Although this acid is not a weak one, it is not quite as strong as acetic acid by which it is precipitated. Sulpharsphenamine shows the same phenomenon of increased p_H on dilution that was previously reported for neoarsphenamine; only a few determinations were made to demonstrate this fact—the p_H in dilute solutions was not usually run on sulpharsphenamine.

In order to prove the presence of free acid in sulpharsphenamine several samples of sulpharsphenamine were ashed in excess sulphuric acid to determine the sodium as sodium sulfate after all of the arsenic had been burned off. The results of the sodium, sulphur and arsenic determinations are given in the following table. Sulfur was determined by the method described by Elvove (3) for total sulphur and arsenic was determined by the Lehmann method.

* Scientific Section, A. PH. A., Baltimore meeting, 1930.

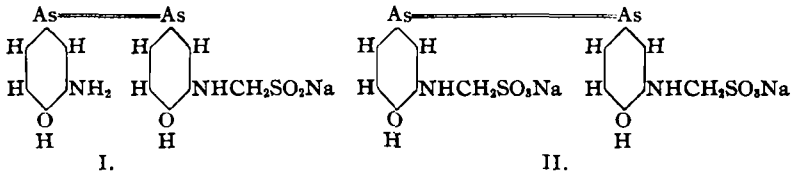
TABLE II.—ANALYSIS OF SULPHARSPHENAMINES FOR SULPHUR, ARSENIC AND SODIUM.

Number.	Sample A.	Sample B.	Sample C.
p_H	2.50	4.36	3.49
Per cent arsenic	20.28	21.30	21.52
Per cent sulphur	12.39	11.31	11.91
Per cent sodium	6.59	7.51	7.49
Atoms of arsenic	2	2	2
Atoms of sulphur	2.86	2.50	2.60
Atoms of sodium	2.00	2.30	2.27

These results show a preponderance of sulphur on an atomic ratio basis and, since the sulphur must be present either as sodium formaldehydebisulphite or sulpharsphenamine because any free sulphur dioxide would have been lost in the preparation of sulpharsphenamine, it must be concluded that the excess sulphur is present as sulpharsphenamine acid thus accounting for the results of the p_H determinations. Also it is noteworthy that the p_H rises as the atomic ratios of sulphur and sodium approach each other. It is apparent that the lowest p_H is found in Sample A where the difference between these two atomic ratios is greatest and highest in Sample B where the difference between these two ratios is smallest.

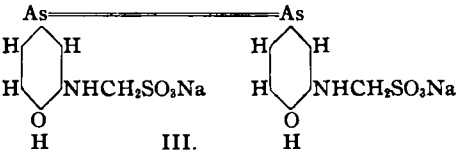
From the foregoing information the question arises as to how two compounds of supposedly so little structural difference can be so widely different in their p_H ranges and in their stability at different p_H ranges; neoarsphenamine is decomposed in the acid p_H range of sulpharsphenamine and sulpharsphenamine becomes less stable when alkalinized up to the p_H range of neoarsphenamine. The only possible conclusion is that there is a fundamental difference in the structures of these two arsenicals. This possibility has been suggested by Newbery and Phillips (4) who pointed out that whereas sulpharsphenamine is prepared by the separate and successive action of formaldehyde and sodium bisulfite on an aqueous solution of arsphenamine hydrochloride (5, 6), sodium formaldehydebisulphite reacts with arsphenamine hydrochloride to yield an altogether different compound. This finding has been confirmed in this laboratory. Furthermore, they pointed out that whereas the sulfur attached to the amino group in sulpharsphenamine could not be oxidized by alkaline iodine, the sulphur attached to the amino group in the compound obtained with sodium formaldehydebisulphite could be oxidized by alkaline iodine solution. Additional work by Newbery and Phillips on aminophenols showed that only the latter type of compound could be obtained from para and meta amino phenols and that the sulpharsphenamine type of compound could be obtained only with ortho-aminophenols, *i. e.*, the classification in which arsphenamine belongs. This latter observation gives a point of attack from which a new structure for sulpharsphenamine may be derived.

The hitherto accepted structures of neoarsphenamine (I) and sulpharsphenamine (II) are given as follows:

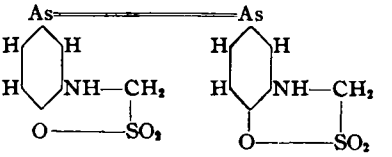


I. II.

If these two structures are compared no difference is noted except the degree of substitution and the presence of one more oxygen atom in the side chain attached to the amino group in sulpharsphenamine. These differences are insufficient to account for the wide difference in the p_H ranges of neoarsphenamine and sulpharsphenamine, the great stability of sulpharsphenamine acid as compared to the instability of neoarsphenamine in acid solution and the difference in the reaction of the sulphur in these two compounds when treated with alkaline iodine solution. However, if the presence of the hydroxyl group in the ortho position to the amino group is taken into consideration a possible structure for sulpharsphenamine can be developed. The structure suggested represents a ring formed by splitting off water between the methylenesulphurous acid group and the orthohydroxyl group to give the structures shown in which III represents the sodium salt and IV the stable free acid.



III.



While no positive evidence of this structure is available no other explanation of the stability of this acid as compared to the instability of neoarsphenamine acid is apparent. A ring structure of Type IV would account for the stability of this material in acid solution, the failure of alkaline iodine to oxidize the sulphur and also the decreased stability in alkaline solution; the alkali would break the ring, form a sodium salt on the methylenebisulphite side chain and result in a compound of the type of structure III which is very similar to neoarsphenamine both in structure and susceptibility to oxidation. The great similarity between the two types of sodium salts is clearly shown by Formulas I and II.

The experiments discussed here show very clearly that there is a considerable structural difference between neoarsphenamine and sulpharsphenamine, the p_H determinations and sodium analyses demonstrating clearly the acid nature of sulpharsphenamine as compared with the alkaline character of neoarsphenamine. It is shown further that sulpharsphenamine is stable at a p_H at which neoarsphenamine would be decomposed. In order to account for these differences a new structure for sulpharsphenamine is suggested involving a ring formation between the phenol group and the sulphurous acid portion of the side chain by splitting off water. It is pointed out that this ring type of structure would account for the three major chemical differences between neoarsphenamine and sulpharsphenamine discussed here and would also account for the greater stability of sulpharsphenamine as compared to neoarsphenamine. The p_H of sulpharsphenamine has been found to range from 2.4 to 4.4.

(1) Smith, Jurist and Christiansen, JOUR. A. PH. A., 18 (1929), 1142.
(2) Clark, "The Determination of Hydrogen Ions," Third Edition (1928), 295.
(3) Elvove, U. S. P. H. S. Reports," June 12, 1925; 40, No. 24, page 1235.
(4) Newbery and Phillips, *J. Chem. Soc.* (1928), 116.
(5) Voegtlin and Johnson, *J. Am. Chem. Soc.*, 44 (1922), 2573.
(6) Christiansen, *Ibid.*, 45 (1923), 2182.

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