[Contribution from the Chemistry Department of Vanderbilt University]

Studies on the Surface Tension of Aqueous Barbituric Acid Solutions

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A study of the surface activity of 13 substituted barbituric acids in aqueous solution is here presented. The effect of sodium chloride on the surface activity of these acids is also presented. A new procedure is described for determining the surface tension of aqueous solutions of slightly soluble solutes by use of a modified single bubble variation of the maximum bubble pressure method. With few exceptions the surface activity was found to increase with molecular weight and with narcotic potency. Sodium chloride raised the surface tension of the solutions of the barbituric acids of low molecular weight and lowered the surface tension of the aqueous solutions of the heavier members of the group.

Since the studies by Tabern and Shelberg[2] on the physical chemical properties of a selected group of substituted barbituric acids, little additional work has been published on this subject. Their studies were undertaken in an effort to correlate the physical properties with the narcotic potency of a group of 15 barbituric acids. Tabern and Shelberg studied the surface tensions of aqueous solutions of these acids at two concentrations, i.e., one part of acid to two thousand parts of water and their saturated solutions. It was felt by the authors of this article that a more extensive study of the surface active properties of the barbituric acids would produce more decisive evidence as to the probable role surface activity plays in the effectiveness of these drugs. Therefore, to extend the study begun by Tabern and Shelberg, data are presented that cover a much larger range of concentrations of aqueous

In making these studies the single bubble variation of the maximum bubble pressure method was employed. Some changes were made in the apparatus described by Brown[3] to make this technique more rapid and less burdensome, without sacrificing precision. It was found that this method is particularly suited to the study of slightly soluble solutes in aqueous solution, and that it gives accurate and reproducible results when allowance is made for a phenomenon that we believe to be associated with surface aging.

Apparatus.—The maximum bubble pressure apparatus used in these experiments was essentially that of Brown[3] and Belton.[4] The following changes were made in the apparatus previously employed and for the accompanying reasons. The changes are listed in the order in which the parts of the apparatus are arranged according to Brown.[3] (1) A dropping funnel was used to add small amounts of mercury to the reservoir (B),[5] thereby, controlling accurately the mercury

Table I
Barbituric Acids in Order of Their Efficacy in Reducing the Surface Tension of Water

	Barbituric acid[d]	Mol. wt.	Solubility, g./l.	M.p., °C.	Slope of salt soln. curve	A.D.,[c] mg./kg.
1	5,5-Dimethyl	156.14	2.419	273	0.162	∞[a]
2	1,5-Dimethyl	156.14		173	.195	∞[a]
3	Barbital (5,5-diethyl)	184.196	6.0	190	.163	234[b]
4	Phenobarbital (5-ethyl-5-phenyl)	232.236	0.97	176	.161	134[b]
5	Diallyl (5,5-diallyl)	208.216	1.465	172	.103	73[b]
6	Evipal (1,5-dimethyl-5-cyclohexenyl)	236.272		145	.045	29[b]
7	Delvinal [5-ethyl-5-(1-methyl-1-butenyl)]	224.258		163	.022	47[b]
8	5-Isopropyl 5-Isobutyl	226.27		157	.146	63.5[a]
9	Nembutal [5-ethyl-5-(1-methylbutyl)]	226.27	1.2	130	− .136	33[b] and 42[a]
10	Amytal (5-ethyl-5-isoamyl)	226.27	0.5	153	− .141	54[b]
11	5-Amyl-5-propyl	240.30		121	− .209	40.8[a]
12	5-Allyl-5-(1-methylbutyl)	238.28		83.5	− .289	28[b]
13	5-Butyl-5-(sec-butyl)	240.30		135	− .189	46.6[a]

[a] T. Butler and M. T. Bush, Proc. Soc. Exper. Biol. and Med., 50, 232 (1942). [b] T. Butler, J. of Pharmacology, 74, 6 (1942). [c] Minimum anesthetic dose for mice. [d] All of the barbituric acids were made available for this study by Dr. M. T. Bush of the Vanderbilt University Medical School.

solutions of a group of thirteen barbituric acids. Seven of the acids have not been studied before in this manner and six are members of the group studied by Tabern and Shelberg. A study was also made of the effect of several concentrations of sodium chloride on the surface tension of aqueous solutions of these acids. These acids are listed in Table I. The numerical designation for each acid in the table is followed throughout the paper.

level and the pressure. (2) Belton and Brown used P_2O_5 to dry the air to be used in blowing the bubbles. This was replaced by a chamber saturated with water vapor to minimize the possibilities of local cooling at the surface of the bubble as it was being blown. (3) The compression chamber (C) has been connected to the manometer (J) and the bubble blowing capillary (G). A stopcock has been placed in the system to make it possible to cut off the capillary from the pressure producing and measuring part of the system and permit the cleaning of the capillary without reducing the pressure in the system. This modification is important because time can be lost in waiting for the manometer fluid to

(1) (a) Abstracted in part from the Ph.D. thesis of Roy J. Kuffner, Vanderbilt University, 1954. (b) Address correspondence to Louis J. Bircher, Vanderbilt University.
(2) D. L. Tabern and E. P. Shelberg, This Journal, 55, 328 (1933).
(3) R. Brown, Phil. Mag., 13, 578 (1932).
(4) J. Belton, Trans. Faraday Soc., 31, 1413 (1935).
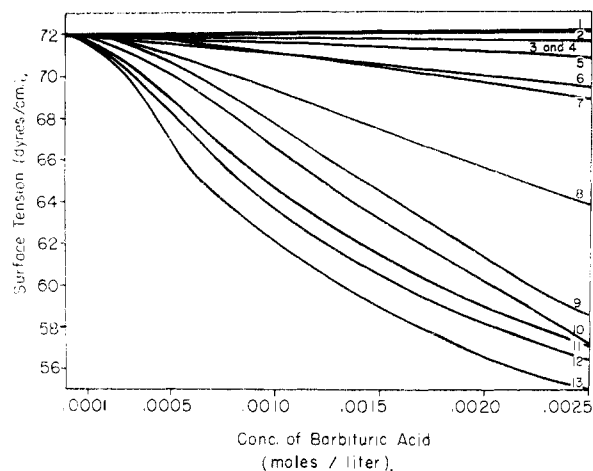(5) All letters refer to the diagram in the article by Brown.

Fig. 1.—Surface tension vs. concentration curves for aqueous solutions of the barbituric acids.

drain down the manometer wall when a pressure differential is impressed across the manometer where none existed previously. (4) The capillary tip (G) has been made replaceable by connecting it to the ground glass joint by means of a Tygon tube. (5) A 25-ml. bulb has been included in the side leveling arm of the bubble chamber to facilitate the mixing of solutions in the chamber. The chamber was also coated with G.E. "silicote." Studies showed that after proper washing the "silicote" had no effect on the surface tension of the solutions used in these experiments.

Experimental

Fifty ml. of solution, the surface tension of which was to be measured, was placed in the bubble chamber (G). The capillary, between 0.005 and 0.010 cm. in radius, was placed in position in the bubble chamber only after pressure, approaching that necessary to blow a bubble in the solution, was created in the capillary. A large positive pressure in the system before putting the capillary in the solution prevents a capillary rise of the solution into the capillary bore. The pressure was maintained in the system at approximately the estimated bubble pressure of the solution to be studied for at least 20 minutes before a reading was made to give the manometer fluid time to drain from the walls of the manometer. This time was found sufficient for drainage and reproducible results. To hold approximate operating pressures in the system while the solutions were being mixed and the capillary cleaned, stopcocks were placed in the system to cut off the chamber from the rest of the chain.

The depth below the surface of the liquid to which the capillary was adjusted was regulated by withdrawing solution by means of a mercury air pump from or adding solution to the bubble chamber. When the level was adjusted so that the tip of the capillary was level with the surface of the solution in the chamber, the pressure was increased until a bubble appeared at the end of the capillary. Starting with the tip at the surface of the solution eliminates the necessity for making a hydrostatic pressure correction. The maximum pressure required to blow a bubble was read. Readings were made until three consecutive readings on a solution checked to ±0.01 cm. The time interval between readings was found to be critical and for these solutions 40 seconds on the average must elapse between the blowing of bubbles. This time was found to vary for the different solutions studied.

In proceeding to the study of a more dilute solution the manometer was disconnected from the capillary and the capillary removed from the bubble chamber. The capillary was cleaned by drawing distilled water through it and dried by drawing air through it. The solution in the bubble chamber was diluted by replacing a given amount of solution with an equal amount of diluent. The latter was thoroughly mixed with the solution by running the mixture in and out of the side arm of the bubble chamber. This procedure also hastens the attainment of the bath temperature by the solution in the bubble chamber. After thoroughly mixing the solutions, the cleaned and dried capillary was connected to the manometer, and the pressure in the capil-
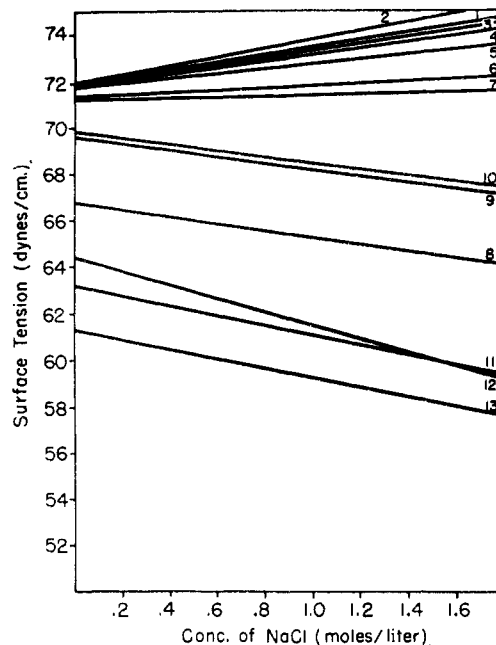

Fig. 2.—Surface tension of aqueous solutions of constant barbituric acid concentration and varying NaCl concentration.

lary was again allowed to approach that of the probable maximum bubble pressure as the capillary is put into place in the bubble chamber. The depth of the capillary tip with reference to the surface was again adjusted for the next run. The data obtained were reproducible to ±0.02 dyne/cm. and the values given in the article are the averages of three readings for each solution. The system was maintained at 20.00 ± 0.02°.

Calculations.—The equation used by Brown and Belton, and also used in this study to determine the surface tension of a solution from its maximum bubble pressure, is

$$\gamma = \frac{rg}{2}\left[hd_1 - {}^2/_3 rd_2 \right]$$

where

γ = surface tension in dyne/cm.
g = acceleration of gravity (979.8 cm./sec.[2] for Nashville)
d_1 = density of manometer fluid (butyl phthalate)
d_2 = density of the liquid being studied
r = radius of the capillary bore
h = max. bubble pressure in cm. of butyl phthalate

The radius of a particular capillary was obtained by determining the maximum bubble pressure of a liquid of known surface tension using this capillary and substituting the values obtained in the above equation.

Results and Conclusions

Figure 1 shows the plots of the measured surface tension of the aqueous solutions of the various barbituric acids vs. the concentration of the acids. Except for Evipal the high molecular weight barbiturates have greater surface activity.

The effects of sodium chloride at varying concentrations on the surface tension of the aqueous solutions of these barbituric acids also were studied. These data are plotted in Fig. 2. An attempt to explain these results suggests that the presence of the salt has two effects: a tendency of a salt to "salt

out" the barbituric acid into the interface and thereby increase the effectiveness of the barbituric acid in reducing the surface tension of the water, and the normal tendency of the salt to increase the surface tension of the water. The curves for the surface tension of solution of barbituric acids 1 through 7, the low molecular weight acids as a function of the concentration of salt (see Table I), have positive slopes, and in all of these instances the normal effect of the salt to increase the surface tension of the water is lessened by the presence of the barbituric acid, and to a greater degree as the molecular weight increases. In the case of barbituric acids 8 through 13, the ones with heavy substituent groups, the slopes are negative, showing the salt is actually enhancing the surface tension reducing properties of the barbituric acid.

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The Preparation and Properties of Complex Fluoroarsenates[1]

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Potassium dihydrogen arsenate, KH_2AsO_4, reacts with a 48% aqueous solution of hydrofluoric acid to give potassium hydroxypentafluoroarsenate(V), $K[AsF_5OH]$. Potassium hexafluoroarsenate(V), $K[AsF_6]$, can be prepared by the action of liquid anhydrous HF on $KAsF_5OH$ or KH_2AsO_4. The reaction is discussed. Procedures for preparing ammoniun and cesium hexafluoroarsenates and hexafluoroarsenic acid, $HAsF_6$, are described. Cesium hexafluoroarsenate is of low solubility in water while NH_4AsF_6, $HAsF_6$ and $KAsF_6$ are water soluble. The data suggest a means for separating the light and heavy alkali metals.

In the pioneer work on the fluoroarsenates[2-4] products which were assumed to contain the hexafluoroarsenate anion, (AsF_6^-), were produced from an aqueous solution containing KH_2AsO_4 and 48% HF. It was reported that the resulting AsF_6^- ion underwent extensive and ready hydrolysis in water solution to give arsenic oxyfluorides.

In contrast to the foregoing reports the results of Ruff, Stauber and Graf[5] suggest more difficult preparation and hydrolysis of the AsF_6^- ion. The compound $NOAsF_6$ (reported as $NOF \cdot AsF_5$ by Ruff) could not be analyzed for arsenic and fluorine without a preliminary sodium fusion of the sample.[6] Difficult hydrolysis of the AsF_6^- ion is also implied in the recent reports of Woolf and Emeleus.[7] The compounds $KAsF_6$ and $NOAsF_6$ were synthesized by methods involving the powerful fluorinating agent bromine trifluoride. The analytical methods used for identification involved preliminary fusions with a mixture of Na_2CO_3 and $NaNO_3$, not direct hydrolysis in aqueous solution. The current paper is aimed at a resolution of the uncertainty which arises from the early literature on the synthesis and analysis of compounds containing the AsF_6^- ion.

The reaction between 48% aqueous hydrofluoric acid and potassium dihydrogen arsenate produces potassium hydroxypentafluoroarsenate(V), $K[AsF_5OH]$, rather than the hexafluoroarsenate salt, $K[AsF_6]$. Anhydrous HF converts the $KAsF_5OH$ to $KAsF_6$. Both the AsF_5OH^- and the AsF_6^- anions give precipitates with nitron acetate or with tetraphenylarsonium chloride, $[As(C_6H_5)_4]Cl$. Lange[4] used the formation of a precipitate with nitron acetate as evidence for hexafluoroarsenate formation in aqueous solution. He erroneously described his precipitate as nitron hexafluoroarsenate monohydrate.

The $[AsF_5OH^-]$ anion hydrolyzed relatively rapidly in water solution. The process was accelerated by acid, base or heat. In contrast the AsF_6^- ion showed no hydrolysis as a result of (1) boiling a strongly basic solution almost to dryness, (2) storing a strongly basic solution for six weeks at room temperature. Conventional tests for determining As(V) such as reduction with KI or precipitation of As_2S_5 with $(NH_4)_2S$ were unsuccessful when applied to the true AsF_6^- ion. Similarly silver arsenate could not be precipitated by adding silver ion to a solution of $KAsF_6$. In contrast one could easily determine arsenic in $KAsF_5OH$ by taking advantage of its ready hydrolysis in boiling NaOH solution. Reduction of As(V) with KI was easily effected in the hydrolyzed solution. After complete hydrolysis of AsF_5OH^- to arsenate, no precipitate of complex salt was obtained with nitron or tetraphenylarsonium chloride.

The properties of the AsF_6^- ion are seen to be quite similar to those of the PF_6^- ion while the AsF_5OH^- ion is much less stable toward hydrolysis. The failure of aqueous hydrofluoric acid to convert AsF_5OH^- to AsF_6^- and the great stability of the latter toward hydrolysis would seem to indicate that a relatively high energy barrier blocks the exchange reaction between the sixth fluoride and hydroxide ion

$$AsF_5OH^- + F^- \underset{slow}{\overset{}{\rightleftharpoons}} AsF_6^- + OH^-$$
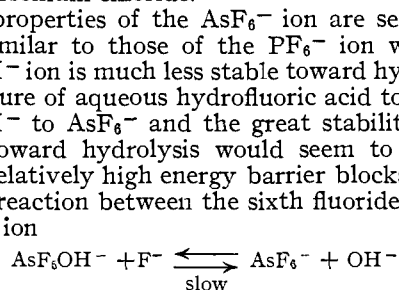
These observations may be rationalized in terms

(1) Abstracted from a thesis submitted on February 9, 1955, to the Horace H. Rackham School of Graduate Studies of the University of Michigan by H. M. Dess in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) M. C. Marignac, *Ann. chim. phys.*, [4], **10**, 371 (1867); *Ann.*, **146**, 237 (1867).

(3) Gmelin, "Arsen," System-Nummer 17, Verlag Chemie, GMBH, Weinheim, 1952, p. 366.

(4) W. Lange and E. Muller, *Ber.*, **63**, 1058 (1930).

(5) O. Ruff, K. Stauber and H. Graf, *Z. anorg. Chem.*, **58**, 325 (1908).

(6) Ruff noted that AsF_5 presents no special analytical problems but did not speculate further as to the cause of the interference in his new complex.

(7) A. A. Woolf and H. J. Emeleus, *J. Chem. Soc.*, 1050 (1950); A. A. Woolf, *ibid.*, 1053 (1950).