

# Study of the Boric Acid-Glycerin Complex II

## Formation of the Complex at Elevated Temperatures

By JOHN J. SCIARRA and ANTHONY J. MONTE BOVI

A study of the boric acid-glycerin complex was conducted at temperatures of 30, 40, 50, and 60° and the effect of increasing the concentration of glycerin upon the solubility of boric acid was studied. This may then be indicative of the degree of complex formation taking place between these two substances. Concentrations of glycerin varying from 0 to 100% were utilized. The results of these experiments show the relationship between (a) solubility of boric acid and (b) temperature and concentration of glycerin. A phase diagram was constructed at these temperatures showing the quantitative relationship among boric acid, water, and glycerin. From a plot of the log solubility of boric acid *versus* the reciprocal of absolute temperature, the heat of solution at various concentrations of glycerin was calculated. It was found that the degree of complex formation between boric acid and glycerin increased with an increase in temperature but showed little, if any, increase with an increase in glycerin concentration from 0 to about 40%. However, above this concentration of glycerin, the degree of complex formation, as indicated by the solubility, increased with an increase in concentration of glycerin.

THE FORMATION of a complex compound between boric acid and glycerin has been known and investigated by many workers. This complex has been detected by many methods, among them being changes in pH (1, 2) and in solubility (3). In most cases the addition of glycerin to boric acid will allow the formation of a complex compound which is soluble to a greater extent than boric acid alone. However, during the course of previous investigations it has been found that boric acid behaves quite differently in glycerin than in the presence of other substances capable of forming a complex compound, such as sorbitol (4), mannitol, fructose, and other similar substances. Some of the differences in behavior between the boric acid-glycerin complex and the boric acid-sorbitol complex have been indicated in a previous publication (5) where the complex formation between these substances was studied at 25°. The results of this investigation prompted further work at elevated temperatures.

An increase in temperature generally will increase the solubility of substances in water and other solvents. The solubility of substances which are favorably affected by an increase in temperature will show a negative heat of solution. The heat of solution of a substance will vary depending upon the concentration of solute in solution. The partial molal or differential heat of solution is defined as  $d(\Delta H)/dn_2$ , where  $\Delta H$  is the heat of solution of a mole of solute in

a quantity of solution so large that the addition of the one additional mole of solute does not appreciably change the concentration of the solution (6).

A solubility study can be used to determine the heat of solution of boric acid in varying concentrations of glycerin. By determining the solubility of boric acid in the various glycerin solvents at several temperatures and plotting these results, according to the van't Hoff relationship

$$\frac{d \ln S}{dt} = \frac{\Delta H}{2.303 RT}$$

which when integrated becomes

$$\log S = \frac{-\Delta H}{2.303 RT}$$

one can calculate the heat of solution. In the van't Hoff equation,  $S$  is the molal solubility of boric acid in the glycerin solvent,  $\Delta H$  is the heat of solution,  $R$  is the gas constant, and  $T$  is the absolute temperature. An error is introduced since  $\Delta H$  is treated as a constant, an assumption which is not entirely true (7).

Boroglycerin glycerite N.F. has been used for many years as an antibacterial substance. This consists chiefly of a 50% (by weight) solution of boroglycerin ( $C_3H_5BO_3$ ) in glycerin. Official directions specify that this product be kept in a dry container (8). This glycerite is also described as a soluble preparation of boric acid (9), however, in certain cases, the addition of water is followed by the precipitation of boric acid. This is due to the hydrolysis of the boroglycerin complex to form boric acid which precipitates when water is not present in sufficient concentration.

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A comparison of this reaction with the reaction taking place between boric acid-sorbitol and water has previously been reported (5). However, to study this reaction more fully, the relationship between the amount of boric acid precipitated and the concentration of glycerin-water solutions was studied by combining various combinations of saturated solutions of boric acid in glycerin and in water at 25°.

### EXPERIMENTAL

Saturated solutions of boric acid in solutions of glycerin and water were prepared in a manner previously reported (5). This method consisted of diluting glycerin U.S.P. containing 99%, by weight, of  $C_3H_5(OH)_3$  with varying quantities of distilled water so that concentrations of glycerin were obtained from 0 to 100%, by weight, in increments of 10%. These solutions were then neutralized to phenolphthalein by the addition of a few drops of 1 *N* sodium hydroxide. An excess of finely divided, crystalline boric acid U.S.P. was added to about 100 ml. of glycerin solvent which had been placed into a 150-ml. glass solubility tube. The tube was placed into a constant temperature water bath at  $30 \pm 0.1^\circ$  and stirred continuously for 24 hours (preliminary experiments showed that equilibrium had been attained during this period). After allowing the undissolved particles to settle to the bottom of the solubility tube, two 25-ml. portions of the clear, supernatant liquid were removed, placed into tared beakers, and quickly weighed. The amount of boric acid in each of these solutions was determined by assaying the solutions according to the U.S.P. assay for boric acid (10). The above procedure was repeated at temperatures of 40, 50, and 60°, all

$\pm 0.1^\circ$ . Constant temperature was maintained through use of a Sargent full visibility, constant temperature water bath.

A different procedure was used to determine the amount of boric acid which would precipitate from saturated solutions of boric acid in both water and glycerin. A saturated solution of boric acid in water was prepared at 25° according to the official method (8), and assayed as above. A similar solution of boric acid was prepared in glycerin [over 99% by weight  $C_3H_5(OH)_3$ ] and assayed. Various quantities of these solutions were added to a 150-ml. solubility tube in the quantities shown in Table I. Each tube contained a total weight of 100 Gm. These tubes were then tightly stoppered and placed into the constant temperature water bath at  $25 \pm 0.1^\circ$  and allowed to stand without agitation. Maximum precipitation of boric acid was obtained at this time. Then two 25-ml. portions of the clear, supernatant liquid were removed and assayed as indicated above.

### RESULTS

From the above results, the solubility of boric acid in the various glycerin-water solvents was calculated at elevated temperatures and expressed as weight per cent of boric acid as shown in Table II. In order to show the effect of temperature upon the solubility of boric acid Fig. 1 was constructed. Figure 2 relates the concentration of glycerin with the solubility of boric acid at the indicated temperatures.

The composition of each of the solutions was calculated on a weight per cent basis and the amount of each component present (boric acid-water-glycerin) is given in Table III. From this data, Fig. 3, which is a phase diagram of this multicomponent system, was constructed.

TABLE I.—PRECIPITATION OF BORIC ACID FROM SATURATED SOLUTIONS OF BORIC ACID IN GLYCERIN AND WATER

Saturated Solution $H_3BO_3$ in Glycerin, Gm.	Saturated Solution $H_3BO_3$ in Water, Gm.	$H_3BO_3$ in Glycerin Fraction, Gm.	$H_3BO_3$ in Water Fraction, Gm.	Total $H_3BO_3$ , Gm.	Amount $H_3BO_3$ Found, Gm.	Amount $H_3BO_3$ Precipitated, Gm.	% $H_3BO_3$ Precipitated
100	0	16.68	0	16.68	16.68	0	0
97.5	2.5	16.26	0.12	16.38	16.40	0	0
95	5	15.85	0.24	16.09	16.06	0.03	0.19
90	10	15.01	0.48	15.49	15.17	0.32	2.07
85	15	14.18	0.72	14.90	12.13	2.77	2.28
80	20	13.34	0.96	14.30	9.72	4.58	32.03
75	25	12.51	1.20	13.71	8.12	5.59	40.77
72.5	27.5	12.09	1.32	13.41	7.73	5.68	42.36
70	30	11.68	1.44	13.12	7.20	5.92	45.12
65	35	10.84	1.68	12.52	6.44	6.08	48.56
60	40	10.01	1.92	11.93	6.05	5.88	49.29
55	45	9.17	2.16	11.33	5.68	5.65	49.87
50	50	8.34	2.41	10.75	5.37	5.38	50.05
45	55	7.51	2.65	10.16	5.16	5.00	49.21
40	60	6.67	2.89	9.56	5.12	4.44	46.44
35	65	5.84	3.13	8.97	4.90	4.07	45.37
30	70	5.00	3.37	8.37	4.63	3.74	44.68
25	75	4.17	3.61	7.78	4.66	3.12	40.10
20	80	3.34	3.85	7.19	4.72	2.47	34.35
15	85	2.50	4.09	6.59	4.72	1.87	28.38
10	90	1.67	4.33	6.00	4.73	1.27	21.17
5	95	0.83	4.57	5.40	4.74	0.66	12.22
2.5	97.5	0.42	4.69	5.11	4.78	0.33	6.46
0	100	0.00	4.81	4.81	4.81	0	0

TABLE II.—SOLUBILITY OF BORIC ACID IN GLYCERIN SOLUTIONS AT ELEVATED TEMPERATURES

Concentration of Glycerin, % w/w	Per Cent Weight Boric Acid			
	30°	40°	50°	60°
0	6.01	7.85	9.90	12.24
10	6.45	7.65	9.80	11.82
20	6.82	7.59	9.56	12.16
30	5.96	7.76	9.81	12.74
40	6.02	7.88	9.63	13.01
50	6.36	8.23	10.60	13.78
60	7.01	9.12	12.29	14.53
70	8.57	10.62	13.25	17.38
80	11.37	13.40	15.96	19.21
90	14.99	17.24	19.77	22.42
100	19.98	21.97	24.34	27.00

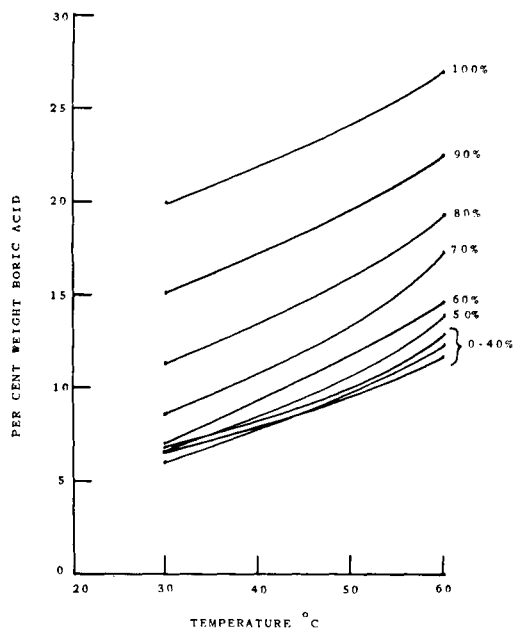


Fig. 1.—Effect of temperature upon the solubility of boric acid in glycerin.

Tables III and IV show the data necessary to plot Fig. 4 and calculate the heat of solution for each of the solvent systems studied. These also show the application of the van't Hoff equation to this system.

Table I shows the calculations involved in determining the amount of precipitation of boric acid taking place when saturated solutions of boric acid in both water and glycerin are combined.

These results are shown graphically in Fig. 5.

### DISCUSSION

The degree of complex formation between boric acid and glycerin was found to increase with an increase in temperature as indicated by the corresponding increase in solubility of boric acid. The temperature effect also increased as the concentration of glycerin increased; that is, temperature had a greater effect at higher concentrations of glycerin. See Table V. This is shown in Fig. 1 where it can be noted that the curves representing from 0 to 40% are quite close to one another, in fact it is difficult to separate them. However, as one approaches

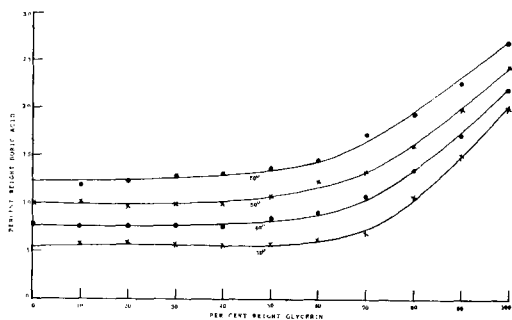


Fig. 2.—Isotherm curves showing solubility of boric acid in glycerin.

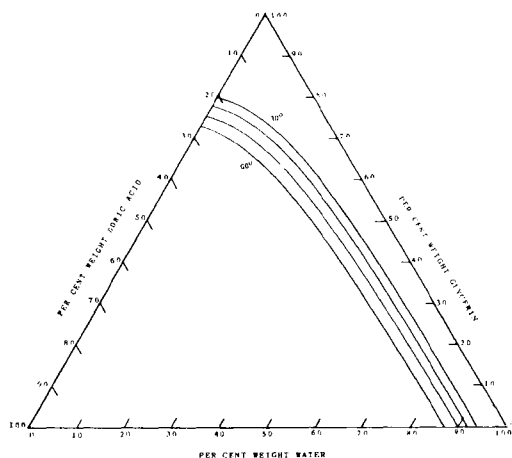


Fig. 3.—Phase diagram of boric acid-water-glycerin system.

50% and higher concentrations of glycerin, the curves are separated by a greater difference. The maximum temperature effect is obtained in going from a solvent containing 90% glycerin to one containing 100%. A similar relationship is found in Fig. 4 where the log solubility is plotted *vs.* reciprocal or absolute temperature. Since straight lines are produced in all cases, it may be assumed that the van't Hoff relationship is applicable to this system. Similar to Fig. 1, 0 to 40% glycerin concentrations show very little difference in solubility, as seen in Fig. 4. This difference becomes greater with increase in concentration of glycerin. In both Figs. 1 and 4 it can be seen that the temperature gradients going from 30 to 40°, 40 to 50°, and 50 to 60° seem to be about the same in all cases. This might be expected from results of prior reports. From Fig. 4, the slope can be determined from which the heat of solution can be calculated in each solvent. It is interesting to note that the slope of the lines for concentrations of glycerin from 30 to 60% are parallel, therefore they would have the same heat of solution. These results would indicate that very little, if any, complex formation takes place between boric acid and glycerin solutions in the range of 0 to 40%. This also seems to be independent of temperature.

A plot of the solubility of boric acid *vs.* concentration of glycerin, as shown in Fig. 2, also shows the

TABLE III.—COMPOSITION OF BORIC ACID-WATER-GLYCERIN SYSTEM AT ELEVATED TEMPERATURES

Composition of Solutions <sup>a</sup>											
30°			40°			50°			60°		
A	B	C	A	B	C	A	B	C	A	B	C
6.01	93.99	0	7.85	92.15	0	9.90	90.10	0	12.24	87.76	0
6.45	84.19	9.36	7.65	83.11	9.24	9.80	80.18	9.02	11.82	79.36	8.82
6.82	74.54	18.64	7.59	73.93	18.48	9.56	71.36	18.08	12.16	70.28	17.56
5.96	65.84	28.20	7.76	64.58	27.66	9.81	63.16	27.03	12.74	61.08	26.19
6.02	56.38	37.60	7.88	55.28	36.84	9.63	54.21	36.16	13.01	52.19	34.80
6.36	46.84	46.80	8.23	45.87	45.90	10.60	44.70	44.70	13.78	43.12	43.10
7.01	37.20	55.79	9.12	36.36	54.52	12.29	35.08	52.63	14.53	34.20	51.27
8.57	27.42	64.01	10.62	26.82	62.56	13.25	26.04	60.71	17.38	24.78	57.84
11.37	17.72	70.91	13.40	17.32	69.28	15.96	16.80	67.24	19.21	16.14	64.65
14.99	8.50	76.51	17.24	8.28	74.48	19.77	8.02	72.21	22.42	7.76	69.82
19.98	0	80.02	21.97	0	78.03	24.34	0	75.66	27.00	0	73.00

<sup>a</sup> A, Boric acid, % w/w; B, water, % w/w; C, glycerin, % w/w.

TABLE IV.—MOLAL SOLUBILITY OF BORIC ACID

Temperature <sup>a</sup>											
30°			40°			50°			60°		
A	B	C	A	B	C	A	B	C	A	B	C
63.94	1.0340	0.0145	85.19	1.378	0.1393	109.88	1.776	0.2495	139.47	2.255	0.3532
68.95	1.11	0.0453	82.84	1.340	0.1271	108.65	1.756	0.2435	134.04	2.167	0.3359
73.19	1.18	0.0719	82.13	1.328	0.1232	105.71	1.709	0.2326	138.43	2.238	0.3498
63.38	1.02	0.0086	84.13	1.360	0.1335	108.77	1.758	0.2450	146.00	2.360	0.3729
64.06	1.04	0.0170	85.48	1.382	0.1405	106.56	1.723	0.2362	149.55	2.418	0.3834
67.92	1.098	0.0407	88.71	1.435	0.1568	118.56	1.917	0.2826	159.82	2.584	0.4123
75.38	1.218	0.0856	99.26	1.605	0.2054	140.12	2.265	0.3551	170.00	2.749	0.4392
93.73	1.515	0.1804	118.81	1.921	0.2835	152.73	2.469	0.3925	210.36	3.401	0.5316
128.28	2.070	0.3160	154.73	2.502	0.3982	189.90	3.070	0.4871	237.77	3.844	0.5848
176.33	2.851	0.4550	208.31	3.368	0.5273	246.41	3.984	0.6003	288.99	4.673	0.6696
249.68	4.037	0.6061	281.55	4.552	0.6582	321.70	5.202	0.7162	369.86	5.980	0.7767

<sup>a</sup> A, Solubility of boric acid, Gm./1,000 Gm. solvent; B, solubility of boric acid, moles/1,000 Gm. solvent; C, log solubility.

TABLE V.—HEAT OF SOLUTION OF BORIC ACID-GLYCERIN SOLUTIONS

Concentration of Glycerin, % w/w	Heat of Solution Cal./Mole/° C.
0	-5,491
10	-4,576
20	-3,890
30	-5,720
40	-5,720
50	-5,720
60	-5,720
70	-5,034
80	-4,118
90	-3,203
100	-2,517

lack of complex formation between these two substances until 45 or 50% concentrations of glycerin are attained. Then the solubility increases sharply as 100% glycerin is approached. A comparison of these results with the results obtained in studying the boric acid sorbitol complex are quite interesting (4). As previously indicated, the boric acid-sorbitol complex is formed in ranges from 0 to 70% sorbitol. This indicates increased stability of the boric acid-sorbitol complex as compared to the boric acid-glycerin complex, especially at low concentrations.

Temperature increases will give a greater area of miscibility to the boric acid-water-glycerin system as seen in Fig. 3. These curves are separated from one another by an equal distance, indicating the temperature effect to be constant.

In order to determine the amount of boric acid which would precipitate from solutions of the boric

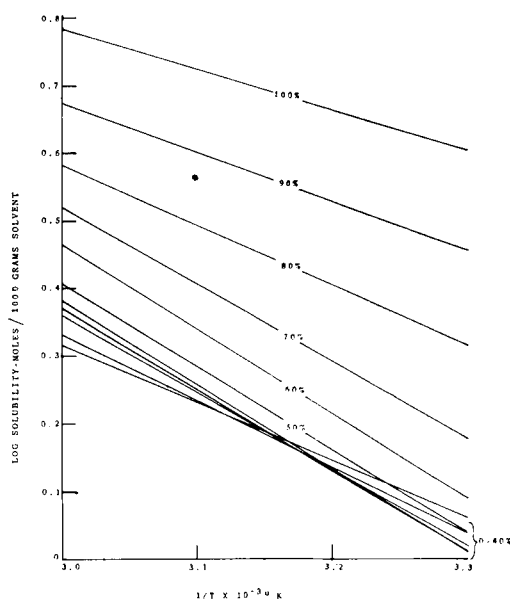


Fig. 4.—Application of data to van't Hoff equation.

acid in glycerin (essentially boric acid-glycerin complex), varying quantities of a saturated solution of boric acid in water (to ensure that the amount of boric acid precipitated from the glycerin did not redissolve in water) was added to the glycerin solution of boric acid. These results are depicted in Fig. 5 where essentially a bell shaped curve is obtained.

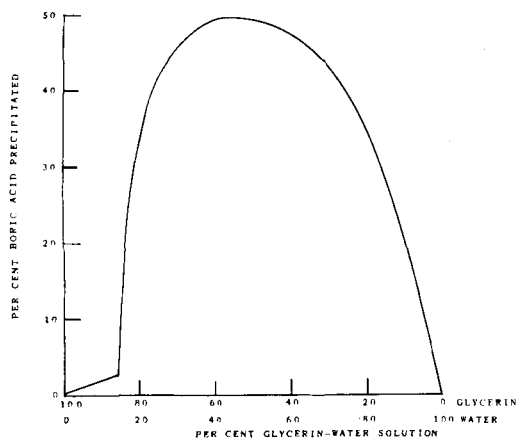


Fig. 5.—Precipitation of boric acid from glycerin-water solutions.

As expected, maximum precipitation of boric acid occurs about 45% water and 55% glycerin. About 15% water can be added without causing precipitation of boric acid. However, additional quantities of water will cause a large increase in the amount of precipitation. This observation would limit the use of boroglycerin glycerite when diluted with certain amounts of water.

#### SUMMARY AND CONCLUSIONS

1. A solubility study of the boric acid-water-glycerin system has been made at temperatures of 30, 40, 50, and 60°.

2. The degree of complex formation between boric acid and glycerin was found to increase with an increase in temperature.

3. Concentrations of glycerin from 0 to 40% had little effect, if any, upon the degree of complex formation as indicated by a solubility determination. This complex was found to increase as the concentration of glycerin was increased from 40 to 100%.

4. The heat of solution for each of the solvent systems was calculated through use of the van't Hoff relationship.

5. Maximum precipitation of boric acid from solutions of boric acid in glycerin was found to take place at a concentration of 45% water and 55% glycerin.

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## Infrared Method for the Determination of Ethanol and Acetone in Thimerosal Tincture N.F.

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The distillation method for determining ethanol in thimerosal tincture N.F. is time consuming and involves special handling to prevent interference of the acetone in the preparation. A shorter method is described based on the extraction of the ethanol into carbon tetrachloride and the measurement of the infrared absorption at 11.37  $\mu$ . The relative freedom from the interference by other alcohols and acetone assures greater specificity than the distillation method. The acetone present in tincture thimerosal N.F. can also be determined using the same extracted solution by reading the absorption of the carbonyl band at 5.86  $\mu$ .

THE DETERMINATION of ethanol in thimerosal tincture N.F. as described in the National Formulary (1) is that of Thorpe and Holmes (2). It has the disadvantage of being time consuming.

It is also possible that it may not give a true estimate of the amount of ethanol in the preparation due to incomplete recovery of the ethanol in the distillate. The method formerly used in this laboratory was a modification of that of Hoff and Macoum (3) using paraformaldehyde and sodium hydroxide to form a nonvolatile reaction product with the acetone before distilla-

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