

Solubilization of Benzoic Acid by Systems Containing Varying Proportions of Benzene and a Nonionic Surfactant

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The solubilization of benzoic acid in the presence of an additive, benzene, has been examined by the potentiometric method. It is shown that in all systems of L1 phase (isotropic aqueous liquid) the solubilization mechanism is governed by the Langmuir isotherm, whereas in emulsions dimerization of benzoic acid apparently occurs.

THE PRESENT authors have previously reported studies of the solubilization of organic acids and amines in surfactant solutions (1-4). In the present paper the effect of an additive, benzene, upon the solubilization of benzoic acid is investigated by the potentiometric method.

DISCUSSION

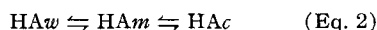
Considerable interest was attached to comparing the solubilization process in systems of different phases. The phases present in the dispersions investigated in this project were therefore identified and part of the relevant ternary phase diagram constructed. Designation of phases is as follows: L1, an isotropic aqueous liquid; L2, an isotropic organic liquid phase; and LC, an anisotropic liquid crystalline phase or mesophase intermediate in structure between the liquid and crystalline states. The molecules of the liquid crystalline phase possess an ordered lamellar arrangement, and the phase exhibits birefringence under polarized light.

The potentiometric method of examining solubilization phenomena has been described in detail in an earlier publication (3). The great advantage of this method of examining solubilization phenomena is that it enables measurement of the activity of solubilized materials in nonsaturated systems; the pharmaceutical and theoretical utility of such measurements have been indicated previously. In essence, this method consists of the measurement of pH values of organic acids in the presence of surfactant and substitution of such values in the Henderson equation. One of the approximations made in the derivation of this equation is that the concentration of hydrogen ions is negligible in comparison with the concentration of unionized acid. For acids of pKa above 4, e.g., benzoic acid, in solutions of pH value between 4 and 10, the error introduced by this assumption is very small. When an organic acid, HA, is present in a surfactant system of L1 phase the equilibrium shown in Eq. 1 will operate.

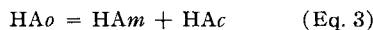


where HA w represents the nonmicellar acid and HA m

the acid bound by the micelles. In (L1 + LC) systems, the following equilibria will exist:



where HA c represents the acid in the liquid crystalline phase. The potentiometric method does not allow separate determination of HA m and HA c ; the value which can be determined is the summated one, HA o .



also



where HA t is the total unionized acid present in the whole system.

Quantitative evaluation of the above equilibria enables considerable information to be gained about solubilization mechanism. Solubilization could be governed by four possible mechanisms.

(a) Solution within the micelle or liquid crystal as a monomer. For this case, Eq. 5 would control the solubilization mechanism.

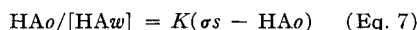


where K_d is a distribution coefficient.

(b) Solution as a dimer. If the solution process involved dimer formation, Eq. 6 would operate.



(c) Adsorption of solubilize would result in the equilibrium being governed by an adsorption equation such as the Langmuir isotherm, Eq. 7.



where K is the binding constant and σs the amount of solubilize that could be accommodated at monolayer saturation.

(d) Complex formation. If the solubilization were due to complex formation, the equilibrium would be governed by the stability constant or constants of the complex or complexes.

EXPERIMENTAL

The materials used were laboratory grade; the benzene¹ was purified by distillation and crystallization, b.p. 80°; the nonionic surfactant, cetomacrogol B.P.C.² was characterized by proton magnetic

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² Supplied by Evans Medical Co. Ltd., Bradford, England.

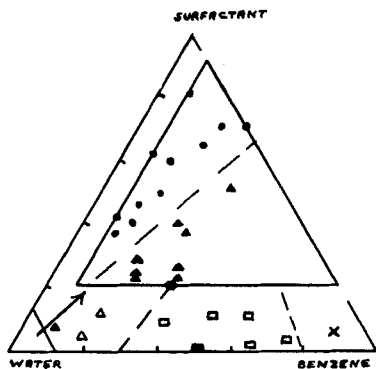


Fig. 1.—Phase diagram for the system cetomacrogol-benzene-water. Key: ●, L1; △, (L1 + LC); □, (L1 + LC + L2); ◊, (L1 + L2); ×, (LC + L2); — — —, approximate position of phase boundary. Solid points represent composition of systems used in potentiometric studies.

TABLE I.—COMPOSITION AND TYPE OF PHASE IN THE DISPERSIONS USED IN THE POTENTIOMETRIC STUDIES

System	% w/v Cetomacrogol	% w/v Benzene	Cetomacrogol-to-Benzene Ratio	Phases Present
A1	20	...	∞	L1
A2	12	...	∞	L1
A3	8	...	∞	L1
A4	4	...	∞	L1
B1	8	1	8	L1
B2	4.8	0.6	8	L1
B3	3.2	0.4	8	L1
C1	10	2	5	L1
C2	6	1.2	5	L1
C3	4	0.8	5	L1
D	10	4	2.5	L1
E1	6	4	1.5	(L1 + LC)
E2	3.6	2.4	1.5	(L1 + LC)
F1	8	8	1	(L1 + LC)
F2	3.2	3.2	1	(L1 + LC)
F3	1.6	1.6	1	(L1 + LC)
G1	1	5	0.2	(L1 + LC)
G2	0.6	3	0.2	(L1 + LC)
H1	0.5	5	0.1	(L1 + LC)
H2	0.3	3	0.1	(L1 + LC)
I	...	5	...	L1 + L2
J	10	50	0.2	L1 + LC + L2

resonance spectroscopy and the mean molecular formula found to be $C_{16}H_{33}O(C_2H_4O)_{24}OH$.

Dispersions containing varying amounts of the three components were prepared, shaken, and the systems allowed to reach equilibrium at 25°. When necessary, the systems were centrifuged for 3 to 5 min. and then re-equilibrated at 25°. The phases present were noted, the systems redispersed, and centrifuged again. Only when the separated phases remained unchanged after being returned to the water bath at 25° following centrifugation was the system assumed to be in equilibrium. All dispersions were examined under polarized light. When birefringence indicated the presence of liquid crystal, such material was examined microscopically under crossed Nicols. Figure 1 shows the number and nature of the phases identified in the various dispersions.

Sodium benzoate,³ 100 mM, was titrated with hydrochloric acid in the presence of varying amounts

³ Supplied by B. D. H. Ltd., Poole, England.

of benzene and cetomacrogol at 25°. The apparatus and techniques used have been previously described (1). The number and types of phases present in the various dispersions were identified in the manner described above before and after titration. In no case did the solubilized benzoic acid alter the number of types of phase found in the dispersions, though of course it must have altered the composition of the phases.

Table I shows the composition of the dispersions used in the potentiometric studies. All binary phase systems, except I, were examined in the form of emulsions. The turning rate of the magnetic stirrer was kept constant at about 75 r.p.m. The volumes of organic phase in the emulsions were estimated in systems in which the phases had been separated by centrifugation.

RESULTS AND DISCUSSION

The phase diagram for the system benzene-cetomacrogol-water shown in Fig. 1 is similar to that reported by Mulley (5). However, the region (L1 + LC) appears to be considerably larger.

The attempts made to examine the solubilization of benzoic acid in systems I and J were unsuccessful.

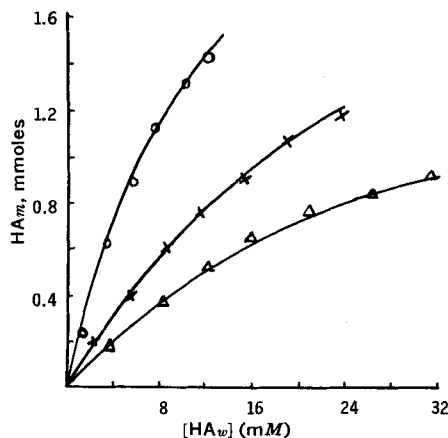


Fig. 2.—Solubilization isotherms for C systems. Key: ○, C1; ×, C2; △, C3.

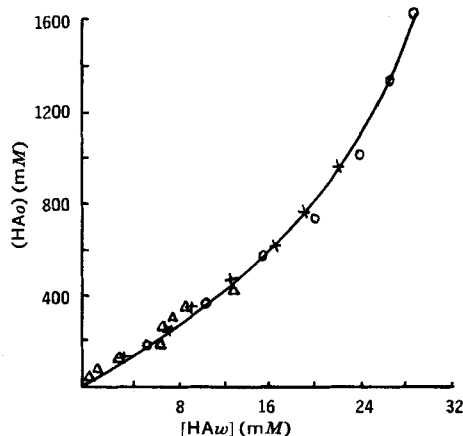


Fig. 3.—Solubilization isotherms for F systems. Key: ○, F1; ×, F2; △, F3.

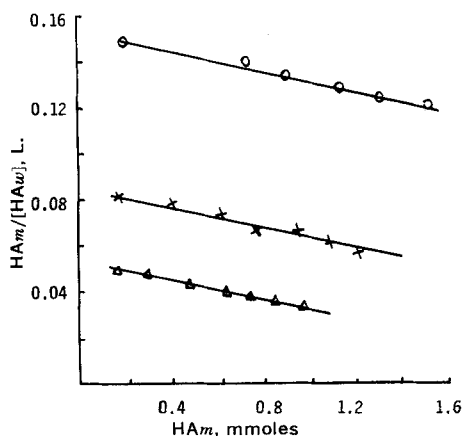


Fig. 4.—Langmuir isotherm plot for *C* systems. Key: O, *C1*; X, *C2*; Δ, *C3*.

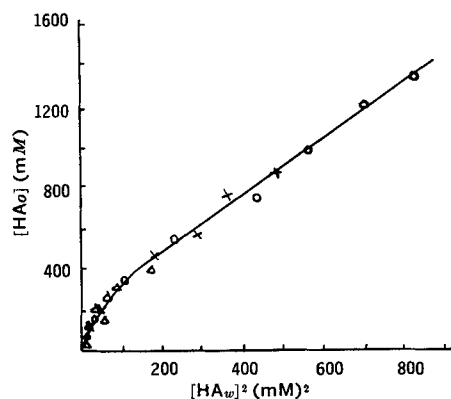


Fig. 5.—Dimerization plot for *F* systems. Key: O, *F1*; X, *F2*; Δ, *F3*.

TABLE II.—SOLUBILIZATION PARAMETERS FOR L1 SYSTEMS

System	K molar ⁻¹	σ_s/G of Surfactant, mmoles
<i>A1</i> ^a	26	2.1
<i>A2</i>	20	2.4
<i>A3</i>	20	2.3
<i>A4</i>	20	2.4
<i>B1</i>	23	2.1
<i>B2</i>	23	2.0
<i>B3</i>	23	2.1
<i>C1</i>	22	2.2
<i>C2</i>	22	2.2
<i>C3</i>	22	2.3
<i>D</i>	40	1.9

^a The results for the *A* systems, which have been previously reported (3), are recorded here for comparison purposes.

TABLE III.—SOLUBILIZATION PARAMETERS FOR THE (L1 + LC) SYSTEMS

System	Max. and Min. Values of K_d^1	
<i>E1, E2</i>	0.4	0.25
<i>F1, F2, F3</i>	3.2	0.65
<i>G1, G2</i>	0.6	0.25
<i>H1, H2</i>	0.5	0.30

In the case of solution *I*, two bulk phases, the benzoic acid liberated in the water did not apparently diffuse into the benzene. The pH values recorded during the titration were the same as those observed in a purely aqueous system. Though the lower L1 phase was stirred magnetically, it was not possible to stir the upper L2 phase. This lack of stirring together with the relatively small interfacial area was probably responsible for the apparent lack of diffusion from the L1 to L2 phase.

In system *J*, pH measurements were unobtainable. The needle on the dial of the pH meter fluctuated violently (± 0.1 pH unit); film formation upon the surface of the glass electrode may possibly be responsible for this phenomenon (6).

Solubilization isotherms, plots of HA_m against $[HA_w]$ for L1 systems and of $[HA_o]$ against $[HA_w]$ for the (L1 + LC) systems were obtained by substitution in the Henderson equation (3).

The graphs so obtained were of two types. Those obtained from the L1 systems were similar to previously reported isotherms. Figure 2 exemplifies them. However, in the (L1 + LC) systems the solubilization isotherms were very different in form. All were similar to that shown in Fig. 3.

Figure 4, a Langmuir plot, shows that the solubilization process in all the *C* systems was governed by the Langmuir isotherm, as was the solubilization process in all the L1 systems. From Langmuir plots the values of K , the negative slope, and σ_s , the intercept on the HA_m axis, were measured. Table II records the adsorption parameters for all the L1 systems. It is noteworthy that with the exception of system *A1* the solubilization parameters for systems of the same surfactant-to-benzene ratio are substantially the same. It is also interesting that the presence of quite large quantities of benzene has, with the exception *D*, little effect upon the solubilization parameters.

Solubilization in the (L1 + LC) systems appears to be governed by a totally different mechanism; the increasing slope of the curve shown in Fig. 3 suggests dimer formation in the liquid crystal. A plot of $[HA_o]$ against $[HA_w]^2$ for the *F* systems is shown in Fig. 5, the plots for the other (L1 + LC) systems were of a similar form, all showing a somewhat abrupt change in slope. This may indicate some fundamental change in the properties of the various systems. As was found in the L1 systems all (L1 + LC) systems with the same surfactant-to-benzene ratio were characterized by the same solubilizing power. Table III records maximum and minimum K_d^1 values.

The change in solubilization mechanism from absorption to dimer formation is probably due to the great difference in interfacial area between the micelles of L1 systems and the liquid crystal of the (L1 + LC) emulsions.

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