Predicting the Effect of Nonionic Surfactants on Interfacial Tensions

By RUSSELL E. PHARES, JR.

The reductions in water–air, oil–air, and water–oil interfacial tensions produced by nonionic surfactants have been successfully predicted using a form of the Langmuir adsorption equation. The reduction in the water–oil interfacial tension produced by a hydrophilic and a lipophilic surfactant acting simultaneously has been successfully predicted using a modified form of the Langmuir equation. The experimental results indicate that all interfacial adsorption sites behave alike, independently of each other. The data also indicate that the lipophilic and hydrophilic surfactants do not interact to reduce interfacial tension more effectively than when used alone. It is suggested that the effect of hydrophilic and lipophilic surfactants on water–oil interfacial tension may serve as an analog for the pharmacological response that would be produced when two drugs which compete for the same sites of action but have different potencies and/or dose response curves are administered together.

DURING THE last few years the nonionic surfactants, such as polyoxyethylene (20) sorbitan monolaurate[1] and sorbitan monolaurate,[2] have become the chosen emulsifiers for many pharmaceutical emulsions; but despite their widespread popularity, little has been published concerning the quantification of their effects. In 1908, Szyszkowski (1) observed that the surface tension of solutions of the shorter-chain normal fatty acids followed the empirical relationship

$$\gamma_0 - \gamma = b \ln [1 + (C/a)]$$

where γ_0 equals the surface tension of the solvent, γ equals the surface tension of the solution, C equals the concentration of the solution, and a and b are constants. For high concentrations, this equation is much like the empirical equation given by Milner (2). These empirical relationships have limited value in formulation work because they do not explain the observable changes in the system under study, they do not permit a meaningful method of comparing surfactants, and they cannot be extended to predict the actions of surfactant blends such as those used in emulsions. Gibbs' equation (3) for calculating the amount of surfactant adsorbed at an interface also has limited value, since a satisfactory experimental method for determining the amount adsorbed at a liquid–liquid interface has not been developed. Even Griffin's empirical method (4) for selecting optimum emulsifier blends does not explain what is actually happening to the surfactant.

THEORY

It has been proposed that the surface tension of a solvent is lowered because of the positive adsorption of surfactant molecules. If surfactants are truly adsorbed, they may be expected to follow a form of the Langmuir equation (5) which can be written

$$Y = Y_m[C/(a + C)] \qquad \text{(Eq. 1)}$$

where Y equals the amount adsorbed per unit area of adsorbent, Y_m equals the maximum amount that can be adsorbed per unit area of adsorbent when the monolayer is complete, C equals the equilibrium concentration of solute, and a equals k_1/k_2, where k_1 is the rate constant for the evaporation of molecules from the surface back into the solution, and k_2 is the rate constant for the adsorption of molecules to the surface. (See *Appendix*.) The validity of using concentration instead of pressure, as given in the original Langmuir equation, has been demonstrated by Barr *et al.* (6).

If it is assumed that the amount the surface tension of a solvent is lowered ($\gamma_0 - \gamma$) is directly proportional to the weight of surfactant adsorbed per unit area of surface multiplied by its activity coefficient (α), then

$$(\gamma_0 - \gamma) = (K)(Y)(\alpha_1) \qquad \text{(Eq. 2)}$$

and

$$\gamma_m = (K)(Y_m)(\alpha_2) \qquad \text{(Eq. 3)}$$

where γ_m is the amount the surface tension will be lowered when the monolayer per unit area of surface is complete, K is a proportionality constant, α_1 is the activity coefficient when weight Y is adsorbed per unit area of surface, and α_2 is the activity coefficient when weight Y_m is adsorbed. Substituting Eqs. 2 and 3 into Eq. 1 gives

$$\gamma_0 - \gamma = \left(\frac{\alpha_1}{\alpha_2}\right)(\gamma_m)\frac{C}{a + C} \qquad \text{(Eq. 4)}$$

When dealing with nonionic surfactants, one would not expect a change in α as concentration changes unless it was a result of van der Waals forces or steric interferences. If there is no interaction, then α_1/α_2 should equal 1. Equation 4, after it is rearranged and α_1/α_2 is set equal to 1, becomes

TABLE I.—EFFECT OF VARIOUS CONCENTRATIONS OF POLYSORBATE 20 ON THE SURFACE TENSION OF WATER

% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$
100	37.4	10	37.4	0.2	32.8	0.02	31.3	0.002	20.0
80	39.8	1	35.3	0.1	33.5	0.01	30.2	0.001	16.5
66.7	41.4	0.8	34.6	0.08	32.7	0.008	29.1	...	...
50	39.8	0.6	34.2	0.06	32.3	0.006	27.6	...	...
20	38.3	0.4	32.7	0.04	32.1	0.004	25.4	...	...

TABLE II.—EFFECT OF VARIOUS CONCENTRATIONS OF POLYSORBATE 20 ON WATER–OIL INTERFACIAL TENSION

% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$
0.1	38.0	0.04	37.7	0.01	34.5	0.006	29.0	0.001	8.5
0.06	38.0	0.02	35.5	0.008	34.0	0.004	27.0	...	...

$$\frac{C}{\gamma_0 - \gamma} = \frac{a}{\gamma_m} + \frac{C}{\gamma_m} \quad \text{(Eq. 5)}$$

If Eq. 5 is valid, then a plot of $C/(\gamma_0 - \gamma)$ against C should give a straight line with a slope of $1/\gamma_m$ and an intercept of a/γ_m. This equation should be valid for water–air and oil–air interfaces and should also be valid for water–oil interfaces in the presence of only one surfactant if the water–oil partition coefficient approaches ∞ for a hydrophilic surfactant or 0 for a lipophilic surfactant.

At a water–oil interface, it is possible to have surfactant molecules being adsorbed from both the water and the oil phases of the system. The water–oil interfacial tension of a system containing both a hydrophilic and a lipophilic surfactant should be predictable if the following conditions are met: (*a*) Equation 5 is valid for the water–oil interfacial tension for both surfactants when they are used alone. (*b*) There is no interaction between the hydrophilic and the lipophilic surfactants.

The following equation, which is derived in the *Appendix*, should predict interfacial tension when the previously stated conditions are true:

$$\gamma = \gamma_0 - \frac{\gamma_{mT}a_S C_T + \gamma_{mS}a_T C_S}{a_S a_T + a_S C_T + a_T C_S} \quad \text{(Eq. 6)}$$

where the subscript T indicates terms associated with the hydrophilic surfactant, and the subscript S indicates terms associated with lipophilic surfactant. Equation 6 can be written in a more general way as

$$(\gamma_0 - \gamma) = (\gamma_0 - \gamma_T) + (\gamma_0 - \gamma_S) \quad \text{(Eq. 7)}$$

where $(\gamma_0 - \gamma)$ is the total reduction in interfacial tension, and $(\gamma_0 - \gamma_T)$ and $(\gamma_0 - \gamma_S)$ are the amounts the hydrophilic and the lipophilic surfactants, respectively, reduce the interfacial tension.

The equilibrium concentration of surfactant in a solution can be calculated from

$$S_0 = (\text{wt. of soln.}) [C_S] + A Y_S \quad \text{(Eq. 8)}$$

where S_0 is the total amount of the surfactant, wt. of soln. in the case of a lipophilic surfactant is the weight of the oil phase plus the dissolved surfactant, C_S is the equilibrium concentration of the surfactant, A is the total interfacial area, and Y_S is the amount of surfactant adsorbed per unit area of interface. When the weight of solution is large compared to the interfacial area, Eq. 8 becomes approximately equal to

$$S_0 = (\text{wt. of soln.}) C_S \quad \text{(Eq. 9)}$$

It is interesting that the following derivation, based upon Gibbs' adsorption equation and the equations presented in this paper, results in Szyszkowski's equation $\gamma_0 - \gamma = b \ln (1 + C/a)$. Equation 10 is obtained by substituting Eq. 2 into Eq. 4 and setting K equal to $RT\gamma_m/\alpha_2 b$, where R is the ideal gas constant, T is the absolute temperature, b is a constant for temperature T, and γ_m, α_2, and a are the same as given previously.

$$Y = (b/RT)[C/(a + C)] \quad \text{(Eq. 10)}$$

Gibbs' equation is

$$Y = -(C/RT)(d\gamma/dC) \quad \text{(Eq. 11)}$$

Equating Eqs. 10 and 11 gives

$$-\frac{d\gamma}{dC} = b \frac{1/a}{1 + (C/a)}$$

or

$$-\frac{1}{b} d\gamma = \frac{1/a}{1 + (C/a)} dC \quad \text{(Eq. 12)}$$

Integrating Eq. 12 between γ_0 at concentration $C = 0$ and γ at concentration C results in Szyszkowski's equation

$$\gamma_0 - \gamma = b \ln[1 + (C/a)] \quad \text{(Eq. 13)}$$

EXPERIMENTAL

The materials used in this work included freshly distilled deionized water, liquid petrolatum U.S.P., and commercial grades of polyoxyethylene (20) sorbitan monolaurate and sorbitan monolaurate. All interfacial tension measurements were made with a Cenco-du Nouy interfacial tensiometer, model 70540, at 20° as outlined in the instruction book (7). All water–air and oil–air interfacial tension measurements were made on 25-ml. samples in 50-ml. beakers. All water–oil measurements were done in 50-ml. beakers on 25-ml. samples of water overlayed with 25 ml. of oil. All calculations were based on the average of five up readings on each sample. All concentrations of surfactants are equilibrium concentrations calculated on the basis of Eq. 9 and are expressed as w/w percentages.
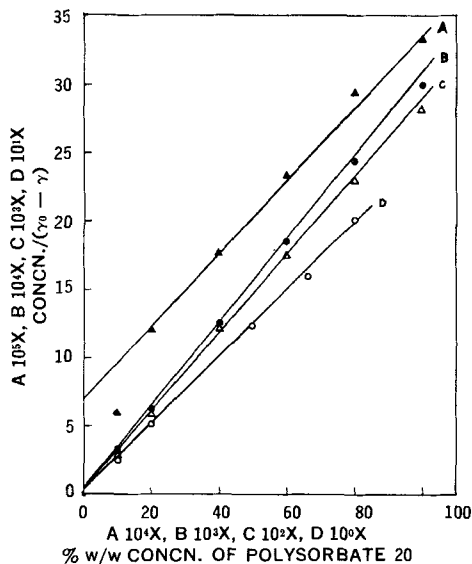
Fig. 1.—Reduction in the surface tension of water at various polysorbate 20 concentrations.
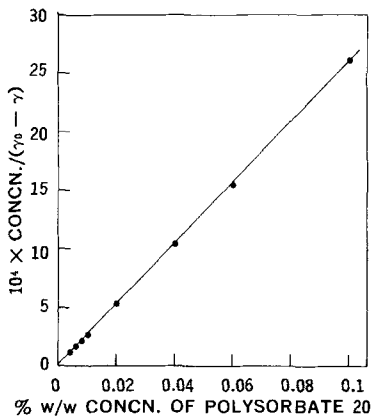

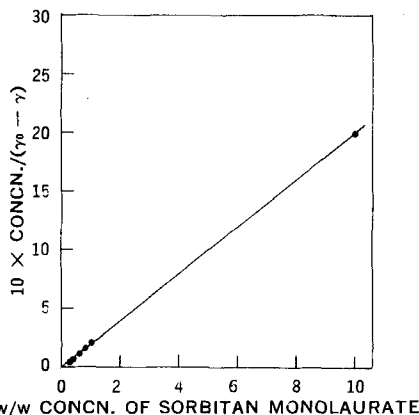Fig. 2.—Reduction in the water–oil interfacial tension at various polysorbate 20 concentrations.

Fig. 3.—Reduction in the surface tension of liquid petrolatum at various sorbitan monolaurate concentrations.
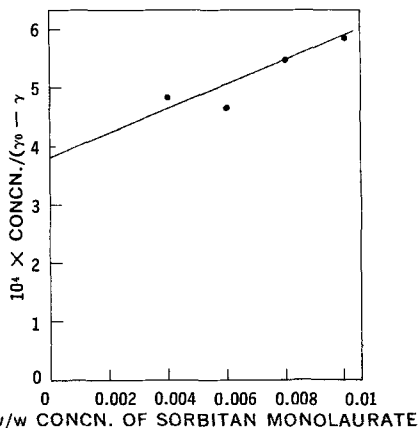

Fig. 4.—Reduction in the water–oil interfacial tension at various sorbitan monolaurate concentrations.

TABLE III.—EFFECT OF VARIOUS CONCENTRATIONS OF SORBITAN MONOLAURATE ON THE SURFACE TENSION OF LIQUID PETROLATUM U.S.P.

% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$
10	5.0	1.0	4.8	0.8	4.8	0.6	4.9	0.4	4.5
0.3	3.8	...	...	...	...	...	...	...	...

TABLE IV.—EFFECT OF VARIOUS CONCENTRATIONS OF SORBITAN MONOLAURATE ON WATER–OIL INTERFACIAL TENSION

% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$	% w/w Concn.	$\gamma_0 - \gamma$
0.01	17.0	0.008	14.5	0.006	13.0	0.004	8.5

RESULTS AND DISCUSSION

Tables I and II summarize the data obtained when the water–air and the water–oil interfacial tensions were determined for various concentrations of polysorbate 20 dissolved in water. A plot of concentration against concentration/$(\gamma_0 - \gamma)$ for the data in Tables I and II is in Figs. 1 and 2. Tables III and IV summarize the data obtained when the oil–air and the water–oil interfacial tensions were determined for various concentrations of

TABLE V.—MEASURED AND CALCULATED WATER–OIL INTERFACIAL TENSIONS RESULTING FROM VARIOUS COMBINATIONS OF POLYSORBATE 20 AND SORBITAN MONOLAURATE

% w/w Concn. Polysorbate 20	% w/w Concn. of Sorbitan Monolaurate[a]									
	0.01		0.008		0.006		0.004		0.002	
	a[a]	b[a]	a	b	a	b	a	b	a	b
0.1	6.2	5.9	7.0	6.0	5.1	6.0	6.4	6.0	5.3	6.0
0.06	6.8	6.4	6.8	6.5	5.4	6.6	6.5	6.6	6.1	6.6
0.04	7.4	6.9	7.8	7.0	6.8	7.0	7.1	7.1	7.8	7.1
0.02	7.9	8.2	9.2	8.4	8.6	8.5	8.6	8.6	8.5	8.8
0.01	9.2	10.5	9.4	10.8	9.3	11.0	11.3	11.3	...	...
0.008	9.6	11.5	10.0	11.8	11.6	12.1	10.0	12.5	...	...
0.006	12.2	12.8	11.5	13.3	12.0	13.8	13.0	14.3	...	...
0.004	13.5	15.0	13.0	15.6	15.0	16.3	15.5	17.0	...	...

[a] a, the measured interfacial tension; b, the calculated interfacial tension.

TABLE VI.—CONSTANTS FOR FIGS. 1–4

Fig.	Slope	Intercept	S[a]	γ_m	a
1A	2.9×10^{-2}	5.2×10^{-5}	2.0×10^{-3}	34.0	1.7×10^{-3}
1B	3.0×10^{-2}	6.6×10^{-5}	4.0×10^{-4}	33.8	2.2×10^{-3}
1C	2.8×10^{-2}	6.4×10^{-4}	4.9×10^{-4}	...	...
1D	2.4×10^{-2}	2.6×10^{-2}	8.7×10^{-3}	...	...
2	2.5×10^{-2}	5.1×10^{-5}	...	39.8	2.0×10^{-3}
3	2.0×10^{-1}	9.8×10^{-3}	8.0×10^{-4}	5.0	4.9×10^{-2}
4	2.0×10^{-2}	3.8×10^{-4}	...	50.3	1.9×10^{-2}

[a] S = standard deviation of the slope.

sorbitan monolaurate dissolved in oil. A plot of concentration against concentration/$(\gamma_0 - \gamma)$ for the data in Tables III and IV is in Figs. 3 and 4. A summary of the constants pertinent to Figs. 1–4 is presented in Table VI. As can be seen from Figs. 1–4, the experimental results seem to follow Eq. 5. Tuck and Flood have shown in some unpublished work presented to the AMERICAN PHARMACEUTICAL ASSOCIATION, New York City meeting, August 1964, that the Langmuir equation can be used for expressing the effect of surfactants on water–air interfacial tension. Since in at least one instance (8) the amount of a surfactant adsorbed at an interface has been shown to be given by Langmuir's equation, since the experimental data fit Eq. 5, and since Tuck and Flood have also shown that surface tension lowering is given by a form of the Langmuir equation, the assumption expressed in Eq. 2 seems valid.

In the second part of the work, the calculated slopes and intercepts of the curves in Figs. 2 and 4 were used to obtain the constants in Eq. 6, which was then used to predict the interfacial tension between water and oil containing various concentrations of polysorbate 20 and sorbitan monolaurate, respectively. The predicted and the experimentally determined interfacial tensions for the various systems are given in Table V. When a simple correlation on the data in Table V was performed, a correlation coefficient of 0.97 was obtained.

It is interesting that if one considers the reduction of water–oil interfacial tension as an analog of a pharmacological response, then the experimental results can be interpreted in terms of what would be expected if two drugs which compete for the same sites of action in the body but which have different potencies and/or dose response curves are administered together. Differences in potency are defined here as differences in the maximums on the

typical dose response curve, while differences in the dose response curves refer only to the shapes of the curves (*i.e.*, the slopes of the straight portions of the curves) but not the maximums. In terms of the notation used in this paper, maximum dose responses or potencies depend upon Y_{mT} and Y_{mS}, while the shapes of the dose response curves depend upon a_T and a_S. When the equations in this work are written in terms of the biological analogs just mentioned, equations mathematically equivalent to those given by Ariens and Simonis (9) for the effect produced by a single drug and the over-all effect produced by two competitive drugs are obtained.

In view of the findings of this investigation and those of Tuck, Flood, Vold, and Groot, it is suggested that sufficiency of the classical criterion of the critical micelle concentration (CMC), such as that given by Osipow (10), be reviewed critically. The results of this investigation suggest that the effect of surfactant concentration on the lowering of interfacial tension can be explained completely without considering CMC; therefore, defining CMC on the basis of the rate of lowering of interfacial tension seems questionable.

SUMMARY

1. The reduction of water–air and water–oil interfacial tensions by polysorbate 20 seems to be described adequately by an equation of the form of Langmuir's adsorption equation.

2. The reduction of oil–air and water–oil interfacial tensions by sorbitan monolaurate also seems to be described adequately by an equation of the form of the Langmuir adsorption equation.

3. There appears to be no interaction between polysorbate 20 and sorbitan monolaurate as far as their abilities to reduce interfacial tension are concerned.

4. All adsorption sites at the water–oil interface appear to be alike.

5. A formula for calculating the fraction of sites filled by each of two different surfactants has been given.

6. A formula for calculating the water–oil interfacial tension when known amounts of polysorbate 20 and sorbitan monolaurate are both present has been given.

7. From this work, it appears that the optimum surfactant blends described by Griffin for emulsions cannot be explained on the basis of producing a minimum interfacial tension between oil and water.

8. Observing the effect of various types of surfactants and surfactant mixtures on water–oil interfacial tensions may help to elucidate the effect on pharmacological response of various drugs and drug combinations, all of which are adsorbed at common sites.

APPENDIX

In 1916, Langmuir (5) published an adsorption equation which can be derived in the following manner. The rate at which molecules will attack a given number of adsorption sites is proportional to the fraction of unfilled sites $(1 - \theta)$ and the number of molecules that are in a position to be adsorbed. The number of molecules that will be in a position so that they can be adsorbed will be proportional to the pressure of a gas or to the concentration of a solution. The rate of adsorption can be written

$$R_a = K_2(1 - \theta)C \qquad (\text{Eq. 1A})$$

where C is concentration, and K_2 is a proportionality constant or rate constant.

The rate at which molecules will evaporate from or leave a given number of adsorption sites is proportional to the fraction of the filled sites (θ). The rate of evaporation can be written

$$R_e = K_1\theta \qquad (\text{Eq. 2A})$$

At equilibrium $R_e = R_a$, so that

$$K_2(1 - \theta)C = K_1\theta \qquad (\text{Eq. 3A})$$

or

$$\theta = \frac{C}{K_1/K_2 + C} = \frac{C}{a + C} \qquad (\text{Eq. 3B})$$

θ, the fraction of sites filled, can be expressed as Y'/Y_m', where Y' is a quantitative measure of some parameter which is directly proportional to the number of sites filled, and Y_m' is the value of Y' when all of the adsorption sites are filled.

A modified form of Langmuir's equation can be derived, as given below, for cases where two different molecules which do not interact with one another are competing for the same adsorption sites.

The rate of adsorption of polysorbate 20 can be written

$$R_{aT} = K_{2T}(1 - \theta_T - \theta_S)C_T \qquad (\text{Eq. 4A})$$

and for sorbitan monolaurate as

$$R_{aS} = K_{2S}(1 - \theta_T - \theta_S)C_S \qquad (\text{Eq. 5A})$$

where $(1 - \theta_T - \theta_S)$ is the fraction of unfilled adsorption sites.

The rate of evaporation of polysorbate 20 from the sites can be written

$$R_{eT} = K_{1T}\theta_T \qquad (\text{Eq. 6A})$$

and for sorbitan monolaurate

$$R_{eS} = K_{1S}\theta_S \qquad (\text{Eq. 7A})$$

At equilibrium $R_{aS} = R_{eS}$, and $R_{aT} = R_{eT}$ or

$$K_{2S}(1 - \theta_T - \theta_S)C_S = K_{1S}\theta_S \qquad (\text{Eq. 8A})$$

and

$$K_{2T}(1 - \theta_T - \theta_S)C_T = K_{1T}\theta_T \qquad (\text{Eq. 9A})$$

By substituting a_S for K_{1S}/K_{2S} in Eq. 8A and a_T for K_{1T}/K_{2T} in Eq. 9A and solving these equations simultaneously for θ_T and θ_S, the following equations are obtained:

$$\theta_T = \frac{a_S C_T}{a_S a_T + a_S C_T + a_T C_S} \qquad (\text{Eq. 10A})$$

and

$$\theta_S = \frac{a_T C_S}{a_S a_T + a_S C_T + a_T C_S} \qquad (\text{Eq. 11A})$$

If $\theta_T = \frac{Y'_T}{Y'_{mT}}$, where Y'_T = the amount, C_T lowers the water–oil interfacial tension $(\gamma_0 - \gamma_T)$ and $Y'_{mT} = \gamma_{mT}$ = the amount the water–oil interfacial tension is lowered when all of the adsorption sites are filled by polysorbate 20, then the amount that a given concentration of polysorbate 20 will lower the water–oil interfacial tension is

$$(\gamma_0 - \gamma_T) = \gamma_{mT}\theta_T \qquad (\text{Eq. 12A})$$

Similarly, it can be shown that the amount that a given concentration of sorbitan monolaurate will lower the water–oil interfacial tension is

$$(\gamma_0 - \gamma_S) = \gamma_{mS}\theta_S \qquad (\text{Eq. 13A})$$

If there is no interaction between polysorbate 20 and sorbitan monolaurate, then the amount that a given concentration of polysorbate 20 and sorbitan monolaurate would lower the water–oil interfacial tension should be

$$(\gamma_0 - \gamma) = (\gamma_0 - \gamma_T) + (\gamma_0 - \gamma_S) \qquad (\text{Eq. 14A})$$

By combining Eqs. 10A, 11A, 12A, 13A, and 14A, one obtains

$$(\gamma_0 - \gamma) = \frac{\gamma_{mT}a_S C_T + \gamma_{mS}a_T C_S}{a_S a_T + a_S C_T + a_T C_S} \qquad (\text{Eq. 15A})$$

REFERENCES

(1) Von Szyskowski, B., *Z. Physik. Chem.*, **64**, 385 (1908).
(2) Milner, S. R., *Phil. Mag.*, **13**, 96(1907).
(3) Martin, A. N., "Physical Pharmacy," Lea and Febiger, Philadelphia, Pa., 1960, p. 552.
(4) Griffin, W. C., *J. Soc. Cosmetic Chemists*, **1**, 311 (1949).
(5) Langmuir, I., *J. Am. Chem. Soc.*, **38**, 2221(1916).
(6) Evcim, N., and Barr, M., THIS JOURNAL, **44**, 570 (1955).
(7) "Cenco-du Nouy Tensiometer," Bulletin 101, Central Scientific Co., Chicago, Ill.
(8) Vold, R. D., and Groot, R. C., *J. Colloid Sci.*, **19**, 384(1964).
(9) Ariens, E. J., and Simonis, A. M., *J. Pharm. Pharmacol.*, **16**, 139, 141(1964).
(10) Osipow, L. I., "Surface Chemistry," Reinhold Publishing Corp., New York, N. Y., 1962, p. 125.