SUMMARY

A rapid and accurate ΔA spectrophotometric method has been devised for assaying vitamin B_6 in B complex and multivitamin preparations. Solutions containing 10 mcg./ml. or 5 mcg./ml. of vitamin B_6 are prepared in glycerinated 0.1 N HCl and phosphate buffer at pH 7, and the absorbance is read at 328 mμ using 0.1 N HCl solution as blank. Results are evaluated after applying correction for absorbance of plain buffers. The method is not applicable when flavors and emulsifying agents are present together.

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Interfacial Properties of Antimicrobial Long-Chain Quaternary Ammonium Salts I

Soluble Films at the Air–Water Interface

By NORMAN D. WEINER and GEORGE ZOGRAFI*

The surface tension of solutions containing selected long-chain quaternary ammonium compounds, having the same chain-length and counterion but differing in their polar group, was measured using the drop-volume method. The Gibbs adsorption equation was applied to obtain the surface concentration for each bulk concentration used. Data obtained in very dilute solutions conform to the equation of state for an ideal two-dimensional "gaseous" monomolecular film; whereas at higher concentrations, the films are in a "liquid-condensed" state. The standard free energy, entropy, and enthalpy for adsorption were calculated from data obtained in the ideal region. It appears that the change in entropy is the major thermodynamic factor involved in the adsorption process under study. Differences in adsorption for these compounds are discussed on the basis of the electronic and steric configuration of the polar groups.

ALTHOUGH surface-active quaternary ammonium compounds are used widely as antimicrobial agents, few detailed studies of their surface properties have been reported. Those studies which have been conducted have dealt primarily with the determination of critical micelle concentrations (CMC) and the effect of chain length and counterions on adsorption at the air–water interface (1–7).

It was the purpose of this investigation to gain insight into the role of the polar group on adsorption of quaternary ammonium compounds at the air–water interface and to quantify these differences by use of surface pressure *versus* area

curves, equations of state, and thermodynamic functions of adsorption.

EXPERIMENTAL

Materials.—Three quaternary ammonium compounds, having the same chain length and counterion but differing in their polar group, were selected. These were dodecylpyridinium chloride (DPC), dodecyltrimethylammonium chloride (DTAC), and dodecyldimethylethylammonium chloride (DEAC).

DPC (obtained from the Richardson-Merrell Pharmaceutical Co.) was purified by the addition of charcoal to a methanol solution of the sample. DTAC was prepared by the condensation of methyl chloride (Matheson Chemical Co.) and N,N-dimethyldodecylamine (Eastman Organic Chemicals); the latter reactant was purified according to Hinsberg (8). The reaction was carried out in a Paar hydrogenator for 12 hr. using ether as a solvent. DEAC was prepared by the condensation of N,N-dimethyldodecylamine and ethyl chloride (Gebauer's Chemical Co.) in a bomb at 100° for 6 hr. All three compounds were washed thoroughly with petroleum ether to remove any unreacted materials and were recrystallized three times from acetone.
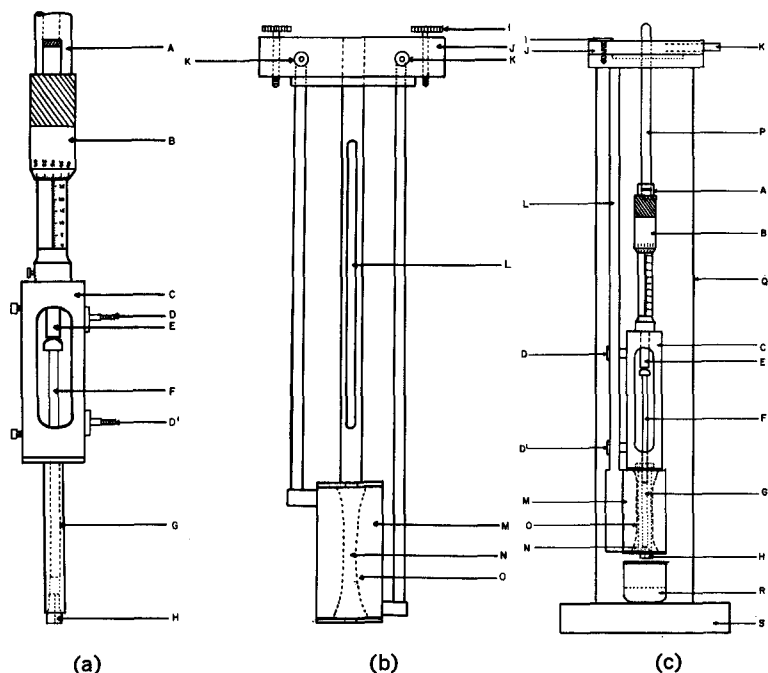
(a)   (b)   (c)

Fig. 1.—Drop volume apparatus for the determination of surface tension. (*a*) Micrometer drop volume apparatus. (*b*) Temperature control jacket for syringe with supporting frame. (*c*) Side view of assembled apparatus before immersion into a water bath (vertical circulation tubes leading from K have been omitted for greater clarity). Key: A, rubber sleeve connecting micrometer friction slip to P; B, modified micrometer; C, micrometer - syringe holder; D, guide screws for positioning C in L; E, micrometer spindle; F, syringe plunger; G, syringe barrel; H, syringe tip; I, locking screw; J, Plexiglas support block; K and K', inlet and outlet tubes for the maintenance of constant temperature; L, support bracket; M, temperature control jacket; N, syringe barrel shaft; O, thin rubber diaphragm; P, micrometer adjustment rod; Q, Plexiglas cylinder; R, solution receptacle; S, support base.

All compounds, recrystallized, had melting points and CMC's which agreed with reported values (7, 9). The purity of the compounds was substantiated further by the absence of a minimum in the surface tension *versus* logarithm molar concentration curves.

Potassium chloride (Mallinckrodt, analytical reagent) was heated to 500° for 6 hr. before use. The surface tension of a 0.1 *M* solution of KCl treated in this manner was 0.1 dynes/cm. higher than distilled water (10), an indication of an absence of surface-active impurities. The water was prepared by distilling deionized water (Barnstead mixed bed) twice; the first distillation was carried out in the presence of basic potassium permanganate. The surface tension of water prepared by this method was always within 0.05 dynes/cm. of the literature value (10).

Surface Tension Measurements.—The drop volume method (11) was used for all surface tension measurements. The apparatus[1] utilized (Fig. 1) was similar to that described by Parreira (7). The principle modifications of the instrument included a thin rubber diaphragm which allowed closer contact between the circulating water used to maintain constant temperature and the syringe, and the use of Plexiglas for the construction of the column in which the apparatus was contained. An Agla micrometer syringe (Burroughs Wellcome and Co.) was used. The syringe tip was cut to provide a flat edge and roughened with medium carborundum powder to insure good wetting. The tip showed no visible flaws under 10 × magnification, and wetting of the sides of the tip was not observed throughout

the study. The radius of the tip, measured with a cathotometer, was 0.2910 cm. Temperature was controlled to within ± 0.05°.

Surface tension measurements of water at 25°, 35°, and 45° and of benzene and hexane at 25° were within 0.05 dynes/cm. of reported values (10). Interfacial tension measurements of hexane–water and benzene–water at 20° were within 0.1 dynes/cm. of reported values (10).

Calculations of surface tension from the drop volume method involve the use of a correction factor, θ, which is obtained from a graph of θ *versus* $r/V^{1/3}$, where r is the radius of the tip and V is the volume of the drop (11). It was found that graphical interpolation of θ from standard graphs (11) involved errors in excess to those warranted by the precision of the instrument. A second-order polynomial expression

$$\theta = 0.41344(r/V^{1/3})^2 - 0.70796(r/V^{1/3}) + 0.90217 \quad \text{(Eq. 1)}$$

was in excellent agreement (± 0.0005) with literature values (11) for $r/V^{1/3}$ values of 0.3 to 1.0. This range of values was well within the limits of all experiments performed in this study.

All solutions were prepared in duplicate. The volume of at least 5 drops was measured for each sample; the volume of a drop was independent of time if the drop was allowed at least 2 min. to form. All surface tension values obtained were, therefore, considered to be equilibrium measurements.

Surface tension *versus* concentration data were obtained for DPC, DTAC, and DEAC in water at 25° and in 0.1 *M* KCl at 17.5°, 25°, and 35°.

RESULTS

To obtain values for the surface excess of each compound from the surface tension *versus* concentration data, the Gibbs adsorption equation (12) was applied. In the presence of excess electrolyte common to the counterion (0.1 *M* KCl), where activity coefficient, $\gamma \pm$, remains invariant to changes in concentration of surface-active agent

$$\Gamma = (1/kT)(d\pi/d \ln c) \qquad \text{(Eq. 2)}$$

where

Γ = surface excess (molecules/cm.^{2}),
k = Boltzmann's constant (ergs/degree-molecule),
T = absolute temperature,
π = surface pressure; surface tension of solvent minus surface tension of solution (ergs/cm.^{2}),
c = bulk concentration (moles/liter).

In the absence of excess common electrolyte,

$$\Gamma = (1/2kT)(d\pi/d \ln a) \qquad \text{(Eq. 3)}$$

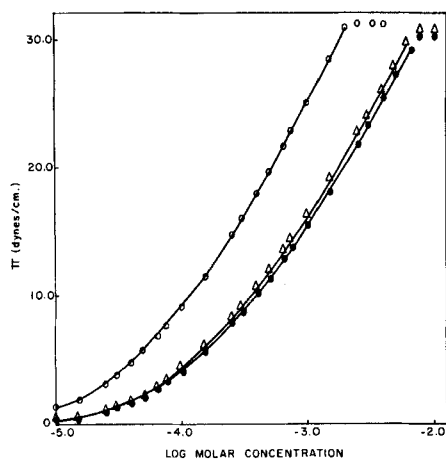where $a = \gamma \pm c$, the bulk activity. The mean

Fig. 2.—Surface pressure (π) *vs.* log molar concentration in 0.1 *M* KCl at 25°. Curves represent theoretical fourth-order polynomial approximations (least-squares fit) for each compound. Key: O, DPC; △, DEAC; ●, DTAC.
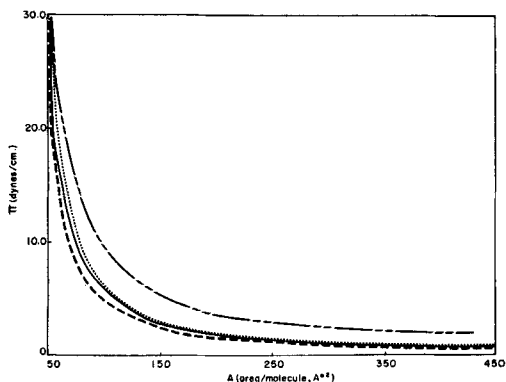
Fig. 3.—Surface pressure (π) *vs.* surface area (A) for DPC. Key: — — — —, distilled water at 25°; ————, 0.1 *M* KCl at 25°; ......, 0.1 *M* KCl at 35°; — — — —, 0.1 *M* KCl at 17.5°.
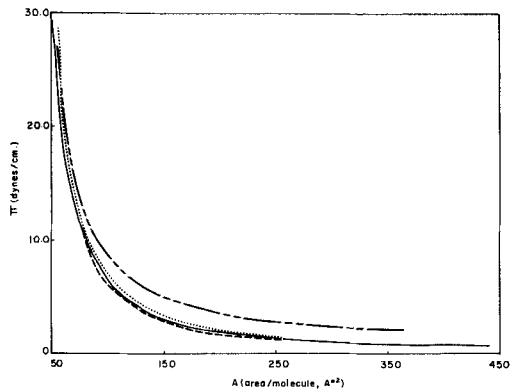
Fig. 4.—Surface pressure (π) *vs.* surface area (A) for DTAC. Key: — — · — —, distilled water at 25°; ————, 0.1 *M* KCl at 25°; . . . ., 0.1 *M* KCl at 35°; — — — —, 0.1 *M* KCl at 17.5°.
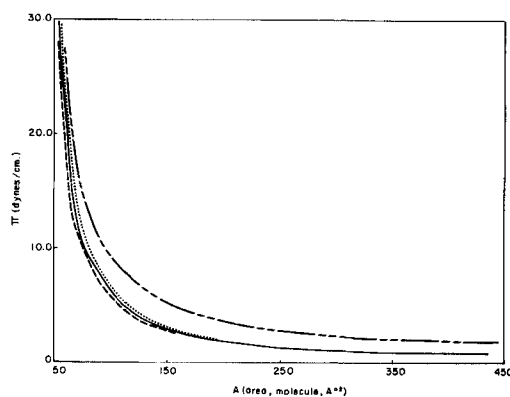
Fig. 5.—Surface pressure (π) *vs.* surface area (A) for DEAC. Key: — — · — —, distilled water at 25°; ————, 0.1 *M* KCl at 25°; . . . ., 0.1 *M* KCl at 35°; — — — —, 0.1 *M* KCl at 17.5°.

activity coefficient, $\gamma \pm$, was calculated from the extended Debye-Hückel equation (13).

To obtain accurate values of $(d\pi/d \ln c)$, it was necessary to estimate the slopes of surface pressure *versus* logarithm molar concentration curves. Since the curves are parabolic in nature, slopes were estimated with polynomial equations using the least squares method (14). An IBM model 7090 digital computer was utilized to obtain the required data.[2] The agreement between experimental and theoretical data was excellent (Fig. 2), and in all cases the standard error of the equations was less than 0.08 for fourth-order equations in the presence of 0.1 *M* KCl and fifth-order equations in the absence of excess electrolyte.

The mean area per molecule, A, expressed in angstrom units, was calculated by taking the reciprocal of the surface excess expressed as molecules per square angstrom. Surface pressure, π, *versus* area, A, curves are shown in Figs. 3–5. These curves represent a two-dimensional analogy to a pressure-volume curve of a gas and give information concerning the degree of packing of the film.

It should be noted that in all cases the films are less expanded in salt solution than in pure water due

to the screening of ionic repulsions by the electrolyte. The slightly greater compressibility of the film at higher temperatures is consistent with the fact that the van der Waal forces of attraction between the hydrocarbon chains decrease with increasing temperature.

To treat the adsorption process thermodynamically, and thereby quantify it with standard thermodynamic functions, surface activities, rather than concentrations, must be used. Since surface activity coefficients are difficult to evaluate, measurements made in very dilute solution, where the surface activity coefficient is equal to unity, are most commonly used to evaluate standard thermodynamic functions of adsorption.

For low concentrations of surface-active agents, a linear relationship exists between surface pressure and bulk concentration

$$(d\pi/dc)_{c \to 0} = \alpha \qquad \text{(Eq. 4)}$$

where α is Traube's constant (15). Langmuir (16) pointed out the theoretical significance of this linear region by showing that the film obeys an equation of state

$$\pi A = kT \qquad \text{(Eq. 5)}$$

which may be considered a two-dimensional ideal gas law.

The choice of a standard state of one molecule per cubic centimeter, as proposed by Ward and Tordai (20), requires a knowledge of the surface film thickness. This is arbitrary of necessity, particularly when applied to ionized surfaces where
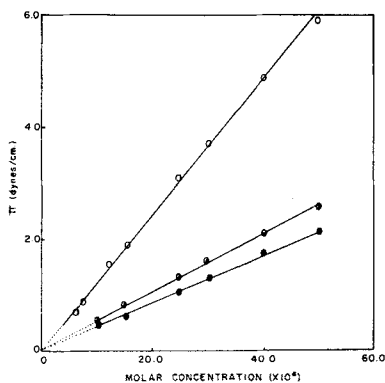

Fig. 6.—Surface pressure (π) *vs.* molar concentration in the ideal region in 0.1 M KCl at 25°. Key: O, DPC; ●, DTAC; ◑, DEAC.

there may be a variation in the thickness of the diffuse double layer with changing surfactant concentration and ionic strength. Betts and Pethica (17) defined the surface fugacity, π^*, as

$$\pi^* = \pi f \qquad \text{(Eq. 6)}$$

where f is the fugacity coefficient, and chose a standard state of unit fugacity. Equation 5 may, therefore, be written more correctly as

$$\pi^* A = \pi f A = kT \qquad \text{(Eq. 7)}$$

Since the value of f approaches unity in the ideal region, values of π in this region may be considered surface fugacities. Using a to denote bulk activity and μ to denote chemical potential

$$\mu^B = \mu_0^B + kT \ln a \qquad \text{(Eq. 8a)}$$

$$\mu^S = \mu_0^S + kT \ln \pi^* \qquad \text{(Eq. 8b)}$$

where the superscripts B and S refer to bulk and surface regions, respectively, and the subscript, 0, refers to the standard state. At equilibrium,

$$\mu_0^B - \mu_0^S = -\Delta G° = kT \ln (\pi^*/a) \qquad \text{(Eq. 9)}$$

where $\Delta G°$ is the standard free energy of adsorption. In dilute regions, where bulk activity can be replaced by concentration and where Eq. 4 is valid,

$$-\Delta G° = kT \ln \alpha \qquad \text{(Eq. 10)}$$

The standard entropy of adsorption, $\Delta S°$, can be calculated from

$$[d(\Delta G°)/dT]_{\pi^*=1} = -\Delta S° \qquad \text{(Eq. 11)}$$

while the standard heat of adsorption, $\Delta H°$, can be calculated from

$$\Delta G° = \Delta H° - T\Delta S° \qquad \text{(Eq. 12)}$$

Figure 6 represents a typical set of plots of surface pressure *versus* molar concentration in the ideal region. The standard thermodynamic functions of adsorption of DPC, DTAC, and DEAC are shown in Table I.

Studies on adsorbed films (18) show that for surface pressures above the ideal region, many films obey the Amagat equation

$$\pi(A - A_0) = xkT \qquad \text{(Eq. 13)}$$

where A_0 is the coarea of the molecule, and x is a measure of the lateral cohesion of the molecule in the film, decreasing as cohesion increases. To obtain A_0 and x, one may plot πA *versus* π, which should give a straight line with a slope of A_0 and

TABLE I.—STANDARD THERMODYNAMIC FUNCTIONS FOR THE ADSORPTION OF QUATERNARY AMMONIUM SALTS AT VARIOUS TEMPERATURES

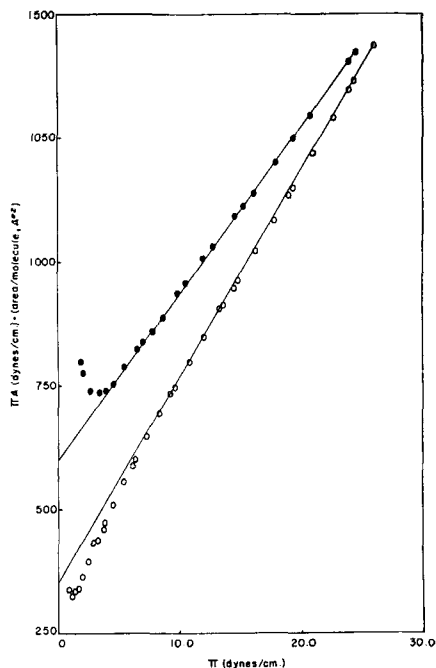| Compd.	KCl Concn., M	Abs. Temp.	α	$\Delta G°$ Kcal. mole	$\Delta H°$ Kcal. mole	$\Delta S°$ e.u.
DPC	0	298.0	3.64×10^3	-4.86	...	...
DPC	0.1	290.5	1.14×10^5	-6.73	0.01	23
DPC	0.1	298.0	1.20×10^5	-6.94	0.01	23
DPC	0.1	308.0	1.13×10^5	-7.13	-0.02	23
DTAC	0	298.0	2.13×10^3	-4.55	...	...
DTAC	0.1	290.5	4.24×10^4	-6.16	-0.06	21
DTAC	0.1	298.0	4.26×10^4	-6.32	-0.06	21
DTAC	0.1	308.0	4.20×10^4	-6.53	-0.06	21
DEAC	0	298.0	2.45×10^3	-4.63	...	...
DEAC	0.1	290.5	4.48×10^4	-6.19	-0.03	21
DEAC	0.1	298.0	4.48×10^4	-6.35	-0.03	21
DEAC	0.1	308.0	4.47×10^4	-6.56	-0.03	21

Fig. 7.—Surface pressure × surface area (πA) *vs.* surface pressure (π) for DEAC at 25°. Key: ●, distilled water; O, 0.1 M KCl.

an intercept of xkT. A typical plot is shown in Fig. 7.

Alexander (19) has shown that combination of the Amagat equation with the Gibbs adsorption isotherm, followed by integration, leads to the results

$$(\ln \pi')/\pi = (A_0/kT) + [(x \ln\pi)/\pi] \quad \text{(Eq. 14)}$$

where $\pi' = c\alpha$. Thus, if a film obeys the ideal gas law at low pressures and the Amagat equation at higher pressures, a plot of $(\ln\pi')/\pi$ *versus* $(\ln\pi)/\pi$ will give a straight line with a slope of x and an intercept of A_0/kT. A typical plot is shown in Fig. 8. Using the values of A_0 and x thus obtained, A can be calculated for each π from the Amagat equation. Therefore, π *versus* A curves as well as values for A_0 can be obtained for many soluble films without the necessity of estimating slopes from surface pressure *versus* logarithm concentration data. Figure 9 compares the π *versus* A curves of DEAC in 0.1 M KCl at 25° from the equations of state, $\pi A = kT$ (0–8 dynes/cm.) and $\pi(A - A_0) = xkT$ (12–30 dynes/cm.), with that obtained by direct application of the Gibbs adsorption isotherm.

Values of A_0 obtained from πA *versus* π curves and from the equations of state described above agree within experimental error. These have been compared with areas calculated from Fisher-Taylor-Hirschfelder molecular models for DPC, DTAC, and DEAC and are shown in Table II. The area of DPC was calculated from models to be 40Å.[2] if the polar group lies flat at the surface, and 25Å.[2] if it is directed vertically to the surface. The most thermodynamically stable configuration of DEAC was assumed for purposes of calculating its area. This configuration is also the most reasonable for

compressed films at an interface since it allows closest packing. In all cases, the dodecyl group was assumed to be aligned vertically to the interface.

Values of x calculated by the various methods were in good agreement. Their significance will be discussed in a subsequent communication concerned with the oil–water interface.

The CMC values of the various compounds at 25°, calculated from the sharp break in the surface pressure *versus* logarithm molar concentration curves (see Fig. 2), are shown in Table III.

DISCUSSION

The effect of the polar group on adsorption can be evaluated best in the ideal region, where strong London-type cohesive forces between the hydrophobic chains as well as electrical repulsion effects are absent, and at very low areas per molecule, where the hydrocarbon chains are vertically aligned, and where the limiting areas are determined by the steric and electronic nature of the polar group.

Ideal Region.—The entropy dependence of the adsorption process, shown in Table I, is in agreement with data calculated by Ward and Tordai for an homologous series of fatty acids, which showed that dependence on entropy becomes more pronounced with increasing chain length (20). This is probably due to the loss of the ice-like structure of water molecules associated with the hydrocarbon chain in
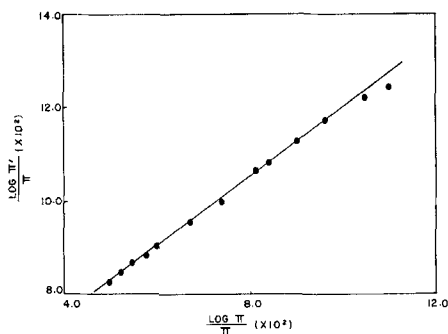

Fig. 8.—Logarithm ideal surface pressure (log π')/ actual surface pressure (π) *vs.* logarithm actual surface pressure (log π)/actual surface pressure (π) for DEAC in 0.1 M KCl at 25°.
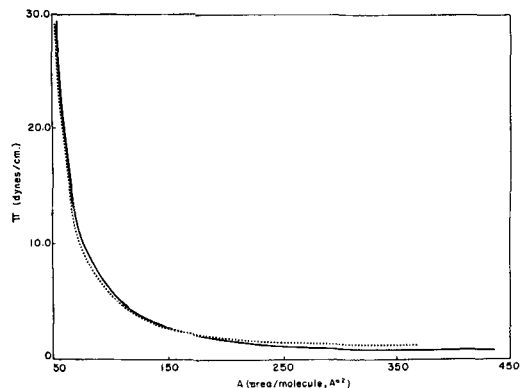

Fig. 9.—Surface pressure (π) *vs.* surface area (A) for DEAC in 0.1 M KCl at 25°. Key: . . . . ., from equations of state; ——, from Gibbs adsorption isotherm.

TABLE II.—COMPARISONS OF COAREAS (A_0) OF QUATERNARY AMMONIUM SALTS AT 25° IN 0.1 M KCl OBTAINED BY VARIOUS METHODS

Compd.	A_0(Sq. Å. per Molecule)		
	From Slope of πA *vs.* π	From Eqs. of State	From Molecular Models
DPC	37	35	25–40
DTAC	37	40	29
DEAC	41	43	31

TABLE III.—CMC OF QUATERNARY AMMONIUM SALTS AT 25°

Compd.	KCl Concn., M	CMC ($\times 10^3$)	CMC$_{water}$/CMC$_{0.1\ M\ KCl}$
DPC	0	14	
			6.1
DPC	0.1	2.3	
DTAC	0	20	
			2.7
DTAC	0.1	7.5	
DEAC	0	19	
			2.7
DEAC	0.1	7.0	

the bulk phase when the surface-active agent is adsorbed to the surface. The loss of one degree of translational freedom and the uncoiling of the chain at the surface probably result in only small over-all entropy effects. The entropic driving force of micelle formation has been explained in a similar manner (21).

Although the chain length plays the predominant role in determing surface activity, a comparison of α values shows that the polar group exerts a small but definite effect; the relative degree of adsorption is DPC >> DEAC > DTAC.

Since electrical and steric factors are negligible in the ideal region, it would appear that differences in adsorption of DPC, DTAC, and DEAC are due to differences in the extent of desolvation of the respective polar groups upon being adsorbed to the surface. A partial desolvation of the polar moiety at the surface is reasonable to expect because of the decreased amount of water in the surface region relative to that in the bulk. The slightly greater surface activity of DEAC, compared to DTAC, is probably due to the entropy gain upon the partial desolvation of the additional methylene group of DEAC in the surface region. This is somewhat analogous to the entropy gained by increasing the chain length. However, it is difficult to speculate concerning the reasons for the greater desolvation of the pyridinium ion, compared to the trialkylammonium ions on adsorption, since many more variables must be considered. For example, DPC contains a planar aromatic polar group with a delocalized charge, while DTAC and DEAC contain tetrahedral ammonium polar groups having point charges. The effect of the configuration of the polar groups at the surface should also be taken into account since this can contribute to their accessibility to water molecules.

The effects of KCl on the surface activity of the compounds investigated provides some evidence for the desolvation mechanism. Assuming that entropy is also the driving force for adsorption in the absence of KCl, the salt effect may be explained as follows.

The greater solubility of the pyridinium ion,

compared to the trimethylammonium ion in the bulk phase, can be assumed since cetylpyridinium chloride is more soluble than cetyltrimethylammonium chloride (22). The trimethylammonium ion would be expected to be slightly more soluble than the dimethylethylammonium ion from simple solubility principles. Assuming the more soluble ion to be hydrated to a greater extent, the order of increasing desolvation in the bulk, with the addition of KCl, should be DPC < DTAC < DEAC, since the less hydrated ion would offer less competition to the KCl for the bound water. This would result in an even greater driving force for adsorption of the more soluble ion in the presence of salt, compared to water, if the desolvation mechanism is primarily responsible for the differences in entropy. The $\Delta(\Delta G°)$ values for DPC, DTAC, and DEAC are -2.1, -1.8, and -1.7 Kcal. per mole, respectively, where $\Delta(\Delta G°)$ is the standard free energy of adsorption of the compound in 0.1 M KCl at 25° minus the standard free energy of adsorption of the compound in water at 25°. The order of $\Delta(\Delta G°)$ values, DPC > DTAC > DEAC, are in full agreement with this mechanism.

Therefore, it would seem that the generally accepted axiom of a decrease in solubility resulting in an increase of surface activity is theoretically sound, based on entropy considerations, when chain length alone is considered. However, if the chain length and counterion are held constant, exceptions to this axiom can occur.

Regions of Low Area.—It has been suggested that values of A_0 obtained from πA *versus* π curves in the regions of low area are usually larger than those calculated from molecular models since the latter does not account for the fact that part of the hydrocarbon chain in coiled form can extend into the aqueous phase (23). Thermal forces also cause the molecules to occupy a slightly larger area than that predicted from models. The values for A_0 shown in Table II are consistent with this reasoning for DTAC, DEAC, and DPC, if it is assumed that the orientation of the pyridinium ion is more vertical than horizontal to the plane of the surface. An orientation tending toward the vertical is more consistent with what would be expected at low areas since a closer packing of the molecules is facilitated.

At fairly high bulk concentrations, near but below the CMC, the change in surface pressure with the logarithm of molar concentration is almost linear, as seen in Fig. 2. This results in a region where the area per molecule at the interface is practically independent of the bulk concentration and surface pressure. Vader (24) termed this the region of saturation adsorption. He suggested that the area at which saturation adsorption commences is due to the presence of a hydration layer around the ionized group which prevents any further significant reduction in area with increasing pressure.

The areas of DPC, DTAC, and DEAC where saturation adsorption begins are all equal to 69 sq. Å. in distilled water and 50, 58, and 60 sq. Å., respectively, in 0.1 M KCl. The similar saturation adsorption areas in water indicate that the combined steric and electronic nature of the three polar groups produce the same over-all effect at low areas. In the presence of salt, however, the electronic repulsive forces at the surface are somewhat diminished due to a swamping effect, and differences

in the now lower values can be attributed to the closer packing of the planar pyridinium ion. It does not seem plausible that the lower saturation adsorption area of DPC in the presence of salt is due to its greater desolvation at the surface since KCl would be expected to desolvate DTAC and DEAC to a greater extent.

A comparison of CMC values of the various compounds in Table III indicate that the addition of salt affects the CMC of DPC to a greater extent than DTAC or DEAC. This can be explained on the same basis as the saturation adsorption phenomenon, where the addition of salts partially eliminates the repulsive effects of the ions and accentuates steric differences.

Thus, it is apparent that the small differences in surface activity due to the polar group may be evaluated by the techniques presented. These techniques, extended to a wider variety of polar groups, including nonionics and anionics, should prove useful to those interested in evaluating the effects of head groups at various interfaces. Future studies will discuss the effect of the polar group at various oil–water and biological interfaces.

SUMMARY

The adsorption of three quaternary ammonium salts, having the same chain length and counterion but differing in their polar group, has been measured at the air–water interface.

Differences in adsorption in the ideal region due to the polar groups have been evaluated thermodynamically and related to the entropy of adsorption. The possible role of ion hydration has been discussed.

Application of two-dimensional equations of state and the Gibbs adsorption isotherm have allowed for the determination of coareas, A_0, which are in good agreement with molecular models for the various compounds.

In regions of high surface concentration, the effect of the steric and electronic nature of the polar group has been evaluated by means of saturation adsorption, coarea, and CMC data.

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____Drug Standards____

Polarographic Determination of Chloramphenicol Preparations

By A. FRANCIS SUMMA

A polarographic method for the determination of chloramphenicol in commercial preparations is presented. The method has the necessary accuracy and precision for use in routine control analysis.

THE U.S.P. XVI assay (1) for chloramphenicol preparations is quite time consuming because it is based on a microbiological method of analysis. Chloramphenicol palmitate and its prepara-

tions, however, are assayed by an ultraviolet spectrophotometric procedure. The spectrophotometric procedure also is used for chloramphenicol preparations as an alternate method. In the analysis of dosage forms, chloramphenicol should be isolated from the excipients or vehicles prior to ultraviolet absorption quantitation, since these materials can lead to erroneously high results. The solubility characteristics of chloramphenicol, however, make isolation by liquid–liquid extraction difficult. Polarographic analysis should be less susceptible to interference from