The Thermodynamics of Micellar Solubilization of Neutral Solutes in Aqueous Binary Surfactant Systems

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1 Introduction

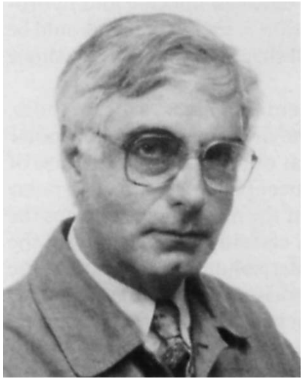
The two main properties of surfactants in water are their ability to adsorb at various interfaces (liquid/air, liquid/liquid, liquid/solid) and to form labile aggregates (micelles) above a critical micelle concentration (cmc). Micelles are able to favour the solubilization of sparingly soluble compounds (ionic or non-ionic) but they may also incorporate various water-soluble amphipathic ions or molecules. As a general rule (with few exceptions), unlike surfactants tend to be co-solubilized in aggregates which we will refer to hereafter as mixed micelles. The formation of mixed micelles may serve many practical purposes: they can decrease the cmc of ionic surfactants, increase the cloud point of a non-ionic surfactant, decrease the Krafft point of an ionic surfactant, modify the foaming properties of the system. A comprehensive survey of the literature on the properties of mixed surfactant solutions has been published recently.[1] The effect of surfactant mixing on the phenomenon of micellar solubilization is much less well documented than the other mixed surfactant properties.

In the case of single surfactant solutions, some general rules have begun to emerge from the wealth of experimental data available,[2] and additivity schemes are being developed[3] which parallel the efforts which were made for the calculation of the partition coefficients of solutes in two-phase systems (*e.g.*, water/octan-1-ol). One of these rules is that the solubilization of a neutral solute is not very dependent upon the charge, the hydrocarbon length, or the type of ionic head-group of a surfactant which forms regular micelles. Mixed-micelle formation may induce different micellar structures, adding a new variable to the investigation of the solubilization effect. The present review is an attempt to organize the sparse literature on this topic. We shall be concerned only with neutral solutes in relatively dilute aqueous binary surfactant systems so that only quantities as close as possible to standard thermodynamic conditions will be discussed. Sophisticated theoretical models have been developed for the description of micellar solubilization in single surfactant solutions either for direct or for reversed micelles.[4] Whatever their practical interest for such systems, the models cannot be applied to mixed micelles and are, therefore, excluded from this review. Many aspects of the micellar solubilization phenomenon are common to single and multi-component micellar systems. Only those studies which are explicitly related to the latter systems will be discussed.

It has been recognized for some time that the change in micelle structure resulting from mixed micelle formation is the main factor responsible for the variation of the solute solubilization. Tokiwa,[5] who was among the first to investigate the fundamentals of micellar solubilization behaviour in mixed surfactant systems, coined this structural feature a compactness factor, a concept which was to be extensively used. He showed that the solubilization of a water-insoluble dye, Yellow OB, in mixtures of a non-ionic surfactant of the dodecylpolyoxyethylene series with nine ethoxylated groups, $C_{12}EO_9$, and various sodium alkylbenzenesulfonates, depended dramatically on the position of the hydrophobic chain with respect to the aromatic group and the sulfonate head-group. A positive deviation from an ideal solubilization behaviour was observed when the hydrophobic chain of the ionic surfactant was separated from the sulfonate group by the aromatic moiety, but in all other configurations, the deviation from ideality was negative. It was concluded that when the mixed micelles are less compact than the single ones, the solubilization should decrease whereas when the mixed system is more compact, the solubilization should be favoured. Although other factors, such as solute hydrophobicity, solubilization site, and micelle surface curvature are important for the understanding of the solubilization phenomenon, they are common to single and to mixed micelles, even if the situation appears more complex in the latter case. Thus, knowledge of the changes of micellar properties upon surfactant mixing is a prerequisite for the interpretation of solute solubilization behaviour in these media.

One of the problems related to the discussion of solubilization data is the evaluation of the reliability of the methods which have been developed to extract relevant thermodynamic constants. Whenever saturation solubilities are needed, the experimental technique is relatively simple; but with the solute activity coefficients unknown, only apparent thermodynamic (distribution or equilibrium) constants can be obtained. The tendency in recent years has been to develop indirect methods which control the activity of the solute; but this can lead to discrepancies appearing among the experimental results because each method is based upon a particular assumption. The technical problems are essentially the same whether solubilization is studied in single or in multi-component micelles, with the exception of the question of the micelle composition, which is the relevant variable when discussing the properties of mixed micelles.

The organization of this review is as follows: in the first part, some of the concepts to be used in the discussion will be introduced. In a second part, the advantages of using the regular solution approximation (RSA) as a basis for the discussion of solubilization in mixed micelles will be proposed. In the third part, systems for which the RSA does not apply will be discussed and some general rules for the prediction of the solubilization behaviour of neutral solutes in mixed micellar solutions will be suggested. Finally, some calorimetric data dealing with the heat changes associated with solubilization in mixed systems will be reviewed.



Claude Treiner obtained his Ph.D. in 1967 from the University of Paris after carrying research with Professor R. M. Fuoss in 1963—1964 at Yale University (U.S.A.). He is Research Director at the Centre National de la Recherche Scientifique. He worked on transport phenomena and on the thermodynamics of solvation in multicomponent systems until the late 1970's. Since then he has shifted his interests towards surfactant solutions and has contributed to areas such as micellar solubilization, polymer–surfactant systems, mixed surfactant properties and, more recently, the coadsorption of surfactant and solute species at solid–liquid interfaces.

2 Theoretical Background

2.1 Mixed Micellar Properties: The Regular Solution Approximation

When two unlike surfactants form a mixed micelle, the micellar composition x, is usually different from the stoichiometric composition α If the cmc's of the two surfactants are very different from each other, the composition of the first mixed micelles formed will be richer in the surfactant with the lowest cmc, whatever the value of α At a higher total surfactant concentration, x will be eventually equal to α As the quantity of interest is the actual micellar composition x, the conditions for which $x = \alpha$ must be known This question has been dealt with by Clint[6] in the ideal case and by Rubingh[7] for the non-ideal case, assuming that all deviations from thermodynamic ideality may be accounted for by activity coefficients of the form adopted for the regular solution approximation (RSA)

The result is

$$x = (C - \Delta) + ((C - \Delta)^2 + 4\alpha\Delta C)^{\frac{1}{2}})/2\Delta \qquad (1)$$

$$\Delta = f_2C_2 - f_1C_1$$

and

$$f_1 = \exp(\beta x^2), f_2 = \exp(\beta(1 - x)^2) \qquad (2)$$

$$\beta = \ln(C_{12}\,\alpha/C_1\,x)/(1 - x)^2 \qquad (3)$$

β is an empirical parameter which may be calculated from cmc determinations at several α values using equation 3 and the same RSA model C_1, C_2, and C_{12} are respectively the cmc's of the pure surfactants and of the mixed micelles, and C is the total surfactant concentration It follows from equation 1 that the larger the difference between the cmc's of the two surfactants and the larger the deviation from ideality displayed by the variation of cmc's with micellar composition, the higher the value of C at which the micellar composition reaches the stoichiometric one Equations 1—3 rest upon the assumption that at a given α value only one type of micelle is formed of composition x We shall come back to this assumption in the discussion section Nishikido[8] has shown that the variation of solubilization of the dye Yellow OB with total surfactant concentration for a mixture of $\frac{1}{2}$Mn(DS)$_2$ + $C_{12}EO_{49}$ was non-linear up to $C = 1\ 10^{-2}$ mol l^{-1} A straight line is observed only above this surfactant concentration From the slope of this line, a solubilization constant can be defined This behaviour was interpreted as reflecting the change of solubilization with micellar composition x at the lowest C values Recent determinations of micellar composition in binary surfactant systems using a cross-flow ultra-filtration technique have confirmed the validity of equation 1[9]

It should be pointed out that alternative thermodynamic approaches have been developed to describe the departure from ideality for Gibbs energy changes of mixed micelles with composition Although admittedly a crude one, Rubingh's approach is well adapted to the present purpose because, as will be shown below, a single empirical parameter relates the deviation from ideality for the variation of solute solubilization with micelle composition to the Gibbs energy of interaction of unlike surfactants within mixed micelles

2.2 Micellar Solubilization in Mixed Micellar Systems

Micellar solubilization data, whether in single or multi-component mixtures, are usually represented using the pseudo-phase or the mass-action model The former model is better the larger the number of aggregates per micelle, the latter one needs the aggregation number N This quantity is seldom known and furthermore it may change with the solubilization of the solute Hence, the pseudo-phase model is most often used and the solubilization data are represented by a partition coefficient P, defined as the ratio of solute concentrations in the micellized surfactant pseudo-phase and in water In the case of mixed micelles, P is generally expressed on the mole fraction basis because the partial molar volumes of binary surfactants, which are necessary if the molar concentration scale is used, are often unknown

Nishikido[8] suggested that the ideal solubilization profile be represented by a relationship which, with the present notation reads

$$P_m = \alpha P_1 + (1 - \alpha)P_2 \qquad (4)$$

where P_m is the partition coefficient in the mixtures, and P_1 and P_2 are the values of P in each single surfactant solution Any deviation from this equation was to indicate a synergistic effect This effect was supposed to be the consequence of change in the compactness of the mixed micelle with respect to that of the single micelle, as a result of intra-micellar interactions This effect, however, could not be quantified and could be misleading Thus, in a study on the solubilization of 2-phenylethanol and benzyl acetate (slightly hydrophilic perfumes) in the mixed NaDS + $C_{16}EO_{20}$ system,[10] the negative deviation from ideal solubilization was attributed to an increased compactness of the mixed surfactants as compared to the single micelle properties, the same phenomenon was used to explain the positive deviation observed for the very large and hydrophobic molecule, Yellow OB, in the same binary mixtures [11]

The RSA theory seems a more easily tractable model for the description of micellar solubilization in mixed micellar solutions O'Connell and Prausnitz have shown that the RSA could be applied to the solubility of inert gases in binary solvents [12] Later on, Blandamer *et al* [13] showed the usefulness of that formalism for the description of the thermodynamic behaviour of hydrocarbon gases in mixed solvents Assuming the pseudo-phase model, Treiner *et al* [14] suggested that the RSA could be applied to the variation of the partition coefficient of a neutral solute with micellar composition according to the relation

$$\ln P_m = x\ln P_1 + (1 - x)\ln P_2 + Bx(1 - x) \qquad (5)$$

P_m, P_1, and P_2 have the same meaning as in equation 4, B has the same origin as that of the β coefficient in equations 1—3 and carries the same level of approximation There is no provision for either solute–solute or for solute–solvent interactions except through the individual P values, and only binary interactions are allowed between the two surfactants Thus, it is clearly assumed that the solute occupancy is small, *i e* the P's are limiting values as for the low gas solubility conditions for which the RSA was originally devised [12] Although we do expect that B will be different from β, some relationship between these two quantities can be envisaged The value of β is determined, as noted before, from cmc determinations Thus, from the knowledge of β, the sign and, probably, the amplitude of the variation of P with x should be predictable The literature[7] shows that β is generally negative, *i e* when two surfactants are mixed, a mixed micelle is favoured over single surfactant micelles, consequently, P should decrease upon surfactant mixing β is only positive in the case of some mixed fluorinated and hydrogenated surfactants because of the well-known repulsion effect between fluorine and hydrogen derivatives According to equation 5, such systems should be more favourable to micellar solubilization than either single micelle

Equation 5 should apply to all neutral solutes Most authors, however, tend to separate the behaviour of strictly non-polar molecules (hydrocarbons) from that of polar ones in the case of very dilute solutions (low solute occupancy) With non-polar molecules, it is usually assumed that the molecule penetrates the micellar aggregate and stays (on a certain time-average) in the micellar hydrocarbon core For polar solutes, adsorption at the micellar surface (in the so-called palissade layer) is assumed

A possible consequence of the penetration of the micelles by hydrocarbon gases or liquids was given a quantitative evaluation by Mukerjee[15] who proposed that the macroscopic Laplace pressure effect could be applied to very small labile bodies such as micelles. As this model has been frequently used by many authors, it is worth recalling. Depending upon the curvature of the micelle surface, the pressure effect will oppose solute penetration. Hence the solubility of hydrocarbon gases in a micellar aggregate, (e.g. for one mole of surfactant) will be lower than in a pure hydrocarbon solvent. In so far as mixed micelle formation induces, among other changes, the variation of the aggregation number and therefore, possibly, the change of the radiius of curvature of the aggregate, the micellar solubilization may be affected by this structural parameter. The basic equation may be put under the form:

$$\ln X_m = \ln X_h - 2\gamma V/rRT \qquad (6)$$

where γ is the surface tension between micelle and water, V the molar volume of the solubilizate, r the micelle radius. X_h and X_m are, respectively, the mole fraction solubilities of the non-polar molecule in a hydrocarbon solvent and in the micelles. The order of magnitude of this effect has been shown to be reasonable for hydrocarbons either in single[16] or in mixed micelles.[17] This approach predicts that a change in micellar shape (*e.g.* from spherical to cylindrical symmetry) should be accompanied by a decrease of solute solubility. The fact that this effect has not been observed does not mean that it does not exist. The micellar structural change is always produced by the addition of salt, and it is assumed that the sole effect of this addition is in terms of structural changes, excluding purely salt effects, which is certainly an oversimplification.

A new calculation based upon equation 18 with an expansion to incorporate activity coefficients has been recently proposed and tested using coefficients determined by the GC method for pentan-1-ol in mixtures of NaDS with a nonylphenol derivative.[19] This approach is based upon the assumption that equation 5 be used as a reference solubilization, any deviation from that equation being considered as a synergistic effect. Such a proposition is questionable since it implies that this equation is strictly valid, which is not the case even for the much simpler systems of non-polar gases in homogeneous solvent mixtures for which it was originally devised.

3 Experimental Findings and Discussion

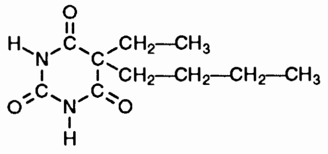
3.1 Partition Coefficient Studies

3.1.1 The Regular Solution Approximation Model

We intend, in this section, to test the applicability of equation 5 as a formal representation of the variation of solute solubilization with micellar composition. Unfortunately, most of the published data are presented as plots of maximum micellar solubilization or P values as a function of the solution composition α, and thus cannot be used quantitatively for the testing of a model. Therefore we use some of our own data and mention the literature results wherever the profile of the variation of the micellar solubilization with micellar composition has been presented.

The following questions should be answered: Does the form of equation 5 correspond to the experimental findings? Is there any correlation between the empirical B values and the intramicellar surfactant interactions as quantified by the β coefficient?

3.1.1.1 Qualitative observations. Figure 1 presents the variation of P with micellar composition as deduced using a solubility method,[21] for a barbituric acid, butobarbital (1), in mixed micelles of an anionic surfactant, sodium decylsulfate (NaD), with a cationic one, decyltrimethylammonium bromide (DTABr). An excellent fit to equation 5 can be obtained using an average B value equal to -4.5 ± 0.1. If the RSA was strictly valid, the dotted line with $\beta = -13.2$ should be obtained.[7] Most solubilization data, whether corresponding to solute-saturated values or to partition coefficients, show the same profile as a function of micellar composition. In fact, systems for which equation 5 is not followed appear as exceptions, which will be dealt with below.



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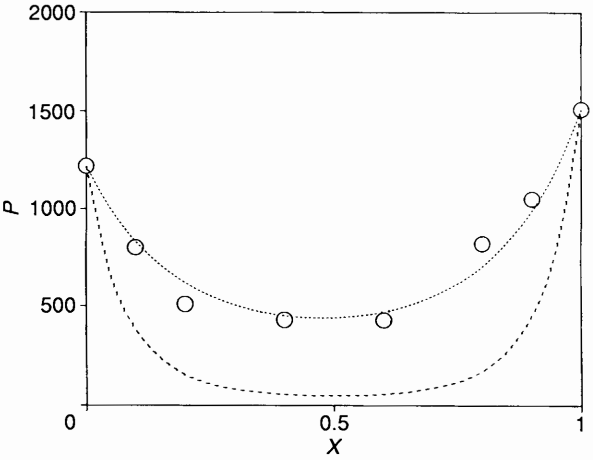

Figure 1 Variation of the partition coefficient of butobarbital as a function of micelle composition for mixtures of sodium decylsulfate + trimethyldecylammonium bromide (ref. 24): ○ experimental values; ------ equation 2 with fitted parameter $B = -4.5$; ---- equation 2 with $\beta = -13.2$ (see text).

A very drastic test of the validity of equation 5 as an analytical relationship with physical significance is provided by surfactant systems with positive β. β is positive for some mixed hydrogenated and fluorinated surfactant binaries as a consequence of the repulsion interaction between these moieties (the cmc's of the mixed micelles are larger than for the pure ones). Care must be exercised when dealing with these mixtures because some of the binaries may demix as a consequence of the repulsion effect, leading to two types of micelles, one richer with one component and the other richer with the second component. Furthermore, addition of a solute may also induce demixing in the case of a binary system which is, by itself, already close to the thermodynamic demixing conditions. In the case of complete mixing, according to equation 5, B should be positive. This prediction is borne out for a number of chemical systems from various laboratories using different experimental techniques. The limiting P values for 1-PeOH in the mixed lithium perfluorooctanoate (LiFOS) and lithium dodecylsulfate (LiDS) binary displays a positive deviation from ideality.[14,21] The same observation has also been made for perfluorobutanol and hexan-1-ol by Meguro and Esumi.[22] Both research groups used the GC method of investigation. Carlfors and Stilbs, using a NMR method, studied a single surfactant mixture of LiFOS + lithium decanoate[23a] with a mole fractional micellar composition $x = 0.125$. The solubilization of benzene was larger in the mixed micelle than in either single surfactant solutions. A positive B value may therefore be inferred from this result. However, in the case of aliphatic alcohols, the micellar solubilization was equal or smaller in the mixed system than in the single ones. Likewise, the variation of P for hexan-1-ol and for heptafluorobutanol which was determined in mixtures of two cationic surfactants, a hydrogenated (trimethyldodecylammonium chloride) (DOTACl) and a fluorinated one (diethanolheptadecafluoro-2-undecanolmethylammonium chloride) (DFDACl), displayed a negative deviation from the ideal mixing rule ($B = -2.0$), although the β coefficient of this surfactant mixture is slightly positive ($\beta = +1.0$).[23b] Note, however, that these mixed surfactant systems may undergo partial demixing as suggested above. In that case, the theoretical model on the basis of which the β value was calculated would not be valid.

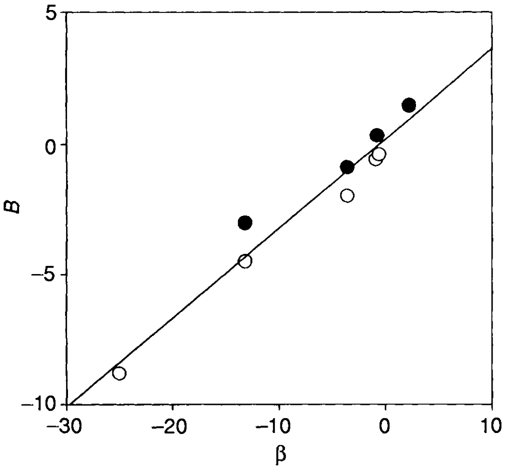

Figure 2 Correlation of solubilization constants *B* (equation 2) with intra-micellar coefficients *β* ● pentan-1-ol (ref 21, GC method), ○ butobarbital (ref 24, solubility method)

It is interesting to note that mixed hydrogenated and fluorinated surfactants do not systematically display positive *β* values Hence the mixed micelles formed by LiFOS with the non-ionic surfactant $C_{12}EO_6$ show a large negative deviation from ideality ($\beta = -5\ 4$) The *B* coefficient for the water-insoluble dye, Yellow OB, is also be negative for this system,[11] in agreement with the prediction of equation 5

Thus, it seems that there are grounds for using RSA for the representation of solubilization patterns in mixed micelles The quantitative relationship between *B* and *β* is now examined

3 1 1 2 Quantitative correlations Figure 2 shows a plot of *B* values, obtained by a fitting procedure similar to that shown for Figure 1, for pentan-1-ol in four series of binary surfactant systems, and for the barbituric acid, butobarbital, in five different surfactant binaries These solubilization data represent the most complete set of results currently available in a variety of surfactant systems ranging from slightly positive to very negative *β* values LiDS + LiFOS ($\beta = +2\ 2$), dimethylbenzyltetradecylammonium chloride TTABzCl + TTACl ($\beta = -0\ 9$), trimethyltetradecylammonium bromide + $C_{12}EO_{23}$ ($\beta = -0\ 8$), NaDS + $C_{12}EO_{23}$ ($\beta = -2\ 5$), NaD + DTABr ($\beta = -13\ 2$), NaDS + DDTACl ($\beta = -25$) *P* results for 1-PeOH were calculated from reference 21, and were taken from reference 24 for the barbituric acid The *β* coefficients were taken from the same references

Taking the nine partition coefficient data sets, one gets a straight line with

$$B = 0\ 194 + 0\ 343\beta \qquad (\sigma = 0\ 95) \qquad (7)$$

The correlation between *B* and *β* is remarkable as it is applied to the micellar solubilization behaviour of two widely different solutes It shows that essentially $B = k\beta$

It would be meaningless to discuss quantitatively the value of the coefficient *k* because, as noted before, *B* is not equal to *β* even for a non-polar gas in a mixed solvents

The question may be raised as to the effect of solute size on *B* values, and thus to the degree of generality of correlations such as displayed in Figure 2 The results obtained for the four barbituric acids of different sizes studied in mixed anionic- + non-ionic and cationic + non-ionic systems, show some indication for a change of *B* with solute size in the homogeneous solute series investigated [20] Hence, in the mixtures of NaDS + $C_{12}EO_{23}$, as *P* increases with solute hydrophobicity, *B* decreases from $-1\ 1$ to $-2\ 2$ In fact, an average *B* value equal to $-1\ 6 \pm 0\ 4$ represents the whole data series In the case of the mixed cationic + non-ionic system TTABr + $C_{12}EO_{23}$, a constancy of *B* with solute size may be safely assumed $B = -0\ 35 \pm 0\ 12$ for the four barbituric acids [20] In the mixed cationic micelles (DOTACl + DFDACl) mentioned above,[23] *B* is stated as being equal for $C_4F_7H_2OH$ and for $C_6H_{13}OH$, although the *P* values are twice as large for the fluorinated alcohol than for the hydrogenated one This may be taken as an additional evidence that the effect of solute hydrophobicity on *B* is not very large, at least in a reduced range of solute size

It should also be pointed out that the addition of salt, which has a considerable influence on the cmc and, to a lesser extent, on *P*, hardly changes *β* or the *B* coefficient, confirming the existence of a correlation between the two parameters Whereas for mixtures of NaDS + $C_{12}EO_{23}$, *β* varies from $-2\ 5$ in the absence of added salt to $-2\ 8$ in the presence of 0 2 molar of NaCl, under the same conditions *B*, for butobarbital only changes from $-2\ 0 \pm 0\ 4$ to $-1\ 7 \pm 0\ 3$ [20]

It was mentioned above that solubilization data may depend somewhat on the experimental method and on the model used for calculating *P* There are very few systems for which a comparison can be made between the results One of these, is the partition coefficient of pentan-1-ol in the binaries NaDS + $C_{12}EO_{23}$ and NaD + DTABr which were determined by the GC method and by calorimetry [25] With both of these techniques, the activity of the solute was kept constant, at a low solute occupancy Nevertheless, differences between GC and calorimetric results have been pointed out in the literature for the solubilization in neutral solutes in single surfactant solutions [26] Using the calorimetric results, one obtains for pentan-1-ol, $B = -1\ 5 \pm 0\ 4$ and $-6\ 2 \pm 0\ 9$ respectively, for the mixed anionic + non-ionic and the anionic + cationic systems The former value is in reasonable agreement with the GC results taking into account the combined uncertainties on these coefficients The latter value is somewhat too negative Again, care must be exercised when results from different techniques are compared *P* values as deduced from calorimetry have been shown to be systematically larger (in absolute values) than those obtained from GC and other experimental techniques (Of course, from the calorimetric method the solute enthalpy changes associated with the solubilization process can be measured simultaneously with the *P* values, which is one of the main advantages offered by this technique) The general trend is nevertheless the same for both methods the larger the value of *β*, the larger the value of *B*

There are other systems which seem to display some of the characteristics of the RSA-type behaviour If the actual data are often lacking, some of the results may still be qualitatively discussed along the lines suggested above Here we draw attention to the solubilization results of Muto *et al* [11] on the water-insoluble dye Yellow OB and the slightly water-soluble one, azobenzene, in mixed micelles of $C_{12}EO_6$ with NaDS, sodium ethyl-hexylsulfosuccinate (AOT), or LiFOS The binary surfactant systems display *β* values equal respectively to $-4\ 0$, $-4\ 2$, and $-4\ 8$ The deviations from ideality of dye solubilities follow the same trend, *i e* the more negative the value of *β*, the larger the decrease of dye solubility upon surfactant mixing The solubility profiles with micellar composition also follow the trend shown in Figure 1 There are slight differences between the behaviour of the two solutes, but they are marginal Likewise, the solubilization of hexan-1-ol in mixtures of a non-ionic surfactant of the Igepal series (nonylphenol with 15 ethoxylated groups) (NEO_{15}) with NaDS and with hexadecylpyridinium chloride (CPyCl),[19] shows a close to ideal behaviour with the cationic surfactant and a significant deviation from ideality with the anionic component, in agreement with the prediction of a more negative *β* with the latter mixture than with the former one The same general trend is displayed for non-1-ane in mixtures of $C_{12}EO_6$ with NaDS and with dodecyltrimethylammonium bromide (DOTABr) [17]

Uchiyama *et al*,[27] using an equilibrium dialysis method, studied the micellar solubilization of 2-phenylethanol in dodecyldimethylamine oxide solutions from acidic to basic solutions, thus forming mixed cationic + non-ionic micelles at intermediate pH values Again, a negative deviation from ideality was observed along the lines outlined above. Here, however, the β value could not be determined.

Mention should also be made of a study of the solubilization of a series of phenols and phenoxide ions in mixtures of CTABr with $C_{12}EO_{23}$.[28] B values could be extracted for only some of the data (the phenols). They were slightly positive (*e.g.* B was equal to +0.13 for phenol and +0.46 for methylphenol), results which are in line with the small negative β values which could be assumed for such cationic + non-ionic mixtures. However, for some of the other phenol derivatives (*e.g.* t-butylphenol), the P *versus* x curve was so distorted with respect to the form of equation 5 that no single B coefficient could be reasonably calculated. A similar situation, although not as dramatic, was observed from an analysis of recent data on the solubilization of perfumes[10] using the present approach. It should be noted that the variation of the cmc with micellar composition for some surfactant binaries may not always be represented by a single β coefficient, as discussed below.

The effect of solute occupancy on the micellar solubilization phenomenon has been studied by Christian *et al.* using vapour pressure or semi-equilibrium dialysis techniques.[10,27] Their data are usually presented using empirical equations of the type

$$P = P^{\circ}(1 - X_p)^2 \qquad (8)$$

where X_p is the solute intramicellar mole fraction and P° the limiting partition coefficient, obtained by data extrapolation to $X_p = 0$. This type of equation may be linked to a Langmuir adsorption model and should break down for solutes which penetrates the micellar structure. No specific effect is observed with mixed micelles when compared to single surfactant solutions as the result of increasing solute occupancy. The apparent partition coefficient decreases as the concentration of solute in the micelle increases. The activity coefficient may be smaller or larger than 1 at low solute concentration and it may decrease or increase with solute occupancy. The activity coefficient of pure hydrocarbons seems to decrease with solute occupancy whereas it increases with polar molecules. The latter situation is demonstrated by the case of 2-phenylethanol and benzylacetate in NaDS + $C_{16}EO_{20}$.[10] At low concentrations, the solute activity coefficient is larger than 1 for the latter compound and smaller than 1 for the former.

3.1.2 Solubilization Behaviour for Solutes which do not Follow the Regular Solution Approximation Model

The micellar solubilization of some neutral solutes in some binary surfactant solutions displays a behaviour which cannot be interpreted within the framework of the RSA. It is interesting to note the characteristics of such systems. It concerns solutes such as orange OOT in mixed zwitterionic + anionic,[29] various dyes in mixed anionic + non-ionic,[8] oleyl alcohol in zwitterionic + anionic,[30] decane in mixed anionic + cationic,[31] or hexane in mixed anionic + non-ionic binaries.[32] For these systems, the micellar solubilization presents a maximum at a particular micellar composition, *i.e.* the B coefficient is positive although the β coefficients are all negative, in contradistinction to the prediction of the RSA.

A thorough analysis of these results shows that, for these systems, important structural micellar changes occur upon mixed micelle formation with consequences on solubilization which depend upon the degree of solute hydrophobicity. The nature of these changes identifies two types of systems. (i) The structural change leads to the formation of mixed micelles with larger sizes than the single ones. (ii) Partial demixing occurs although the β coefficient of the RSA is negative. These two situations are considered below.

3.1.2.1 Mixed micelles of larger size. In some cases, it is observed that the change of size of mixed micelles with composition does not display a regular pattern.

This may be the case with the mixing of cationic surfactants where the difference is the length of the hydrocarbon chains (a decrease of aggregation number is observed upon surfactant mixing).[33] However, the largest structural micellar changes are expected for systems which display strong intra-micellar interactions. This is the case for zwitterionic + anionic and anionic + cationic mixtures. The phenomenon is well known in the case of formation of coacervates. Milliaris *et al.*[33] deduced from fluorescence-decay measurements that the size of the mixed micelles of NaDS + DOTABr is larger than either single micelle. Likewise the size of the mixed micelles of ammonium decanoate with ammonium perfluorooctanoate is a maximum around a micellar composition $x = 0.5$, as deduced from neutron scattering experiments.[34]

Formation of micellar structures of larger size than the individual micelles does not systematically induce positive solubilization changes. For example, B is negative for barbituric acids or 1-PeOH in anionic + cationic mixtures[20,21] but positive for decane[31] in the same binaries. On the other hand, nonane in mixtures of ionic + non-ionic surfactants does not present a solubilization maximum and the size of the mixed micelles varies monotonously with micellar composition.[17] Thus, neither large solute hydrophobicity nor increased micellar size alone can lead to a positive synergistic effect (positive B value). Both of these conditions should be fulfilled. It may be argued that a large hydrophobic dye molecule needs more volume to be easily accommodated, which is not the case for a smaller molecule.

These observations bring prompt consideration of the solubilization site in micelles. The problem is not greatly different in mixed micelles than in single ones but it has more relevance to the present situation in connection with the use of the β coefficient as a guide to the prediction of solubilization effects. This coefficient obviously describes various interactions between hydrocarbon moieties, dipoles, and ions in the mixed micelle and therefore should be considered as the sum of partial values corresponding to the contribution of each portion of the mixed micelle to the overall interaction. Such an approach is presently fruitless. Nevertheless, one may consider that β has its fullest control over solubilization only if the solute site is close to the micellar region where the main interaction between the unlike surfactant takes place. If a hydrocarbon molecule resides, on average, in the hydrocarbon core, the solute solubilization change with micelle composition should be close to ideal. That this is not the case with mixed anionic + cationic or zwitterionic + anionic (but close to it with nonane in mixed non-ionic + ionic micelles) is due to the increase in micellar size with such binaries upon surfactant mixing, as indicated above. Thus, one expects that the closer the solubilization site to the micellar surface (the so-called palissade layer), the better the conditions for the RSA application. This is most certainly the reason for the excellent correlation observed between B and β observed in Figure 2, both solutes investigated being relatively small and polar hydrophobic molecules.

Mixed non-ionic + ionic micelles introduce an additional complication. Contrary to mixed ionic surfactants, most of which have rather close hydrocarbon lengths, non-ionic surfactants present a long polar chain, which is several times longer than that of the hydrocarbon chain. Thus, upon mixing, a portion of the polar chain may not come into contact with the ionic surfactant. This is clearly seen by the rather small dependence of β upon the number of polar groups attached to the hydrocarbon chain of non-ionic surfactants. Nishikido has indicated[35] with a series of dodecylpolyoxyethylene compounds that only the first six polar groups should be considered as being affected by the mixing with NaDS. Thus, at least three solubilization sites should be considered in mixed micelles comprising ionic and non-ionic surfactants: the hydrocarbon core, the region of interaction between the ionic head-group and the polar moieties, and finally the fraction of the polar chain without interaction with the ionic head-groups. Only the second region should be concerned with the β value.

3.1.2.2 Demixing in ionic + non-ionic binary systems. The above discussion rests to a large extent on the assumption that the mixing of surfactants leads to the formation of only one type of mixed micelles, the composition of which may be calculated using equations 1—3 The thermodynamic treatment based upon the RSA indicates that micellar demixing should occur only if β is equal or larger than 2 Evidently, this limiting value rests upon the validity of the RSA model as applied to mixed micelles It has been shown experimentally that some mixed hydrogenated and fluorinated surfactants form two types of micelles, one richer in one component and the other with the second component [36] The micellar compositions being different, one would expect different *P* values in each type of micelle, however, the micellar composition should remain constant in the demixing domain and so also should the solubilization constants The results available do not display this behaviour

It seems that the phenomenon of micellar demixing does not concern only systems with fluorinated components but also fully hydrogenated mixed anionic + non-ionic binaries Uchiyama *et al* have indicated[27] that the mixing of NaDS with long chain hexadecylpolyoxyethylene surfactants leads to two kinds of micelles The β values for these systems are not known The same conclusion was reached by Abe *et al* [30 37] from similar cases of mixtures of an anionic surfactant with a non-ionic component bearing 40 oxyethylene groups Uchiyama suggested that the demixing could be the reason for positive solubilization changes without offering additional explanations The same possibility arises with the positive solubilization changes observed with the dye Yellow OB in mixtures of NaDS with polyoxyethylene surfactants where the number of polar groups extends to EO = 49 oxyethylene groups

The extensive surface tension results of Carrion Fite[38] yield the variation of cmc of mixtures of NaDS + nonylphenol derivatives, bearing 5 to 30 ethoxylated groups It appears that Rubingh's model does reproduce the experimental results when the number of polar groups on the non-ionic component is equal to 10, 15, and 20, *i e* , a single β value is sufficient to represent the variation of cmc with micellar composition However for the extreme cases of EO = 5 and 30, β varies widely with micellar composition, hence with EO = 5, β varies from − 1 8 to − 7 1 in the whole micellar composition range, for EO = 30, the variation is from − 2 8 to − 6 0 To adopt an average β value would be meaningless The RSA model obviously breaks down when the non-ionic components posess a very small or a large number of polar groups and the more likely interpretation is that these systems demix even though the β parameter is negative In such cases, the RSA approach to micellar solubilization is no longer appropriate

A tentative interpretation of the effects observed with the non-ionic surfactants may be suggested The non-ionic compounds which are used in most fundamental studies on micellar solubilization are homogenous compounds with a high degree of polydispersity They form therefore, by themselves, mixed micelles For dodecyl derivatives, which are the most commonly used non-ionics, the components with the shortest polar chain would not be soluble in water They are in fact co-solubilized in the micelle by the major water-soluble components and constitute a factor in the destabilization of the system A monodisperse anionic component such as NaDS should mix more easily with the non-ionic surfactant components bearing the shortest polar chains In other words, the role of the ionic component would be to solubilize (extract) the lower non-ionic homologues from the polydisperse non-ionic surfactant If that is the case, then the miscelles formed by the remaining components with the largest polar chains would present a lower degree of polydispersity and therefore a higher degree of micelle stability These micelles could then be better solubilizing agents than the single non-ionic micelles Although this picture appears as an *ad hoc* hypothesis, it seems a plausible one Indirect evidence in favour of such a mechanism is provided by the work of Nishikido on mixed manganese dodecylsulfate and dodecyloxyethylene surfactants with widely different number of polar groups the single ionic micelles are poor solubilizating agents for Yellow OB when compared to the non-ionic ones [8]

3 1 3 Solubilization in Mixed Micelles of Phospholipids and Bile Salts

The case of the mixed phospholipids + bile salts system should be considered separately Although these naturally occurring surfactants form mixed micelles in water in a large isotropic domain, the structure of the aggregates is completely different from the more classical cases considered above Because of their non-toxicity these surface-active agents have been used in various pharmaceutical formulations for drugs such as benzodiazepines,[39] progesterone,[40] or vitamin K_1 [41] Cholesterol solubilization and transportation occur through the same mechanism involving mixed micelle formation These systems have been the subject of many investigations Mixed micelles are formed in water (the so-called L_1 phase), vesicles may be present and mesomeric phases also form at larger concentrations It is generally admitted that disc-shaped bimolecular leaflets of lecithin molecules form the core of the mixed micelle with the hydrocarbon sides of the bile salts associating with their counterparts on the lecithin disc The addition of lecithin to a bile salt may increase considerably the solubilization of a hydrophobic drug molecule as a consequence of the formation of mixed micelles Hence, at a one to one ratio, the mixed micelles increase the solubility of Vitamin K_1 by a factor of 30 [41] The type of bile salt may influence strongly the synergistic mixing effect It is noteworthy that the solubilization capabilities of sodium dehydrocholate towards diazepam, a very hydrophobic drug molecule, is much lower than that of other bile salts such as sodium cholate, glycholate, or taurocholate It is not known, however, if the structural changes upon mixing of the four bile salts with the lecithin used in this investigation are comparable Shankland observed that the increase of drug solubility is related to the increasing size of these mixed micelles depending upon the micelle composition [42] This observation is in qualitative agreement with the general conclusions outlined above cholesterol, progesterone, or benzodiazepines are large hydrophobic molecules which need larger micellar structures to be accomodated, mixed micelles of phospholipids and bile salts may serve such a purpose

3.2 Enthalpimetric Studies

Contrary to the case of single surfactant solutions,[43] the enthalpy and entropy changes associated with micellar solubilization in binary surfactant solutions have been scarcely studied It is classically observed in the investigation of the thermodynamics of hydrophobic solutes in aqueous solutions that the solute excess or standard enthalpy and entropy functions tend to be of opposite sign so that the corresponding Gibbs energy is a smooth function of solute concentration or, in the case of mixed solvents, displays relatively small changes in magnitude with solvent composition Thus, one may expect that the standard enthalpy function in mixed micelles might reveal the behaviour of a solute in a more subtle way than the Gibbs energy The RSA again may serve as a base line for interpretation purposes The standard enthalpy function of transfer takes the classical form

$$\Delta H^\circ_{\mathrm{t\,m}} = x\Delta H^\circ_{\mathrm{t\,1}} + (1 - x)\Delta H^\circ_{\mathrm{t\,2}} + x(1 - x)RT^2\delta B/\delta T \quad (9)$$

where the ΔH_{t}'s are the standard enthalpies of transfer of the neutral solute from the mixed micelles to pure water and *T* the temperature There are very few data against which the validity of equation 9 could be tested As an example, β is found equal to − 3 0 for the system sodium dodecylsulfonate + $C_{12}EO_8$, whereas the derivative of β with respect to temperature is 0 027 K^{-1} [44]

Figure 3 presents the variation of the standard enthalpy of transfer for acetophenone[45] and benzyl alcohol[46] from the mixed cationic micelles of TTABzCl + TTACl to water as deduced from calorimetric experiments A quasi-ideal behaviour is observed for acetophenone The slight positive deviation from ideality is in agreement with equation 9, assuming a small positive value for the last term of this equation of the order of

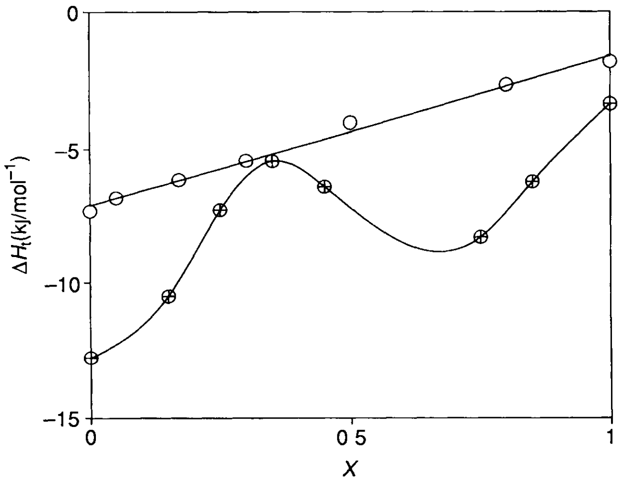

Figure 3 Variation of the enthalpy of transfer of acetophenone (○) (ref 45) and benzylalcohol (⊕) (ref 46*a*) in mixtures of trimethyltetradecylammonium chloride + benzyldimethyltetradecylammonium chloride

magnitude as that cited above The corresponding profile of the variation of *P* with micellar composition displays a regular solution pattern, with $B = -1\ 8$ (not shown) [45] However, benzyl alcohol shows two extrema with large enthalpy variations as a function of micelle composition As the mixed cationic system displays a close to ideal behaviour ($\beta = -0\ 9$)[46a] such results indicate that, upon solubilization, benzyl alcohol induces considerable micellar structural changes even when the solute concentration is kept at a relatively low solute occupancy (in the present case, $x < 0\ 20$) The calorimetric method can be used for the simultaneous determination of the solute standard Gibbs energy and of the enthalpy of transfer, from which the corresponding entropy term is calculated Figure 4 presents the results obtained for the enthalpy and the entropy of transfer for the aromatic alcohol in the same mixed micelles A typical example of enthalpy/entropy compensation is observed This type of profile closely resembles that observed for the same type of solutes in mixtures of hydrophobic solvents and water However, the apparent similarities could be misleading In the case of mixed aqueous systems, the solvent structural changes determine the solute thermodynamic profiles, whereas in the case of mixed micelles such as the cationic ones investigated, the solute molecule imposes the micellar structural changes responsible for the large thermodynamic changes observed as a function of micelle composition The RSA cannot be applied to such systems and, more to the point, thermodynamics alone does not indicate the type of structure which produces such complicated profiles

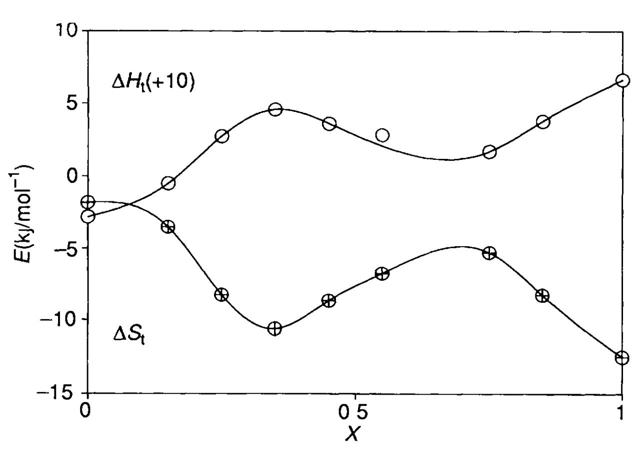

Figure 4 Variation of ΔH_t and of $T\Delta S_t$ for benzylalcohol in mixtures of trimethyltetradecylammonium chloride + benzyldimethyltetradecylammonium chloride (ref 46*a*) A value of 10 kJ mol has been systematically added to all ΔH_t values for reasons of clarity

4 Conclusions

The behaviour of neutral solutes in binary surfactant systems may be rationalized with a few general rules

(1) If the solute molecule possesses a polar moiety and is of medium size, it must be adsorbed at the micellar surface and the solubilization should follow the RSA predictions outlined above In most cases, surfactant mixing is unfavourable to micellar solubilization and the larger the interaction between the two surfactants, the larger the decrease of solubilization upon surfactant mixing The condition for application of the RSA should however be fulfilled, and, in particular, a single type of mixed micelles should be formed at a given solution composition

(2) If the solute is very hydrophobic (whether a pure hydrocarbon or not) and of a large size and if one suspects that strong intra-micellar interactions take place between the surfactants, a positive synergistic effect may be expected An increase of micelle size with surfactant mixing should also be observed Hydrocarbons solubilized in mixed micelles with no large structural changes present a close to ideal behaviour

(3) In the case of mixtures of ionic + non-ionic surfactants in which the non-ionic component presents a high polydispersity index, the ionic surfactant might induce the formation of two types of micelles by solubilizing the more hydrophobic components of the non-ionic surfactant and possibly, as a consequence, favour the solubilization capabilities of the mixed system

(4) The formation of mixed micelles of phospholipids and bile salts may also favour the solubilization of large hydrophobic molecules

Finally, the enthalpy changes associated with the solubilization of solutes in mixed micelles may display rather complex features and the conditions for applications of the RSA model are more stringent for the enthalpy function than the Gibbs energy, as expected The available data indicate that even at low solute occupancy, mixed micelles may undergo profound structural changes upon solute solubilization

5 References

1 Mixed Surfactant Systems', Surfactant Science Series, No 46, ed K Ogino and M Abe, M Dekker, N Y , 1993
2 (*a*) D Attwood and A T Florence, 'Surfactant Systems , Chapman and Hall, London, 1983, (*b*) L Sepulveda, E Lissi, and F Quina, *Adv Colloid Interface Sci* , 1986, **25**, 1
3 (*a*) C Treiner and M H Mannebach, *J Colloid Interface Sci* 1987, **118**, 243, (*b*) K T Valsaraj and L J Thibodeaux, *Sep Sci Technol* , 1990, **25**, 369, (*c*) B H Lee, S D Christian, E E Tucker, and J F Scamehorn *J Phys Chem* , 1991 **95**, 360
4 (*a*) E B Leodis and T A Hatton, *J Phys Chem* , 1990, **94**, 6400, (*b*) M Aamodt, M Landgren, and B Jonsson, *J Phys Chem* , 1992, **96**, 945
5 F Tokiwa and K Tsujii, *Bull Chem Soc Jpn* , 1973, **46**, 1338
6 J H Clint, *J Chem Soc Faraday Trans I* 1975, **71** 1327
7 D N Rubingh, 'Solution Chemistry of Surfactants', Vol 1, ed K L Mittal, Plenum Press, N Y 1979
8 N Nishikido, *J Colloid Interface Sci* , 1977, **60**, 242
9 A Makayssi, D Lemordant, and C Treiner, *Langmuir*, 1993, **9**, 2808
10 M Abe, K Mizogushi, Y Kondo, K Ogino, H Uchiyama, J F Scamehorn E E Tucker, and S D Christian, *J Colloid Interface Sci* , 1993, **160**, 16
11 Y Muto, M Asada, A Takasawe, K Esumi, and K Meguro, *J Colloid Interface Sci* , 1988, **124**, 632
12 J P O'Connell, *Ind Eng Chem Fundam* , 1971, **17**, 658
13 M J Blandamer, E Godfrey, and J R Membrey, *J Solution Chem* 1974, **3**, 881
14 C Treiner, J F Bocquet, and C Pommier, *J Phys Chem* , 1986, **90**, 352
15 P Mukerjee, *Kolloid Z Z Polym* , 1970, **326**, 76

16 P L Bolden, J C Hoskins, and A D King Jr , *J Colloid Interface Sci* , 1983, **91**, 454

17 A J I Ward and K Quigley, *J Disp Sci Technol* , 1990, **11**, 143

18 (*a*) N Nishikido, *Langmuir*, 1991, **7**, 2076, (*b*) N Nishikido, *Langmuir*, 1992, **8**, 1718

19 C M Nguyen, J F Scamehorn, and S D Christian, *Colloids Surf* , 1988, **30**, 335

20 C Treiner, M Nortz, C Vaution, and F Puisieux, *J Colloid Interface Sci* , 1988, **125**, 261

21 C Treiner, A Amar Khodja, and M Fromon, *Langmuir*, 1987, **3**, 729

22 K Esumi and K Meguro, 'Solution Chemistry of Surfactants', Vol 11, p 151, ed K L Mittal and D O Shah, Plenum Press, 1990

23 (*a*) J Carlfors and P Stilbs, *J Colloid Interface Sci* , 1985, **103**, 332 (*b*) K Tamori, A Ishikawa, K Kihara, Y Ishii, and K Esumi, *Colloids Surf* , 1992, **67**, 1

24 C Treiner, M Nortz, and C Vaution, *Langmuir*, 1990, **6**, 1211

25 R Bury and C Treiner, *J Solution Chem* , 1989, **18**, 499

26 R de Lisi, C Genova, and V Turco Liveri, *J Colloid Interface Sci* , 1983, **95**, 428

27 H Uchiyama, S D Christian, J F Scamehorn, M Abe, and K Ogino, *Langmuir*, 1991, **7**, 95

28 J W Cabera and L Sepulveda, *Langmuir*, 1990, **6**, 240

29 T Iwasaki, M Ogawa, K Esumi, and K Meguro, *Langmuir*, 1990, **7**, 30

30 M Abe, T Kubota, H Uchiyama, and K Ogino, *Colloid Polym Sci* , 1989, **267**, 365

31 D R Scheuing and J G Weers, *Langmuir*, 1990, **6**, 665

32 G A Smith, S D Christian, E E Tucker, and J F Scamehorn, *J Collloid Interface Sci* , 1989, **130**, 254

33 A Malliaris, W Binana-Limbele, and R Zana, *J Colloid Interface Sci* , 1986, **110**, 114

34 S J Burkitt, R H Ottewill, J B Hayter, and B T Ingram, *Colloid Polym Sci* , 1987, **265**, 628

35 N Nishikido, Y Moroi, and R Matuura, *Bull Chem Soc Jpn* , 1975, **48**, 1387

36 P Mukerjee and A Y S Yang, *J Phys Chem* , 1976, **80**, 1388

37 (*a*) H Uchiyama, Y Tokuoka, M Abe, and K Ogino, *J Colloid Interface Sci* , 1989, **132**, 88, (*b*) M Abe, N Tsubaki, and K Ogino, *J Colloid Interface Sci* , 1985, **197**, 503

38 F J Carrion Fite, *Comm Jorn Com Esp Deterg* , 1984, **15**, 379

39 M Rosoff and A T M Serajuddin, *Int J Pharm* , 1980, **6**, 137

40 G P Martin, I W Kellaway, and C Mariott, *Chem Phys Lipids*, 1978, **22**, 227

41 M Nagata, T Yotsuyanagi, and K Ikeda, *J Pharm Pharmacol* , 1988, **40**, 85

42 W Shankland, *Chem Phys Lipids*, 1970, **4**, 109

43 R de Lisi and S Milioto, *Chem Soc Rev* , 1993, 67

44 M J Hey and J W MacTaggart, *J Chem Soc Faraday Trans 1*, 1985, **81**, 207

45 A Makayssi and C Treiner, *Coll Polym Sci* , 1992, **270**, 1124

46 (*a*) R Bury, E Souhalia, and C Treiner, *J Phys Chem* , 1991, **95**, 3824, (*b*) R Bury, C Treiner, J Chevalet, and A Makayssi, *Anal Chim Acta*, 1991, **251**, 69