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On the Concept of Driving Force Applied to Micelle and Vesicle Self-Assembly†

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Micellar kinetics are considered from the viewpoint of the various surfactant exchange processes which can take place and the overall driving force for dissolution/formation of micelles. The ideas are then extended to include vesicle self-assembly processes. The kinetics of these systems are usually easier to study experimentally, since the rate processes are slower, which means that structural characterization of intermediates might then be possible. Specifically, kinetic data are reported for the formation and breakdown of vesicles involving the following synthetic surfactants: sodium 6- or 7-tridecylbenzenesulfonate (SLABS), for which the system is perturbed by changing the ionic strength in order to form or break vesicles, and hexadecyldecyldimethylammonium bromide ($C_{16}C_{10}$DMABr), where vesicles are broken down to mixed micelles on addition of a single-chain alkyltrimethylammonium bromide cationic surfactant. We demonstrate that the rate of the vesicle formation/breakdown transformation is dependent on how far the final concentrations are away from the phase transition concentration conditions for formation/breakdown of the vesicles.

Introduction

Surfactant molecules are capable of forming a wide variety of aggregate states in aqueous solution: for example, micelles (spherical and nonspherical), vesicles, and lyotropic liquid-crystalline phases.[1−5] Normally, micelles are near to spherical, with a radius given by the extended hydrocarbon chain length of the surfactant—and they are essentially monodisperse.[6−9] At higher concentrations of surfactant, micelles can grow to form elongated structures—rods and disks. These are precursors for the formation of various lyotropic liquid-crystalline structures (hexagonal and lamellar).[10−15] These sphere-to-rod (disk) transformations can be spontaneously induced for single-chain surfactants by increasing the ionic strength (e.g. by simple addition of electrolytes such as sodium chloride to water).

With double-chain surfactants, a preferred aggregate structure is based on the formation of extended bilayer sheets. Vesicles can also be thought of as a dispersed lamellar (L_α) phase. Both unilamellar vesicles (ULV's) and multilamellar vesicles (MLV's) can be formed. The name liposome is the name given to closed bilayer structures formed from phospholipids; however, these systems are more difficult to study from the viewpoint of spontaneous self-assembly, as experimentally closed bilayer structures are generally formed from lamellar phases with input of energy.

For vesicles formed by synthetic surfactants, sonication procedures are not usually required, or recommended, as it is possible to generate a ULV surfactant system without input of energy to the system.[16−18] When no external energy is applied to the system to create the vesicles, we describe the process of vesicle formation as spontaneous. In this paper, we have studied vesicle systems based on two different surfactant types: (1) sodium 6- and 7-tridecylbenzenesulfonate (6-SLABS and 7-SLABS) (anionic surfactants), which form vesicles on addition of NaCl to a solution in water (see Figure 1a and b for the relevant formulas), and (2) hexadecyldecyldimethylammonium bromide ($C_{16}C_{10}$DMABr) (a cationic surfactant), which forms vesicles spontaneously on dissolving the solid in water (see Figure 1(c).

The time dependence of vesicle stability is more complex: SLABS vesicles tend to flocculate and/or grow over time (hours) from ULV's to form MLV's or a lamellar phase.[19,20] In contrast, mixtures of anionic and cationic surfactants only produce a stable system after weeks to months.[19,20] It is possible that the catanionic system

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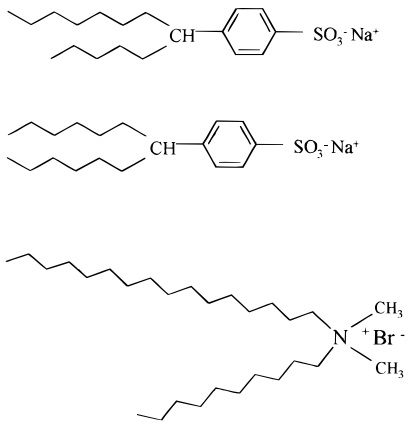

Figure 1. (a) 6-SLABS. (b) 7-SLABS. (c) $C_{16}C_{10}$DMABr.

reaches a state of true thermodynamic equilibrium, as a result of electrostatic balance and the ability to form stable layers of different bending curvature. This is achieved by self-adjustment of the composition of the surfactants in the inner and outer layers of the membrane.[21−23]

Vesicle structures are more permanent than micelles in the sense that they are less dynamic, for example, in terms of surfactant monomer exchange. Although micellar structures are thermodynamically stable, there are two distinct dynamic processes that have been identified in micellar solutions. These are characterized by the so-called fast and slow relaxation times.[24−26]

Micelles have often been portrayed as static spherical aggregates of rather ordered rigid monomeric units,[6] but the now generally accepted view is that the headgroup/water interface is rough, leading to wetting of the methylene chain in the vicinity of the headgroups; in addition, the surfactant chains are significantly kinked.[7,27] The interior of the micelle has a density similar to that of the corresponding liquid hydrocarbon.

Micellar surfactant is in dynamic equilibrium with monomer surfactant in the bulk aqueous solution, such that surfactant in solution is continuously exchanged with surfactant in the micelle. This results in fluctuations in the micelle aggregation number. Considering the case of a micelle with the most probable aggregation number, the entry rate constant of a surfactant is likely to be essentially diffusion-controlled, and the exit rate constant of a monomer will then vary proportionately with the cmc or surfactant chain length.[24] This exchange process determines the so-called "fast relaxation time", which is typically measured in the microsecond time range. As a result of these surfactant exchanges, the aggregation number of an individual micelle will fluctuate in real time over a time scale longer than microseconds. When, as a result of these fluctuations in a nonperturbed system, the micelle aggregation number drops below a critical size for stability, the micelle will necessarily rapidly disintegrate. To preserve the overall state of equilibrium, a replacement micelle should then spontaneously form in another part of the solution, to keep the overall concentration of micelles unchanged.

The breakdown of micelles can also be "induced" by applying an external perturbation to the system, for example, a temperature, pressure, or concentration jump. In this case, there will usually be a change in the concentration of micelles, since the system must adjust to the new final thermodynamic state of the system; any such change can then be readily measured. Let us now compare the rate of breakdown of micelles under the influence of an applied perturbation, for example a concentration jump from a concentration > cmc to a concentration < cmc, which will lead to dilution of the system as described above, with that in the absence of such a perturbation. The rate of breakdown should depend on the extent of the perturbation, since, following the perturbation, the micelles will suddenly be in a situation where they are in a state far from equilibrium. In particular, the monomer concentration in the bulk solution will have been reduced by the dilution so that the rate of entry of surfactant into the micelle is reduced, facilitating breakdown. The exit rate of surfactant from the micelle will be unaffected. In comparison, we would expect the breakdown under unperturbed conditions to be rather slow. Using small perturbation relaxation techniques, for example a temperature or pressure jump, the slow relaxation time for a range of surfactants is found in the millisecond to second region.[24] This so-called slow relaxation is also related to the overall stability of the micelle, which is conventionally measured through the cmc. The lower the cmc, the more stable the micelle. An understanding of these kinetic processes is essential for understanding many important processes, for example, dynamic surface tension effects. Kinetic information also aids our general understanding of such familiar processes as wetting and solubilization (detergency).

In contrast, vesicles are far less susceptible to breakdown as a result of monomer exchange processes in the absence of a driving force, since the exit rate constant for a monomer surfactant will be a lot slower and the state of aggregation a lot greater.[28,29] The concept of a critical concentration (analogous to the cmc), namely the critical vesicle concentration (cvc), for formation of aggregates is less well developed for vesicles, although, for synthetic surfactants, cvc values in the micromolar range have been reported, and these are probably typical values.[40a] Because of this enhanced stability, there is an obvious attraction in the utilization of vesicle systems for molecular targeting and delivery, and there has been much recent interest in using vesicle systems for drug delivery.[30]

Polymerization of styrene in cationic vesicles[31] and formation of nanoparticles in catanionic vesicles[32] are typical of reactions which have been carried out recently in vesicle systems. Attempts have also been made to polymerize the surfactant in the vesicles to give them added structural rigidity and stability.[33a] Vesicles can also be used as a template to control the process of self-assembly in mixed vesicle systems.[33b]

In this paper, the kinetics of formation and breakdown of vesicles formed by an anionic double-chain surfactant—

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SLABS—have been systematically studied on changing the salt and surfactant concentrations. We have also studied the breakdown of cationic vesicles of hexadecyldecyldimethylammonium bromide ($C_{16}C_{10}$DMABr) on addition of a single-chain surfactant (*N*-alkyltrimethylammonium bromide) to form mixed micelles. These experiments are carried out with a view to elucidating the driving force for the reaction; in a related series of measurements, we are trying to establish the type of intermediate structures that might be involved.

Two similar double-chain C-13 alkylbenzenesulfonate surfactants (SLABS) have been studied. These form micelles in aqueous solution in the absence of salt. However, when small amounts of electrolyte are added (in excess of ~23 mmol dm^{-3} NaCl), vesicles are spontaneously formed.[40a,b] These vesicle structures are then reasonably stable over a period of hours/days. The onset of vesicle formation is characterized experimentally by the determination of the critical salt concentration (csc), needed to induce the formation of vesicles from smaller aggregates or monomers, which are the stable state at concentrations below the csc. We have measured the csc parameter for a number of electrolyte systems, using simple turbidity measurements to detect the onset of vesicle formation.[40d]

We have also studied the effect of temperature on vesicle formation, and for SLABS systems at an appropriate salt concentration, we can effect a transition in the direction of vesicle formation on lowering the temperature.

It is perhaps surprising that relatively few conventional kinetic studies have been performed on vesicle systems. Indeed for many years it was supposed, but for no obvious reason, that synthetic surfactants could not form vesicles even though phospholipids readily form structures of this type, more usually referred to as liposomes. However, some 20 years ago, Kunitake observed vesicle formation with the cationic surfactant didodecyldimethylammonium bromide.[34] More stable systems are formed by mixing, in approximately equal proportions, cationic and anionic surfactants. These systems may indeed be thermodynamically stable,[19] such that meaningful phase diagrams can be constructed. Vesicles can also be formed from micelles by reducing the pH into a relatively narrow pH range, for example, using oleate/oleic acid, such that the headgroups are part charged rather than fully ionized.[35] In both situations, the stability will be largely due to different compositions of the two surfactants on the inside and the outside of the vesicle bilayer, which allows the production of a curved bilayer film which is relatively unstrained. However, the use of a combination of surfactants does not appear to be a necessary requirement for spontaneous self-assembly to vesicles, as in this study a single surfactant is used. There are other known cases; for example, Corti has reported spontaneous vesicle formation from a single ganglioside, which is a glucosidic amphiphile of biological origin.[36] In this case, vesicles form at concentrations as low as ~0.1 mmol dm^{-3}.

A convenient method to induce the breakdown of vesicles (liposomes), which does not involve a concentration or temperature jump, is to add a single-chain surfactant, for example sodium dodecyl sulfate (SDS), to a vesicular assembly. The result will be the formation of mixed micelles. The onset of the vesicle ⇔ micelle transition for a SLABS/SDS system, as the concentration of SDS is increased, is rather abrupt and indicates cooperative phase-transition-like behavior. A detailed thermodynamic and kinetic analysis of systems of this type has recently been carried out.[37] The kinetic analysis gives a Hill coefficient of ~8, which implies that eight single-chain surfactants have cooperated in the bilayer to disrupt the vesicles. The associated thermodynamic analysis reveals that 1 in 10 of the surfactant molecules in the bilayer is single-chain at the critical concentration of added SDS required to break down the vesicles. Related studies have also been carried out for phospholipids and natural membranes mixed with single-chain surfactants.[38,39a,b]

Experimental Section

The surfactants sodium *p*-6-tridecylbenzenesulfonate (6-SLABS) and sodium *p*-7-tridecylbenzenesulfonate (7-SLABS) (Figure 1a and b) were pure samples obtained as a gift from Dr. Peter Garrett of Unilever, Port Sunlight Laboratory, U.K. All other chemicals were standard reagents and were used without further purification.

The surfactant hexadecyldecyldimethylammonium bromide ($C_{16}C_{10}$DMABr) was synthesized from *N*,*N*-dimethylhexadecylamine and 1-decyl bromide.[44] The appropriate microanalyses and NMR spectra of the product were satisfactory.

All other single-chain surfactants used (decyltrimethylammonium bromide, dodecyltrimethylammonium bromide, and tetradecyltrimethylammonium bromide) were purchased from Fluka and used without further purification.

The structural characterization of vesicles was achieved using a combination of methods, including photon-correlation spectroscopy, video-enhanced light microscopy, and cryo-electron microscopy. The onset of vesicle formation, and hence the determination of the csc and the cvc, was measured by 180° optical turbidity measurements at a wavelength where the surfactant does not absorb, for example 300 nm. The determination of cvc values has been described previously.[40a] The determination of cmc values was generally carried out using a combination of spectrophotometry, surface tension, and conductivity measurements.[40a,b] Values of the cmc obtained by various methods were in excellent agreement.

Kinetic measurements were carried out using a Hewlett-Packard diode-array spectrophotometer and/or a Hi-Tech small-volume single-mixing stopped-flow instrument (dead time ~ 5 ms) in absorbance (turbidity) mode at 300 nm.

Results

The SLABS System. The cmc of 6-SLABS in water has been determined by spectrophotometry at 262 nm, surface tension, and electrical conductivity. All methods are in excellent agreement and give a cmc of 0.0014 (±0.0001) mol dm^{-3} at 298.2 K.[40a,b] The cmc is found to be essentially independent of temperature. There is no significant light scattering from this system above the cmc, which suggests the micelles formed are small.

The cmc for 7-SLABS is found to be significantly increased,[40b] to 0.0020 (±0.0001) mol dm^{-3}, consistent with packing parameter considerations:[41] since the more rect-

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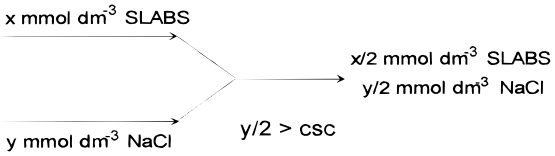
angular molecular structure of 7-SLABS disfavors micelle formation as compared with 6-SLABS. Confirmation that small micelles form in water in the case of the SLABS surfactants was provided by translational diffusion coefficient measurements using fluorescence correlation spectroscopy (where the aggregate (micelle) contained a solubilized molecule of Rhodamine 6G). It was found that the size of the diffusing entity in water was comparable to that of a sodium dodecyl sulfate micelle.[41] In the case of 6-SLABS, on addition of electrolyte, for example to 30 mmol dm^{-3} NaCl, there is an increase in turbidity as a result of the spontaneous formation of much larger aggregates. Cryo-electron microscopy measurements confirm that unilamellar vesicles are exclusively formed.[40c] There is no significant light absorption by the benzene chromophore of the SLABS surfactants at wavelengths >290 nm, so 300 nm was chosen as a convenient wavelength for monitoring changes in turbidity associated with vesicle formation/breakdown. From photon correlation spectroscopy measurements, we found the SLABS vesicles to be somewhat polydisperse, with a mean diameter of 250 nm.[40d]

Vesicles can be readily prepared by spontaneous self-assembly on mixing a salt solution with a SLABS surfactant solution at a concentration which can be either below or above the cmc in water. The vesicles form spontaneously over a few minutes, no sonication being required. Previously, it has been reported that sodium p-heptylnonylbenzenesulfonate could form vesicles following sonication, and these were stable for many weeks before reverting back to a liquid-crystal form.[42] Kaler et al.[19,20,43] reported on the ageing and stability of vesicular dispersions formed by the same surfactant. They reported that the systems were unstable over times on the order of 24 h but were more stable in the presence of salt (NaCl), which is apparently linked to a lowering of the surfactant solubility in water. It was therefore of interest to establish the extent to which the SLABS systems, which form vesicles spontaneously and without the input of energy, are thermodynamically stable. The stability of our system was therefore checked by measuring the turbidity over a period of days, gently shaking the solution before measurements were taken. The turbidity is essentially unchanged. However, if a sample is left undisturbed in the spectrophotometer cell over the full period, changes are observed and the formation of a small number of considerably larger structures is indicated. As the turbidity remains the same, this observation indicates the likely formation of "flocs" of vesicles, which can be redispersed on gentle shaking.

These results tend to confirm our belief that, for the SLABS system, even vesicles which form spontaneously will not be stable over the long term. Instability initially takes the form of formation of flocculated vesicles followed (although not observed by us) by the fusion of vesicles to give a final stable lamellar phase which would not be expected to be so readily redispersed.

The onset of vesicle formation as the electrolyte concentration is increased occurs rather abruptly at a particular concentration of salt, which we have assigned as the critical salt concentration (or csc value). The csc for 7-SLABS is at a significantly lower concentration than that for 6-SLABS, which is consistent with vesicle formation being easier with the more symmetrical 7-SLABS. Again, this is to be expected on geometrical arguments, since as discussed above, the simple packing parameter arguments favor bilayer structure formation for 7-SLABS. The micelle-to-vesicle transition takes place for 6-SLABS at NaCl concentrations between 16 and 30 mmol dm^{-3} whereas for 7-SLABS the corresponding salt concentrations are between 5 and 10 mmol dm^{-3}. The csc value can be conveniently taken as the midpoint of the transition region in a plot of turbidity against added salt concentration, and the csc values are ~23 mmol dm^{-3} for 0.5 mmol dm^{-3} 6-SLABS and ~7 mmol dm^{-3} for 7-SLABS.

Scheme 1



It should be noted that the turbidity for electrolyte concentrations > csc was constant, indicating that the size of the vesicles is unchanged with an increase in salt concentration (up to 100 mmol dm^{-3}). This was confirmed by photon-correlation spectroscopy measurements of the translational diffusion coefficient.

The transition region becomes sharper as the SLABS concentration is increased, but the csc is independent of the total concentration of SLABS, providing that the concentrations are all in the millimolar region.

However, it is found that temperature has a large effect on the csc, the value decreasing from 28 mmol dm^{-3} at 35 °C to 10 mmol dm^{-3} at 10 °C for 6-SLABS. This means that if a salt concentration of 23 mmol dm^{-3} is employed, at 10 °C the system will contain 100% vesicles, whereas at 35 °C the system will be 100% monomers or small weakly scattering aggregates. It is interesting to speculate on the state of the system just before the onset of turbidity. There is the possibility that micellar-type aggregates might be present, in the form of small rods or disks. These structures may be precursors of vesicles and so may be relevant to mechanistic considerations involved in the self-assembly/disassembly of vesicles.

Kinetic Aspects. *(I) Vesicle Formation Kinetics.* The spontaneous formation of vesicles is readily followed by the increase in turbidity of the sample with time. Slow changes can be most conveniently followed using a conventional spectrophotometer, whereas faster changes (<10 s) can be monitored using the same turbidity detection method, but using a stopped-flow instrument. A simple experiment is to start with monomers/micelles in water and "jump" the ionic strength (electrolyte concentration) into a region (>csc) where the vesicles are stable. A reaction scheme for this process for 6-SLABS is shown in Scheme 1. In all experiments, 1:1 mixing is employed.

The kinetics are relatively simple in this configuration, and the spontaneous formation of vesicles occurs on a time scale of a few minutes, depending on the concentration of salt.

The simplest kinetic treatment would be based on the determination of a half-life for the reaction, where $t_{1/2}$ is the time taken for the turbidity to reach half its maximum value. A typical kinetic profile is shown in Figure 2a; it is found to correlate with that of a first-order transient. Since all the curves for this process approximate reasonably well to a single exponential, it is possible to define an apparent first-order rate constant such that:

$$k_{app} = \ln 2/t_{1/2} \quad (1)$$

It is of particular interest to investigate how the final salt concentration influences the kinetics of vesicle formation. An increase in the salt concentration will provide a greater driving force for the reaction, and it is

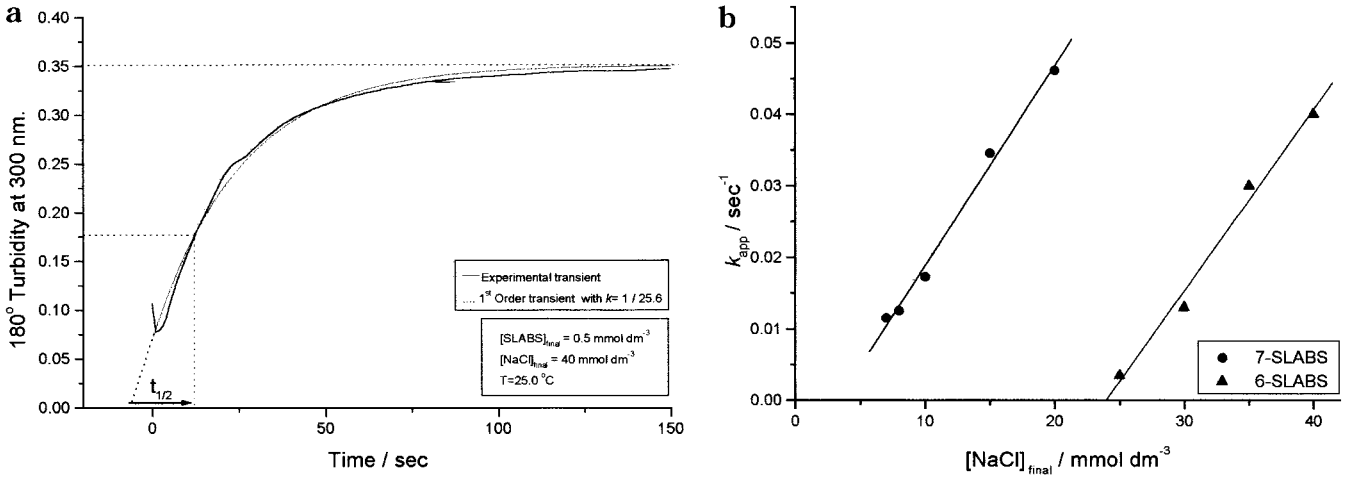


Figure 2. (a) Typical transient curve for the formation of vesicles at $T = 25.0$ °C. (b) Formation rates of SLABS vesicles on addition of salt above the "critical salt concentration" of the system. $[SLABS]_{final} = 1$ mmol dm^{-3}, $T = 25.0$ °C.

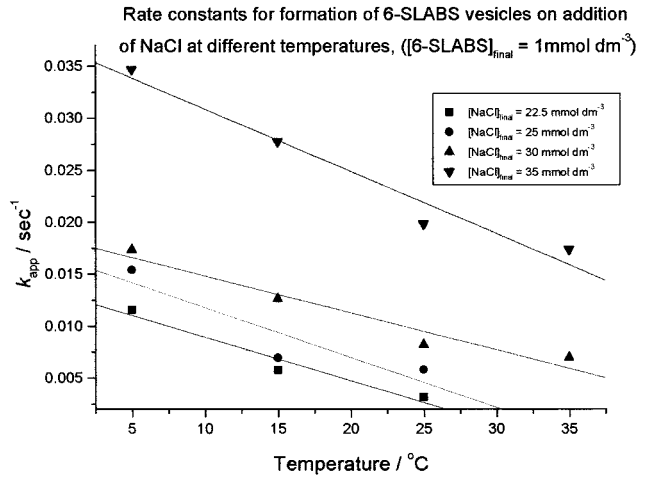


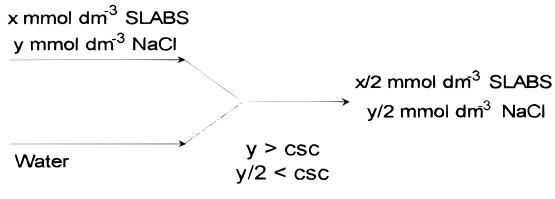
Figure 3. Temperature dependence of rate constants at different NaCl concentrations; $[SLABS]_{final} = 1$ mmol dm^{-3}.

apparent that the larger the salt jump, the greater the tendency will be to form vesicles, which we would expect to be manifested in the observed rates. The size of vesicles is unchanged over the final salt concentration range, corresponding to 30 to 50 mmol dm^{-3} when NaCl is used as the promoter of vesicle formation. A plot of k_{app} versus the final salt concentration (Figure 2b) shows that the rate of formation of vesicles does indeed depend on the NaCl concentration, and the form of the plot is essentially linear for 6- and 7-SLABS. If very high concentrations of salt are employed (>100 mmol dm^{-3}), the linear relationship breaks down, and this is likely to be associated with the preferred formation, in the reaction medium, of lamellar structures rather than vesicles.

The salt is essentially operating through a medium effect, and in this experiment we have a particularly dramatic salt effect in which the free energy barrier for the assembly reaction is systematically decreased as the salt concentration is increased. As the temperature is lowered, it is found that the rate of the self-assembly reaction increases, as shown in Figure 3. As the temperature is lowered, the csc decreases, as already discussed, so if the salt concentration is kept constant, there will be a larger driving force at lower temperatures. This effect apparently overrides the usual effect of the rate of a reaction increasing with an increase in temperature.

(II) Vesicle Breakdown Kinetics. A kinetic scheme for this reaction is shown in Scheme 2:

Scheme 2



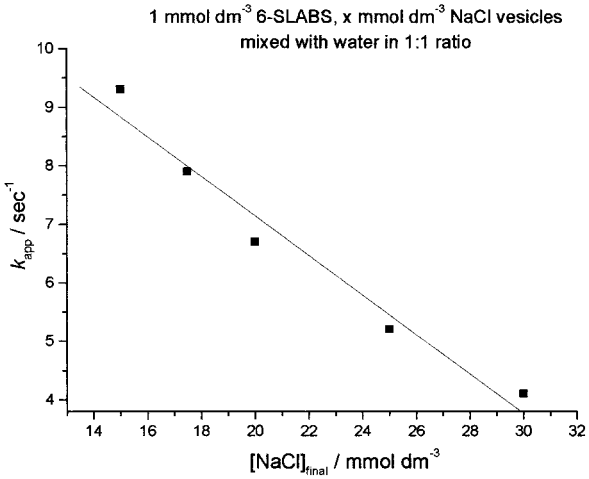


Figure 4. Rate constants for vesicle breakdown on dilution with water; $[6\text{-SLABS}]_{final} = 0.5$ mmol dm^{-3}; $T = 25.0$ °C.

The reaction was monitored on two different time scales: stopped-flow for the period 10 ms to 10 s and conventional spectrophotometry for longer time scales. However, we observe in practice two time regimes for disruption of vesicles—a first step which has $t_{1/2} < 100$ ms and which represents 1% of the total amplitude, and a slow step which represents the bulk of the change. For 6-SLABS, the value of $t_{1/2}$ for this slow step decreases dramatically as the salt concentration y is increased in the region 27−40 mmol dm^{-3}, that is, as the final salt concentration (y/2) approaches the csc (i.e. 23 mmol dm^{-3} NaCl). As for the vesicle formation step, as the salt driving force for the reaction is decreased, the reaction rate slows down. However, the rate does not depend significantly on the SLABS concentration x in the region 0.5−2 mmol dm^{-3}. The data can again be analyzed on the basis of a first-order rate constant (Figure 4).

In conclusion, it is clear that the kinetics of both vesicle formation and breakdown are strongly dependent on the precise salt conditions and temperature.

Cationic Surfactant System. Some cationic surfactants are know to form vesicles spontaneously.[34,44,45]

DODAB (dioctadecyldimethylammonium bromide) forms vesicles in water at temperatures above the phase-transition temperature of the bilayer lipids (~45 °C).[31,46,47] The vesicles can then be extruded to give unilamellar vesicles; these have been reported to have a nonspherical facetted morphology,[31] but they exhibit excellent stability over a time period of several months. In this respect they behave like phospholipids because the monomers are very insoluble in water at room temperature and so monomer exchange is very slow, as it is expected that there will be a correlation between monomer insolubility and stability. As the chain length of the surfactant gets shorter, the monomers become more soluble in water and the stability is expected to decrease.

The cationic surfactant based on a C-16/C-10 combination is more readily solubilized in water due to the presence of a short chain, and this also results in the vesicle bilayer being fluid at temperatures close to ambient. Bending is likely to be facilitated by the asymmetry of the tails aligning the short chain in such a way as to ease the bending on "edges", so that a more spherical structure can be predicted.[22] The vesicles formed are polydisperse, as determined by photon correlation spectroscopy measurements.[40d] They have not been extruded for the kinetic studies reported in this paper, as the focus of the work is on the breakdown of spontaneously formed vesicles. Relative to the di-C_{18} system, these vesicles are not very stable. The long-term instability has not been investigated in detail, but a slow decrease in turbidity is observed over a period of days. Therefore vesicle solutions were prepared immediately prior to use.

This system is different from the SLABS system discussed previously in that it appears that micelle formation precedes the formation of vesicles. The cmc of $C_{16}C_{10}$DMABr is determined by surface tension measurements to be 5.4×10^{-6} mol dm^{-3} at 298.2 K. The cvc is measured to be 1.4×10^{-4} mol dm^{-3} at 298.2 K; this is found by monitoring the turbidity increase at 300 nm due to formation of larger aggregates. The vesicle system can be broken down into mixed micelles on addition of a single-chain surfactant, this has previously been studied in the case of the SLABS/SDS system.[37] It is known that single-chain surfactants, in fact, intercalate into the vesicle bilayer, resulting in vesicle growth.[48] However, above a certain concentration of added single-chain surfactant, the vesicles will break down spontaneously into mixed micelles. In this study, the main emphasis is placed on the breakdown kinetics of $C_{16}C_{10}$DMABr vesicles on addition of an *N*-alkyltrimethylammonium bromide and the aim is to study the effect of the concentration of the single-chain surfactant on vesicle breakdown, which is providing the driving force on this occasion.

The single-chain surfactant C_nTAB, where $n = 10$, 12, and 14, is added to the vesicle solution of $C_{16}C_{10}$DMABr in a 1:1 mixing ratio. For concentrations of added C_nTAB lower than the critical breakdown concentration (cbc) for the vesicle-to-micelle transition, an increase in turbidity is observed which is due to the incorporation of the single-chain surfactant into the vesicle bilayer. When the C_nTAB concentration is high enough (i.e. above the cbc), fast vesicle breakdown occurs within ~5 s, the rate being dependent on the nature and concentration of the single-chain surfactant. There exists an excellent correlation between the rate of breakdown and the concentration of C_{14}TAB added, as shown in Figure 5. Similar results have been obtained for the C_nTAB surfactants where $n = 10$ and 12.

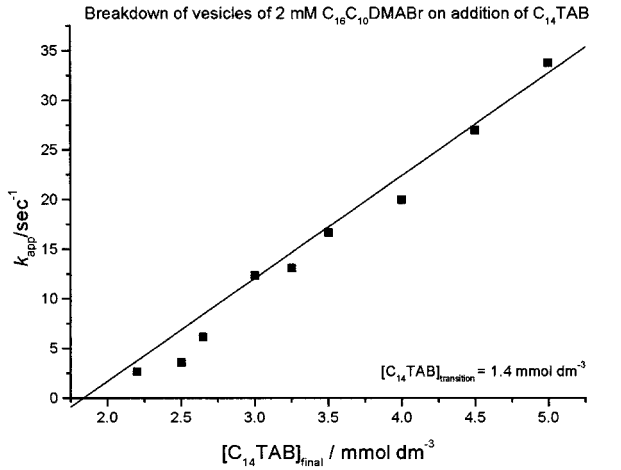
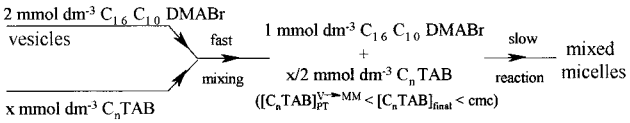
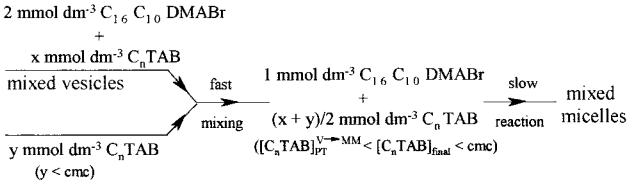


Figure 5. Breakdown of 2 mmol dm^{-3} $C_{16}C_{10}$DMABr vesicles on addition of C_{14}TAB; $T = 25.0$ °C.

Scheme 3



Scheme 4



For this reaction the mechanism would be as in Scheme 3.

Vesicle breakdown can also be achieved starting from mixed vesicles of $C_{16}C_{10}$DMABr and the single-chain surfactant, breakdown of vesicles being induced on addition of more single-chain surfactant, as in Scheme 4.

When the concentration of C_nTAB initially present (x) is close to that corresponding to the cbc, only a small amount of additional single-chain surfactant is needed to disrupt the vesicle structure. Accordingly, the rates of breakdown according to Scheme 4 are generally faster than those in the case of Scheme 3.

However, the rate of breakdown is again strongly correlated to the concentration of the added single-chain surfactant, which is providing the "driving force" (Figure 6).

Discussion

It is interesting to speculate on the intermediates which might be involved in these complex kinetic pathways, which necessarily involve the rearrangement of large numbers of surfactant molecules. It is easier to visualize the mechanism of the breakdown process in contrast to assembly, and there are two possibilities. In the case of SLABS, a likely first step on decreasing the salt concen-

(45) Wagenaar, A.; Rupert, L. A. M.; Engberts, J. B. F. N. *J. Org. Chem.* **1989**, *54*, 2638.
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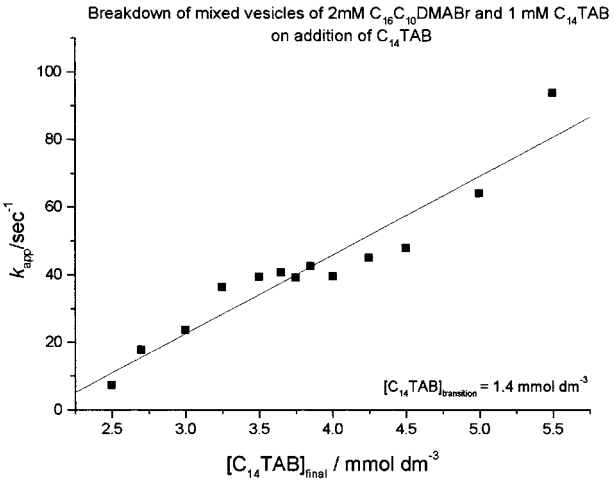

Figure 6. Breakdown of mixed vesicles of 2 mmol dm^{-3} $C_{16}C_{10}$-DMABr and 1 mmol dm^{-3} C_{14}TAB on addition of more C_{14}TAB; T = 25.0 °C.

tration to below the csc is that the mechanism of exchange of monomer surfactant will be perturbed such that more surfactant will exit from the external surface than is replaced. In addition, the headgroup−counterion interaction will be changed, in the sense that headgroup−counterion neutralization will be reduced, leading to increased repulsion between the surfactant headgroups, which is again likely to lead to expelling of surfactant from the outside surface into the bulk aqueous solution. This would then result in an imbalance in the number of surfactant molecules on the two sides of the vesicle bilayer. Because the flip-flop of surfactant between the internal and external surfaces is generally slow on the time scales we are investigating, this process will end in the development of a critically unstable vesicle which is then likely to rupture into fragments, probably disklike. Depending on the final value of the ionic strength, we might expect these fragments, which might be slightly distorted micelles, to be relatively stable, and indeed we are presently probing the structure of these entities using the fluorescence correlation technique referred to previously.

Recent studies with "giant" vesicles, which can be directly visualized by video-microscopy techniques, have shown that when they are placed in an unstable environment, vesicles can either shrink or experience bilayer undulations followed by rupture.[49] In our system, we feel the latter mechanism is more likely.

(49) Luisi, P. L. ETH Zurich, personal communication.

The process of spontaneous assembly of vesicles is not so easy to visualize. Again the first step is likely to involve the assembly of surfactants into rods or, more likely, disks. These could then join together and eventually form closed bilayer spheres. There is a driving force for this, as the edges of the sheets will have a relatively high free energy and so there will be a strong tendency for the edges to seal. An alternative scenario might involve the disjoining of large disklike structures followed by assembly of the bilayer by addition of surfactant. In any event, the system will be driven by the need to minimize the contact between the hydrocarbon chains and water and considerations of the bending energy/elasticity.

In the case of the cationic system, the mechanism of induced disintegration is likely to involve the following steps:

(1) Incorporation of the single-chain surfactant into the vesicle such that the mole fraction of the mixed surfactant system in the bilayer is in excess of that corresponding to a vesicular structure, such that mixed micelles are favored. We argued in a previous paper[37] dealing with SLABS/SDS that this step introduces cooperativity through the invading surfactant functioning as a small cooperative unit of approximately eight SDS molecules. This is the case for measurements made close to the cbc. In the studies reported here, there is excess surfactant present to drive the dissolution of the vesicles and we see a more straightforward first-order dependence on the concentration of added single-chain surfactant in excess of the cbc, the rate increasing linearly with the concentration of added surfactant. In this case, there is no need for the invading surfactant to function in a cooperative way.

(2) When sufficient single-chain surfactant is present in the vesicle bilayer, mixed micellar domains will form within the bilayer, and so the process of disintegration will take place.

The general ideas which we have developed in this paper to explain the dynamics also appear to be valid for other vesicle-forming systems. In particular, we have studied the rate of dissolution of mixed surfactant vesicles formed from CTAB/SOS systems, and these studies will be described in more detail in a subsequent paper.

One can also speculate that the assembly and disassembly processes might progress via different pathways. Since these changes to the system are induced by large perturbations, it is possible for the reactions to proceed by routes involving different energy surfaces, and so the intermediates need not necessarily be the same in the assembly and disassembly processes.

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