

## Novel Vesicles from Single-Chain Surfactants

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We have studied aqueous mixtures of tetradecyldimethylaminoxid ( $C_{14}$ DMAO) and calciumdodecyl sulfate  $Ca(DS)_2$ . Surface tension measurements show a stronger synergism for these mixtures than for the combination of  $C_{14}$ DMAO and sodiumdodecyl sulfate SDS. With an increasing mole fraction of dodecyl sulfate  $X_{DS}$ , for 100 mM solutions one observes a viscoelastic  $L_1$ -phase, a birefringent  $L_\alpha$ -phase, and a viscous  $L_1$ -phase on the dodecyl side. The maximum of the viscosity in the first  $L_1$ -phase occurs around  $X_{DS} = 0.28$ . At this composition, the viscosity is more than 4 orders of magnitude higher than the viscosity of the single-component solutions. Rheological measurements show that the birefringent  $L_\alpha$ -phase is composed of densely packed multilamellar vesicles. For concentrations above 100 mM, the  $L_\alpha$ -phase has a yield stress value that is large enough to suspend small dispersed air bubbles. SANS measurements show that the interlamellar spacing between the bilayers at 100 mM is  $\sim 800$  Å and is independent of  $X_{DS}$  within the existence region of the liquid crystalline phase. To our knowledge, this is the first time that a vesicle phase from combination of a single-chain zwitterionic surfactant and a Ca salt of a single-chain anionic surfactant has been reported. The large synergism between the two surfactants is likely to be the result of strong binding of Ca ions to two dodecyl sulfate ions. The Ca ions act as links for two ionic surfactants, and by doing so, the  $Ca(DS)_2$  behaves like a double-chain surfactant. In addition, it is conceivable that the Ca ions coordinate to the polar oxygen of the aminoxide.

### Introduction

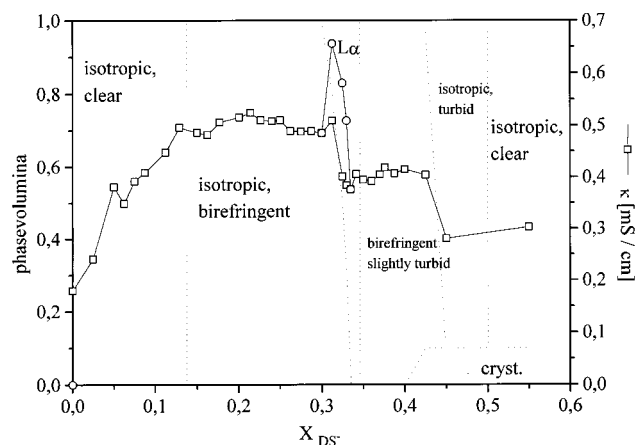
It is well-known that vesicles can be prepared by mechanical manipulation of phospholipid dispersions. Several techniques are available now which give reproducible size distributions for the vesicles. Vesicle phases from phospholipids are of much interest in biochemistry and in pharmaceutical applications as drug delivery systems.<sup>1</sup> Vesicles are also formed from different types of surfactants. Vesicles are formed in solutions of double-chain ionic surfactants such as dialkyldimethylammonium bromide and in many solutions of perfluorosurfactants or in mixtures of various surface-active perfluorocompounds.<sup>2,3</sup> They are produced when cationic and anionic surfactants are mixed. The vesicle phases are usually formed when one of the surfactants is present in a small excess. The systems precipitate when the stoichiometry between the two surfactants is exactly 1.<sup>4</sup> When the vesicles are prepared from the two surfactants, their ionic charge from the excess surfactant is shielded by the salt that is produced from the counterions of the two ionic surfactants. This is important for the understanding of the macroscopic properties of the vesicle phases. Charged vesicle phases without shielding can be prepared by mixing small amounts of ionic surfactants to  $L_3$ -phases from ionic surfactants and cosurfactants.<sup>5</sup> It is theoretically argued that the vesicles are formed in these systems by the influence of the charge density on the Gaussian bending constant.<sup>6</sup> It was shown recently, however, that shearing forces that result from the mixing of the two solutions might also be responsible for the formation of the vesicles.<sup>7</sup> Vesicles were not formed when the  $L_3$ -phase was ionically charged without shear forces. Instead a well-defined  $L_\alpha$ -phase is produced. Very recently, thermodynamically stable vesicles were formed in mixtures of ionic surfactants, nonionic surfactants, and cosurfactants.<sup>8</sup>

Vesicles can also be produced in a small temperature range of solutions of the nonionic surfactant alkylpolyglycolates.<sup>9</sup> Vesicle phases which are ionically charged and are not shielded by excess salt have interesting rheological properties. These phases are highly viscoelastic and have a yield stress value even when the concentration is as low as 2% surfactant.<sup>10</sup>

In the present work, we report the preparation of charged vesicle phases that are produced without the use of cosurfactants. Such phases are important for many applications where cosurfactants cannot be used. The vesicle phases are simply produced by mixing micellar solutions of alkyldimethylaminoxide and the Ca salt of dodecyl sulfate. Both surfactants form normal micellar  $L_1$ -phases on their own. We prepared the samples by mixing a 100 mM solution of  $C_{14}$ DMAO with a 50 mM solution of  $Ca(DS)_2$ . The properties of the solutions will be presented as a function of the mole fraction  $X_{DS}$  of dodecyl sulfate. The formation of the vesicles in these mixtures is most remarkable, and as far as we know, it was observed by us for the first time. Mixtures of alkyldimethylaminoxide and the Na salt of dodecyl sulfate do not form vesicles.

### The Phase Diagram

In Figure 1 the sequence of phases is shown that is produced by mixing solutions that were 100 mM in  $C_{14}$ DMAO and 50 mM in  $Ca(DS)_2$ . Because of the low solubility of  $Ca(DS)_2$  in water at room temperature, the samples were prepared at 50 °C and then thermostated at 25 °C. The Krafft temperature of  $Ca(DS)_2$  is  $\sim 50$  °C.<sup>11</sup> In mixtures with  $C_{14}$ DMAO, the Krafft temperature is reduced and solutions with a mole fraction  $X_{DS}$  up to 0.4 are thermodynamically stable at room temperature. From  $X_{DS} = 0$ –0.3, we note a single transparent solution that becomes more viscous with increasing  $X_{DS}$ . Between  $X_{DS} = 0.3$  and 0.35, we note macroscopic phase separation into a upper



**Figure 1.** Phase diagram and conductivity of mixtures of 100 mM  $C_{14}$ DMAO and  $DS^-$ , Ca salt at 25 °C when  $DS^-$  is the mole fraction of  $DS^-$ .

birefringent  $L_\alpha$ -phase and an isotropic  $L_1$ -phase at the bottom. Between  $X = 0.35$  and  $0.42$ , there is a single transparent slightly birefringent phase. The birefringence decreases in the solution at rest with increasing DS content. The birefringence becomes large when the samples are tilted or the phase flows.

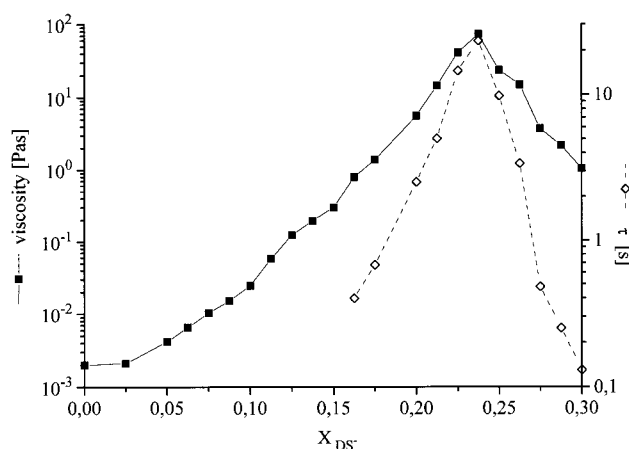
The samples with  $X > 0.45$  are slightly turbid and again separate in two phases. Furthermore, the upper phase contains small crystals of  $Ca(DS)_2$ . We have characterized the different phases with various physicochemical methods. Some of these results are shown in the following discussion.

### Conductivity Results

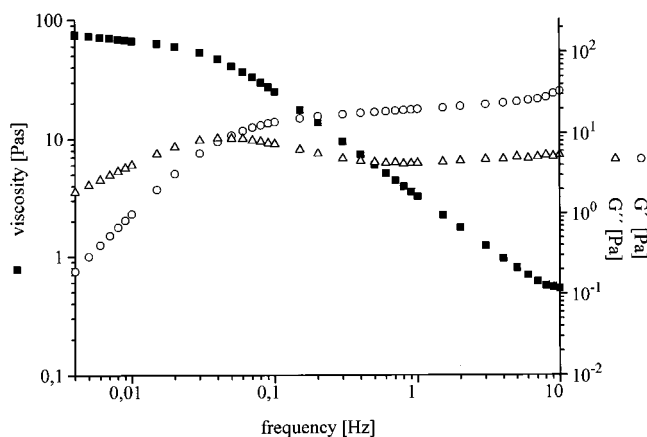
The conductivities of the samples are included in Figure 1. The conductivities rise more or less linearly with the content of dodecyl sulfate up to  $X = 0.15$  and then remain about constant up to the phase boundary. The results indicate that the  $Ca^{2+}$  ions begin to bind to the micellar interface as soon as the mole ratio reaches about 0.15. For a further increase of  $X_{DS}$ , the effective charge density of the micelles remains constant and all added  $Ca(DS)_2$  remains in the condensed state. In the birefringent phase, the conductivity is about  $1/3$  lower than in the  $L_1$ -phase. This is an indication that some of the counterions that have contributed to the conductivities in the  $L_1$ -phase are now trapped inside the vesicles of the  $L_\alpha$ -phase and can no longer contribute to the conductivity. In general, the decrease of the conductivity that is caused by the transformation of the  $L_1$ -phase to the  $L_\alpha$ -phase is usually much larger in other systems. The small decrease is thus an indication that the  $L_\alpha$ -phase consists mainly of unilamellar vesicles and not so much of multilamellar vesicles. It could also mean that the interior of the vesicles is not electroneutral and that some of the  $Ca^{2+}$  ions have been transferred to the outside of the vesicles. It is, however, known that in general bivalent counterions bind much stronger to micellar interfaces of ionic surfactants than univalent ions. The dissociation degree of  $Ca^{2+}$  and  $Ni^{2+}$  dodecyl sulfate, for instance, is about 0.1, in contrast to 0.3 for SDS.<sup>12</sup>

### Rheological Properties

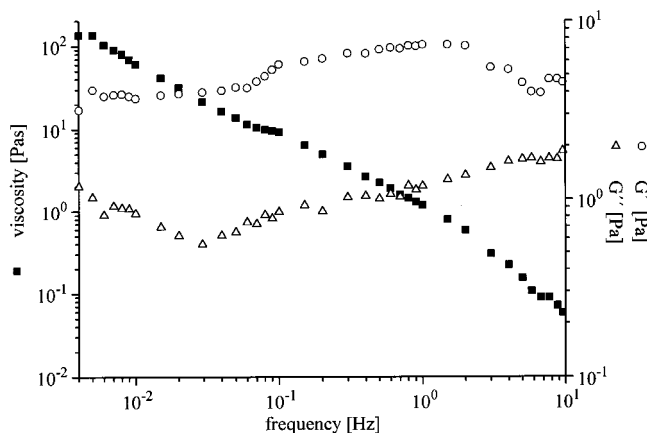
The zero-shear viscosities and the structural relaxation times of the mixed samples are shown in Figure 2. Both parameters increase strongly and pass over a maximum with an increasing mole fraction of  $DS^-$ . The increase in the  $L_1$ -phase corresponds to more than 4 orders of magnitude. For comparison, the viscosity increases by a factor 10 when  $C_{14}$ DMAO is mixed with SDS for the same total concentration. The maximum of



**Figure 2.**  $\eta^\circ$  and  $\tau$  against  $X_{DS^-}$  in mixtures of 100 mM  $C_{14}$ DMAO and  $DS^-$ , Ca salt at 25 °C.

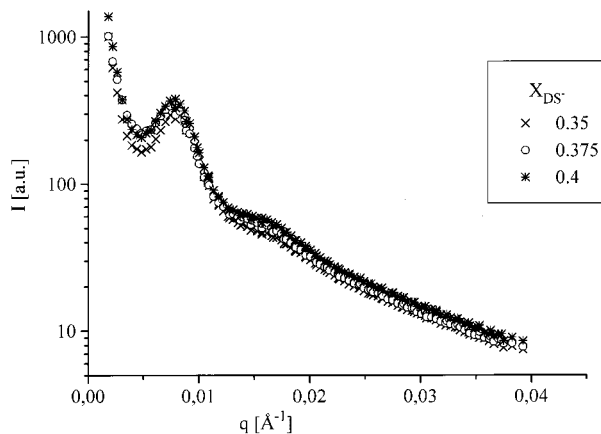
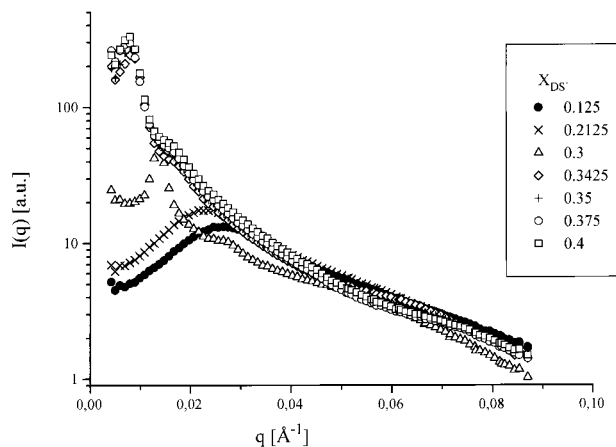


**Figure 3.** Rheogram of a mixture of 100 mM  $C_{14}$ DMAO and  $DS^-$ , Ca salt,  $X_{DS} = 0.24$  at 25 °C.



**Figure 4.** Rheogram within the  $L_\alpha$ -region of 150 mM  $C_{14}$ DMAO and  $DS^-$ , Ca salt with  $X_{DS} = 0.38$  at 25 °C.

the viscosity in the mixture with SDS is at a mole fraction of 0.1. The mixed surfactant solutions of  $C_{14}$ DMAO and  $Ca(DS)_2$  behave somewhat similar to mixtures of  $C_{14}$ DMAO and SDS in the presence of excess salt. Around the viscosity maximum the  $L_1$ -phases are highly viscoelastic and the shear moduli, and the structural relaxation times can be easily measured by oscillating rheological measurements. A typical rheogram for such a situation is shown in Figure 3. All viscoelastic solutions behave like Maxwell fluids with a single shear modulus  $G^\circ$  and a single relaxation time  $\tau$ . The zero-shear viscosity is thus given by the product of  $G^\circ$  and  $\tau_s$  ( $\eta^\circ = G^\circ \tau_s$ ).<sup>13</sup> The increase and decrease of the viscosity in the viscoelastic region is mainly



**Figure 5.** (a) SANS spectra of mixtures of 100 mM  $C_{14}$ DMAO and  $DS^-$ , Ca salt at 25 °C, where  $X_{DS^-}$  is the mole fraction of  $DS^-$ . (b) Details of Figure 5a.

given by the change of the structural relaxation time, and the shear modulus changes very little. The systems in this respect behave similarly to other viscoelastic surfactants when for a given surfactant concentration the salinity or an additive concentration is varied. It is noteworthy that the viscosity decreases again toward the phase boundary of the  $L_\alpha$ -phase. This situation has been observed before on other systems, and it could be due to a transition in the micellar structures from a situation with entangled rods from individual micelles to a real network from branched micelles.<sup>14</sup>

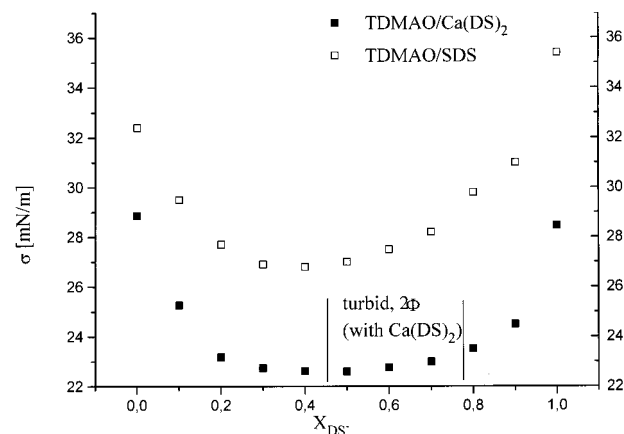
In contrast to the viscoelastic solutions of the  $L_1$ -region which have finite structural relaxation times and therefore a zero-shear viscosity, the viscoelastic  $L_\alpha$ -phase has a yield stress value. The samples behave, therefore, as a Bingham fluid. A typical rheogram of such a phase is shown in Figure 4. The storage modulus of the phase is frequency independent and about 1 order of magnitude larger than the loss modulus. The yield stress value of the phase can easily be recognized by the fact that small air bubbles that are dispersed in samples do not rise. In this respect, the phases of  $C_{14}$ DMAO and  $Ca(DS)_2$  behave in the same way as other charged multilamellar vesicle phases with different chemical compositions.<sup>10</sup>

Classic  $L_\alpha$ -phases with extended bilayers behave very differently at a total concentration of 100 mM. The shear modulus of such phases is much lower than that for the present system. In addition the optical appearance and the texture of the birefringence for the investigated systems are different from those properties of normal  $L_\alpha$ -phases. We are convinced, therefore, that the  $L_\alpha$ -phase in the systems studied consists of densely packed vesicles.

### Small-Angle Neutron Scattering Data

Some SANS curves are shown in Figure 5 a and b. For samples in the  $L_\alpha$ -region, the scattering curves show the typical scattering behavior of  $L_\alpha$ -phases with charged bilayers. One observes the first and second maximum from which one can obtain the interlamellar distance between the bilayers. The scattering curves for three different compositions within the  $L_\alpha$ -region are practically identical. The interlamellar scattering maximum gives an interlamellar distance of  $d = 2 \pi / q_{\max} = 800 \text{ \AA}$ . This separation of the bilayers is consistent with the concentration of the surfactant and the thickness of the bilayers that can be calculated from the scattering curves at high  $q$ .

The scattering curves in the  $L_1$ -phase show a typical correlation peak. The data can be fitted with the scattering function of charged cylindrical micelles. The mean separation distance



**Figure 6.** Surface tension of mixtures of 10 mM  $C_{14}$ DMAO and  $DS^-$ , Ca salt at 60 °C and 100 mM  $C_{14}$ DMAO and  $DS^-$ , Na salt at 25 °C, where  $X_{DS^-}$  is the mole fraction of  $DS^-$ .

**TABLE 1: Radius  $r$  of Cylindrical Micelles and Their Mean Separation Distances  $d$  in Mixtures of 100 mM  $C_{14}$ DMAO and  $DS^-$ , Ca Salt at 25 °C from SANS Data**

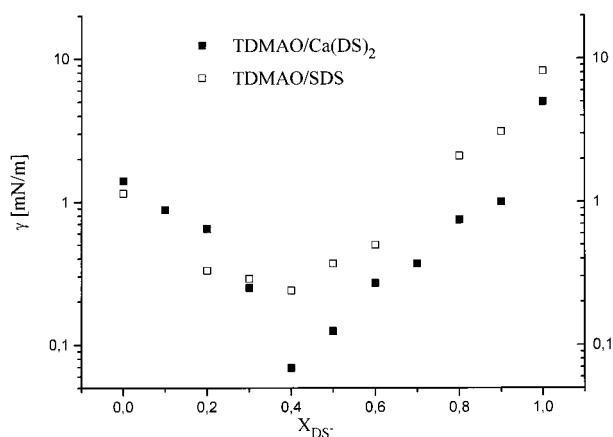
mole fraction of $DS^-$	$r$ [Å]	$q_{\max}$ [Å <sup>-1</sup> ]	$d$ [Å]
0.125	20.2	0.0266	236
0.2125	21.1	0.0243	259
0.3	21.6	0.0137	460

between the micelles and the radius of the cylindrical micelles can be evaluated from the scattering data. The results are given in Table 1. It is somewhat surprising that the mean distance in the  $L_1$ -phase depends somewhat on the mole fraction of  $DS^-$ . Otherwise, the scattering data are very similar to the scattering curves for other surfactant systems with entangled threadlike micelles.<sup>15</sup>

### Surface Tension Measurements

In Figure 6 the surface tension values for  $C_{14}$ DMAO/ $Ca(DS)_2$  mixtures are plotted against the mole fraction of  $DS^-$ . These data were measured by the de Noüy ring method using a Lauda TCE 1 C ring tensiometer. To avoid the problem that is associated with crystal precipitation and the formation of liquid crystalline phases, the measurements were carried out at a total concentration of 10 mM and at a temperature of 60 °C.

In spite of the low concentration, the solutions with  $0.42 < X_{DS^-} < 0.75$  were turbid and in a two-phase region. This situation did not effect the measurements. The surface tension shows a deep minimum for the mixtures. Interestingly, the values of the



**Figure 7.** Interfacial tension of mixtures of 10 mM  $C_{14}$ DMAO and  $DS^-$ , Ca salt at 60 °C and 100 mM  $C_{14}$ DMAO and  $DS^-$ , Na salt at 25 °C against decane, where  $X_{DS^-}$  is the mole fraction of  $DS^-$ .

two components are about the same. At the minimum, the surface tension is only 22.5 mN/m. This is an extremely low value for a hydrocarbon surfactant and is in the range of silicon surfactants.

The surface tension values for the combination  $C_{14}$ DMAO/SDS are also shown in Figure 6. These values are considerably higher than those for the  $C_{14}$ DMAO/ $Ca(DS)_2$  combination. The  $C_{14}$ DMAO/SDS combinations were measured for a total concentration of 100 mM and at 25 °C.<sup>16</sup> There is no phase separation under these conditions for this system. The large differences for  $C_{14}$ DMAO in the two plots comes from the temperature difference. With increasing temperature,  $C_{14}$ DMAO becomes more lipophilic and the surface tension is therefore lowered.

### Interfacial Tension Measurements

The interfacial tensions for the  $C_{14}$ DMAO/ $Ca(DS)_2$  and  $C_{14}$ DMAO/SDS combination against decane were measured by the spinning drop technique using a Krüss SITE 04 spinning drop tensiometer. They are given in Figure 7.<sup>16</sup> On the  $DS^-$ -rich side, the values for the  $Ca(DS)_2$  combination are considerably lower than those for the SDS combination. In particular, there is a deep minimum for the  $Ca(DS)_2$  mixture. The value of the minimum is below 0.1 mN/m.

### Theoretical Considerations

The CMC of  $Ca(DS)_2$  is about a factor 4 lower than that of SDS.<sup>17</sup> This is a consequence of the  $Ca(DS)_2$  system being more lipophilic than SDS because the micelles in  $Ca(DS)_2$  are less charged than for SDS. The  $Ca^{2+}$  ions bind strongly to the micellar interface and shield the charge density from the  $SO_4^{2-}$  headgroups extensively. Conductivity data show that only about 1  $Ca^{2+}$  ion in 10 is in the diffuse double layer and contributes to the conductivity while the other  $Ca^{2+}$  ions bind strongly to the interface. On a microscopic level, the  $Ca^{2+}$  ions act like cross-links between two  $DS^-$  ions and the  $Ca(DS)_2$  system behaves, therefore, more like a double-chain zwitterionic surfactant than a single-chain ionic surfactant.

Nevertheless, compensation of the charges at the interface is not sufficient for the pure system to form a  $L_\alpha$ -phase in dilute solution. It is likely that the system cannot form bilayers on its own because the steric repulsion between the bulky sulfate groups is too large and does not allow the dense packing in the dilute phase that is required for the formation of the  $L_\alpha$ -phase.<sup>18,19</sup> It is only when the repulsion between the headgroups

is reduced by the incorporation of an alkyldimethylaminoxide when the formation becomes possible. It is suggested, therefore, that the large observed synergism between  $Ca(DS)_2$  and  $C_{14}$ DMAO has its origin in the bulkiness of the sulfate headgroups. The two surfactants together can, therefore, pack more densely than the two compounds on their own. Another approach toward explaining the appearance of vesicles only in mixtures of the two surfactants would be from the side of pure  $C_{14}$ DMAO. An increase of ionic surfactant increases the surface charge density of the bilayer, thus decreasing the Gaussian bending modulus, which in turn favors formation of vesicles where the product  $C_1C_2$  of the two main curvatures is positive.

It is, however, also clear that replacement of the sodium ions by  $Ca^{2+}$  ions in other ionic surfactants should always lead to a strong increase of the lipophilicity of the system.

### Conclusions

We have studied the synergistic behavior of the surfactant mixtures tetradecyldimethylaminoxide and the Ca salt of dodecyl sulfate.

The investigations were carried out in aqueous solutions with a total concentration of 100 mM. The two single-chain surfactants show a highly synergistic behavior that is reflected in a minimum of the surface and the interfacial tension with an increasing mole fraction of  $DS^-$ , the formation of highly viscoelastic solutions, and the formation of a liquid crystalline  $L_\alpha$ -phase around a mole fraction of  $X = 0.4$ . It is believed to be the first time that a liquid crystalline  $L_\alpha$ -phase between a single-chain zwitterionic and an ionic surfactant has been observed. The  $L_\alpha$ -phase has a yield stress value that is large enough to suspend small air bubbles in the phase.

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