Carbon-13 Nuclear Magnetic Resonance Study of Mixed Micelles. Variation of Interchain Distances and Conformational Equilibria

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Observed ^{13}C NMR chemical shift changes with respect to their single micelles upon mixed-micelle formation of potassium dodecanoate and short-chain potassium carboxylates (hexanoate up to an including decanoate) are described in all but one case to increasing distances between the apolar ends of the long amphiphile chains as compared with its single micelle. Only for dodecanoate–hexanoate micellar systems can a different conformational equilibrium of the dodecanoate chain not be excluded. Furthermore, recently observed solvent effects upon mixing of *n*-alkanes of different chain lengths are compared with both the decanoate and nonanoate chemical shift changes upon mixing with the dodecanoate amphiphiles. This leads to the conclusion that the former detergents are mainly subject to increased intermolecular chain packing. Observed effects for the octanoate and heptanoate are not as pronounced, and these surfactants should be considered as borderline cases, while the hexanoate undergoes conformational changes toward more extended forms. Finally, it is observed that maximally ca. 1 equiv of hexanoate or ca. 2 equiv of heptanoate can be incorporated into micelles of potassium dodecanoate. At higher percentages of short-chain surfactants, these maximally incorporated mixed micelles coexist with short-chain monomers up to the concentration where the free short surfactants reach their critical micelle concentration and may form micelles. We postulate that a statistical distribution of dodecanoate molecules in short-chain micelles is attained.

Introduction

Short-chain lecithins exist as large micellar aggregates in water above a given critical micelle concentration (cmc). The cmc depends on the fatty acid chain length.[1] Lipid micelles are of biological interest for the following reasons: (1) The so-called polar discontinuities (i.e., local micelle formation) within a phospholipid bilayer alter the permeability of the cell membrane to vital compounds[2,3] and also play a major role in the process of cell division.[2,4] (2) Furthermore, there is a large enhancement of the rate of hydrolysis of phosphatidylcholines by phospholipases in the micellar state compared with the monomer.[5,6]

It is generally presumed, that conformational changes in head-group and/or lipid chains are important in connection with the above-mentioned phenomena,[3,7] as well as their relative orientations.

Recently, much work has been done explaining the acyl chain conformation of long-chain phosphatidylcholines in different states[8,9] (see Figure 1). The *sn*-1 chain is orientated perpendicular to the bilayer surface and the *sn*-2 chain is bent at the C-2 carbon atom and runs from thereon parallel with the *sn*-1 chain.[8,9] In order to gain more insight into the conformational behavior of phospholipids, Roberts et al.[10] applied ^1H NMR techniques to several phosphatidylcholines in different mixed micelles. The observed magnetic nonequivalences of the α protons of the *sn*-1 chain and also the *sn*-2 chain were explained in terms of different conformational equilibria for the two chains.[8] Because of the difference in effective lengths of the *sn*-1 and *sn*-2 chains, phospholipid micelles as such qualify as mixed micelles to a certain extent.[11]

On the other hand, single micelles of simple detergents are studied frequently by means of a wide variety of physical methods.[12] A number of discrepancies, notably about the cmc, still exist between the different analytical methods.[13,14] More details regarding dynamics and conformational equilibria of the acyl chains have been reported by Lindman et al.[13,15,16] in a number of papers. Topics as solubilization and aggregation numbers were also included using ^{13}C NMR.[17]

Specific statements regarding mixed micelles of CTAB (cetyltrimethylammonium bromide) and TTAB (tetradecyltrimethylammonium bromide) were reported by Lindman et al.[18] The difference in chain lengths of the partners in these micelles is of the same order of magnitude as that which might prevail in phospholipid micelles (with nominally equal *sn*-1 and *sn*-2 chain lengths). The different chemical shifts of the terminal methyls of the TTAB and CTAB constituents were explained in terms of in-

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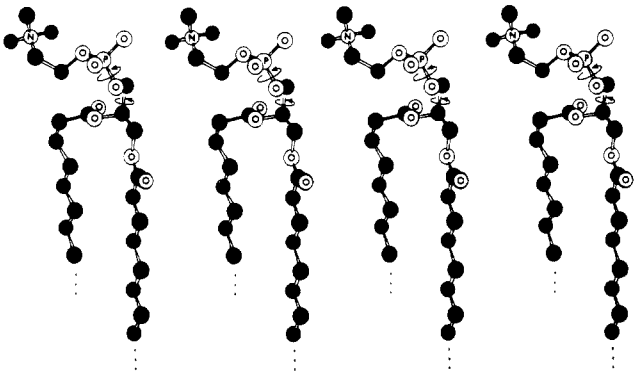

Figure 1. Average orientation of lecithin head groups and the conformational nonequivalence of lecithin acyl chains in lipid bilayers according to Seelig.[8-10]

creased chain folding of the longer chain near the apolar end. A similar explanation has been offered previously for the solubilization of 1-decanol in sodium octanoate micelles.[17]

In our opinion, alternative descriptions involving the occurence of chain separation and, consequently, changes in van der Waals solvent effects on the chain should be considered as well. A recent publication by Roberts et al.[19] concerning ^{13}C NMR of simple phospholipid micelles has been taken into account neither solvent effects nor the model experiments of Lindman et al.[17,18] regarding mixed micelles. This prompts us to report our own results and views on a number of mixed micelles in different ratios and with partners of different chain length.

Experimental Section

Potassium alkanoates were prepared by neutralizing the corresponding carboxylic acids (Fluka AG) with potassium hydroxide (Merck AG) and purified by recrystallization from methanol. Stock solutions of 1.5 M were prepared with deionized water and stabilized with 0.1 M of potassium hydroxide. Mixed-micelle solutions were obtained from the stock solutions by adding the appropriate amounts. The resultant solutions were sonicated for 15 min. at 25 °C and then allowed to stand for 5 days before measurement.

All ^{13}C NMR spectra were run at 62.93 MHz on a Bruker WM 250 spectrometer under proton noise decoupling. The deuterium signal from C_6D_6 was employed as external lock signal. All chemical shifts are related to Me_4Si (C_6D_6 at 128 ppm downfield from Me_4Si). Eight transients corresponding to a spectral width of 2000 Hz were accumulated in 32K data points limiting the resolution to 0.005 ppm. Pulse width was set to a 90° flip angle.

Results

^{13}C NMR chemical shifts of the micelles have been assigned by combining literature data[16,17] and relative relaxation time values, assuming that T_1 values increase toward the apolar ends.[20-23] Results are presented in Table I.

When mixed micelles are formed, the ^{13}C NMR chemical shifts of the constituents chains change with respect to the single micelles (see Table II).

When the dodecanoate solution was diluted from 1.5 to 0.15 M, no changes in chemical shifts were observed. This indicates, that no changes in aggregation numbers occur in this concentration range.[13]

TABLE I: ^{13}C NMR Chemical Shifts of the Single-Micelle Solutions (1.5 M), Relative to Me_4Si[a]

carbon atom	n-C_{12}	n-C_{10}	n-C_9	n-C_8	n-C_7	n-C_6
2	38.40	38.48	38.45	38.39	38.34	38.22
3	26.90	26.89	26.83	26.73	26.59	26.15
4	30.47	30.23	30.13	29.89	29.40	31.68
5	30.33	30.23	29.90	29.39	31.78	22.40
6	30.47	30.06	29.81	32.13	22.76	14.00
7	30.20	29.93	32.33	22.90	14.17	
8	30.47	32.46	23.06	14.19		
9	30.04	23.09	14.25			
10	32.52	14.25				
11	23.12					
12	14.25					

[a] C_6D_6 at 128 ppm downfield from Me_4Si.

Discussion

For the hexanoate NMR measurements indicate formation of aggregates of ca. five molecules of amphiphile in water.[13] Other experimental methods really indicate formation of micelles with larger aggregational numbers.[14] The octanoate forms micelles with an average aggregation number of ca. 17,[13,24] while the dodecanoate forms much larger micelles.

Previous reports[12,25] revealed no appreciable interaction of water with the hydrophobic core of closely packed surfactant micelles such as sodium dodecanoate.[26,27] Contradictory results have been shown to be due to deficiencies in the analytical procedures.[28,29]

The ^{13}C NMR chemical shifts of the ω-methyl groups fall roughly into three groups: 14.00 ppm for the hexanoate, 14.18 ± 0.01 ppm for the heptanoate and the octanoate, and 14.25 ppm for the nonanoate, the decanoate, and the dodecanoate micelles. Similar observations, albeit with larger discrepancies (due to nonnegligible through-bond δ effects of the polar head group in the hexanoate chain) can be made for the ω-1 methylene chemical shifts. Corresponding shift differences are observed for carboxylic acids in chloroform. However, these compounds may form inverse micelles in $CHCl_3$. A comparative study was also carried out for solutions of n-alkyltrimethylammonium bromides[11] in chloroform and water (below the cmc for the latter solvent). (We thank one of the referees for bringing this to our attention.) The results indicate clearly that the variation within a homologous series of the ^{13}C NMR shifts of inverse micelles and of monomers do not differ significantly. Therefore, we would like to suggest that the observed shift differences for the methyl carbons of the alkanoate micelles indicate the formation of three different micellar solutions. Solutions of n-alkanes do not show a comparable behavior.[30] The reason for the differences

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TABLE II: (De-)shielding Effects upon Mixed-Micelle Formation As Compared with the Corresponding Single-Micelle Solutions

effective concn, M	mixing ratios[a]	carbon atom	dodecanoate[b] 2	3	7	9	10	11	12	shorter amphiphiles 2	3	4	5	6	7	8	9	10
1.00:0.50	2:1		+0.05	+0.01	−0.02	−0.05	−0.04	−0.03	−0.02	+0.02	+0.08	+0.13	+0.12	+0.08				
0.75:0.75	1:1			−0.01	−0.12	−0.19	−0.16	−0.13	−0.09	+0.02	+0.04	+0.11	+0.07	+0.03				
0.50:1.00	1:2		+0.09	−0.01	−0.11	−0.21	−0.17	−0.13	−0.08	+0.02	+0.04	+0.09	+0.06	+0.03				
0.38:1.12	1:3		+0.08	−0.01	−0.08	−0.18	−0.15	−0.10	−0.09	+0.01	+0.04	+0.06	+0.07	+0.04				
0.30:1.20	1:4		+0.09	−0.01	−0.12	−0.22	−0.16	−0.11	−0.04	+0.01	+0.04	+0.06	+0.06	+0.04				
0.17:1.33	1:8		+0.09		−0.15	−0.24	−0.20	−0.12	−0.02	+0.01	+0.03	+0.04	+0.05	+0.04				
1.00:0.50	2:1		+0.10	+0.03	−0.04	−0.08	−0.06	−0.04	−0.03	+0.01	+0.03	+0.06	+0.09	+0.07	+0.10			
0.75:0.75	1:1		+0.11	+0.04	−0.03	−0.11	−0.09	−0.06	−0.03	+0.02	+0.04	+0.08	+0.10	+0.09	+0.11			
0.50:1.00	1:2		+0.10	+0.01	−0.10	−0.22	−0.18	−0.13	−0.07	+0.01	+0.02	+0.05	+0.06	+0.04	+0.05			
0.38:1.12	1:3		+0.07	+0.01	−0.10	−0.23	−0.19	−0.16	−0.05	+0.00	+0.02	+0.05	+0.05	+0.05	+0.05			
0.30:1.20	1:4		+0.09	−0.01	−0.09	−0.26	−0.22	−0.16	−0.05	−0.00	+0.01	+0.04	+0.04	+0.03	+0.03			
0.17:1.33	1:8		+0.08	−0.18	−0.00	−0.51	−0.58	−0.17	−0.05	−0.00	+0.01	+0.03	+0.04	+0.03	+0.03			
0.75:0.75	1:1		+0.12	+0.05		−0.08	−0.06	−0.04	−0.02	−0.01	−0.03	+0.08	+0.09	+0.08	+0.12	+0.16		
0.50:1.00	1:2		+0.11	+0.04		−0.12	−0.14	−0.14	−0.09	+0.01	+0.02	+0.04	+0.06	+0.06	+0.08	+0.10		
0.75:0.75	1:1		+0.13	+0.08		−0.02	−0.02	−0.02	−0.05	−0.01	−0.01				+0.05	+0.05	+0.14	
0.50:1.00	1:2		+0.16	+0.08		−0.05	−0.05	−0.03	−0.09	−0.00	−0.01				+0.03	+0.03	+0.11	
0.75:0.75	1:1		+0.13	+0.07			−0.01	−0.01	−0.06	−0.01	−0.02					+0.01	+0.03	+0.10
0.50:1.00	1:2		+0.14	+0.07			−0.06	−0.00	−0.09	−0.01	−0.01					+0.00	+0.02	+0.07

[a] Mixing ratios are defined as the quotient of the concentrations of the dodecanoate and the shorter amphiphile. [b] Spectral assignments of the C-4, C-5, C-6, and C-8 atoms of the dodecanoate chain were impossible because of overlapping signals, just as the carbon atoms corresponding to the vacancies in the table. About the C_α and C_β downfield effects of the dodecanoate surfactant in its mixed micelles, one can only speculate. Small deviations in the basicity may bring about these divergences on the $\Delta\delta$ values.

between *n*-alkanes and substituted derivatives over such long distances must be due to propagation of conformational disturbances caused by the substituents. Through-bond substituent effects are measurable only over small distances (maximally five bonds) and thus can hardly contribute. The fact that comparable shift differences are found in the inverse micelles and in the monomers indicates that conformational freedom is not impaired significantly in the latter.

Before discussing our results, we would like to describe our models of single and mixed micelles in some detail. In Figure 2a, the conventional picture of a micelle is presented. The rodlike shape of the surfactant chains is *not* meant to represent all-anti conformations. On a time-average basis, all monomers forming the micelle will be equivalent. This pertains also to the number and positions of gauche conformations.[30]

Recently, theoretical descriptions of micelles have been put forward by Dill and Flory[31] and Haan and Pratt.[32] These descriptions are based on a space-lattice model combined with Monte Carlo type simulations. In the former case, a cubic lattice is used without weighing different chain conformation according to their different energies. In the latter model a diamond lattice is combined with weighing based on a number of interaction energies between head groups and chains, both intra- and intermolecular. In these two respects, the Pratt model seems more realistic than the Flory model. Both descriptions share the disadvantage of not being able to accomodate chain conformations of the crank-shaft type as proposed many times for lipid bilayers[33] and polymer chains.[34] Simulations take these "kinks" also into consideration.[35]

With regard to single micelles, consideration of lattice models instead of conventional micelles would not influence the discussion of our NMR results.

(a) With complete filling of all outer lattice sites by chain segments (we would like to consider methylene groups rather than chain segments, as this would be more realistic from a practical point of view), the long amphiphile chains would have to assume lateral displacements (gauche conformations in reality) at or very close to the ω_s carbon atom. This leads to open lattice sites in the center of the micelle and, eventually, to smaller micelle diameters.[31] This conforms to the strategy taken by, e.g., Lindman et al.[18]

(b) Without complete filling,[31] open lattice sites are created between two adjacent long chains (between the ω_{s+1} carbons). These vacancies "move" with time over that complete layer,[31] thus creating larger *average* distances between two adjacent long chains. The same occurs for layers farther inside the micelle core, *but to a lesser extent.*

(c) Alternatively, the number of lattice sites within a given layer could be adapted for mixed micelles compared with the single micelles. So complete filling over all lattice sites is maintained. However, these sites have to be larger. This would lead to essentially the same consequences and conclusions as in consequence b.

We are thus left with two basically different possibilities: increased "folding" (with respect to their single micelles) of the long chains in the mixed micelles (see consequence a) or rather constant equilibria of the long chains (with respect to their single micelles) leading to larger average

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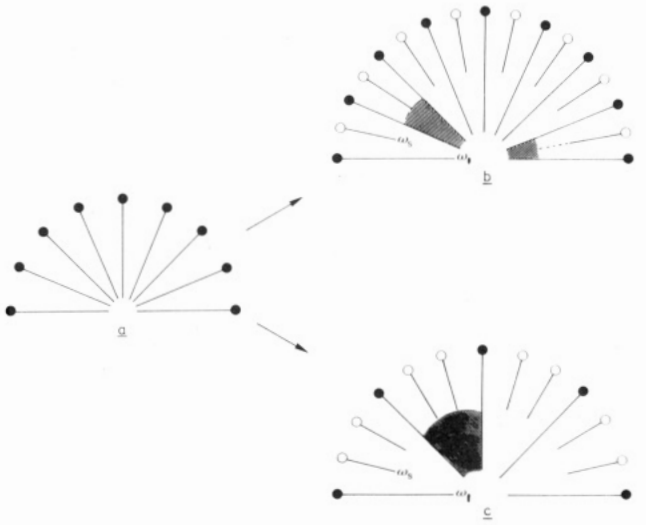
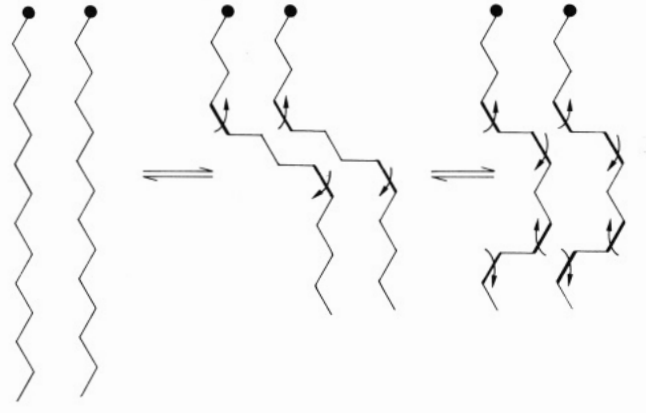


Figure 2. Model for mixed-micelle formation: (b) for the 1:1 mixing ratio; (c) for the 1:2 mixing ratio; the methyls of the long and short surfactants are denoted by ω_l and ω_s, respectively; intramicellar cavities (shaded areas) decrease in size upon elongation of the alkyl chain length of the short surfactant (b) and increase in size upon lowering the mixing ratio (c); open circles represent the head groups of the short amphiphiles and full circles represent the head groups of the long (dodecanoate) amphiphiles; dimensions are not correct. Rodlike shapes of the alkyl chains do *not* represent all-extended conformations. Only a schematic representation is offered. The actual conformational behavior can, in our opinion, be viewed for instance as follows



or any other conformation in which kinks are confined to certain nonneighbor layers. In reality, the assembled kinks will move in time about the longitudinal directions of the chains. Kinks in the shorter amphiphiles in mixed-micellar systems also have the above-mentioned requirements. The motional freedom in the ω_s–ω_l part of the longer chains may be larger.

interchain distances (see consequences b and c). Both processes would lead to increased shielding for the ω_s–ω_l parts of the long-chain surfactant molecules but with *different relative magnitudes*. Therefore, we fell that we are able to interpret our ^{13}C NMR results accordingly. This may be clarified below for a simple example. The shieldings, concomitant with gauche conformations in the alkyl chains, are given in Table III. These values are derived from literature data.[30,36-39] Shieldings arising from increased distances between the long amphiphile chains

TABLE III: ^{13}C NMR Shieldings (in ppm) That Gauche Conformers Induce on the Individual Carbons of the C_7–C_{12} Fragment of an All-Extended Dodecanoate Chain for Mixed Micelles of Heptanoate and Dodecanoate[a]

	C_{12}	C_{11}	C_{10}	C_9	C_8	C_7
I			−4	−2	−2	−4
II		−4	−2	−2	−4	
III	−5	−2	−2	−4		
calcd[b]	−0.07	−0.13	−0.20	−0.17	−0.10	−0.13

[a] From ref 36-39. I: gauche C_8–C_9; II: gauche C_9–C_{10}; III: gauche C_{10}–C_{11}. [b] As a typical example only decimal figures best resembling the experimental values (i.e., the 1:2 mixing ratio of Table I) are mentioned. For applied conformational ratios, see text.

should reflect the relative sensitivities or site factors of the methyl and the various methylene groups.[40,41] In practice this means that relatively large effects are observed for the methyl signals:[30] ca. 3 times larger than for methylene carbon signals. (For different methylenes, the variance of the extra interchain distances along the direction of the chains would have to be considered as well, in theory.)

Now, consider, e.g., the dodecanoate–heptanoate mixed micelle. At a mixing ratio of 1:2, the following shieldings were observed for the dodecanoate chain with respect to its single micelle (see Table II): −0.10 ppm for C-7; −0.22 ppm for C-9; −0.18 ppm for C-10; −0.13 ppm for C-11, and −0.07 ppm for C-12. In order to explain these changes as far as possible in terms of conformational changes, one would have to assume the following percentages of *extra* gauche conformers: 1.4% of III, 2.5% of II, and 3.2% of I (see Table III). Even with this conformational rearrangements, we did not succeed in reproducing the relative shift differences at C-9 and C-10 of the dodecanoate chain. Strictly speaking, such an explanation is not at odds with the Dill–Flory model since in the latter only relative positions of chain segments, each containing approximately 3.6 methylene groups, can be described. Also, the interchain distances between the dodecanoate amphiphiles may be only 10–30% larger than in the single micelles (sum of van der Waals radii). This suffices to cause sizable shielding.[46]

When the concentration of the short-chain amphiphile is raised, the changes described above will be larger, but we expect that the maximum effects remain on the same carbon atoms of the long chains. This is borne out by our results. In addition, the possibility of a maximum solubility of the shorter amphiphile into the longer detergent micelles has always to be taken into account.

The consequences of our model in terms of ^{13}C NMR chemical shift differences can be summarized as follows:

(i) Shielding effects are to be expected for the ω_l through the ω_{s+1} carbon atom of the dodecanoate chains, caused by a diminuation of deshielding van der Waals interactions and possible conformational changes. These effects will be enhanced upon solubilization of more short-chain amphiphile.

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(ii) The methyl carbons of the short amphiphiles will approach the ω_{s+1} carbon atom of the longer dodecanoate chain. Consequently, a maximal shielding upon mixed-micelle formation will appear at or near the ω_{s+2} carbon of the dodecanoate. There will be a gradient of shielding, decreasing toward the terminal methyl carbon of the long surfactant. The small shielding observed at ω-Me of the dodecanoate is to be ascribed to a slightly looser packing caused by the incorporation of the smaller surfactants near the polar head groups (see Figure 2b).

(iii) For the short-chain surfactant, deshielding with respect to its single micelle is to be expected because of two reasons. First, the chain is transferred from a medium consisting of short alkyl chains plus water to longer dodecanoate chains.[40-42] Second, the packing in the mixed micelle presumably will be tighter than in the short-chain single micelle, causing smaller interchain distances. If only solvent effects participate, the deshieldings should reproduce the respective site factors, thus leading to maximal differences for the methyl carbons.[30,40-42] If conformational changes contribute also, relative (de-)shieldings as indicated in Table III should occur.

The observed insensitivities of ^{13}C NMR chemical shifts of the dodecanoate micellar solution upon dilution over the concentration range (1.5–0.15 M) indicate that no changes in aggregation numbers and concomitant changes in chain conformations occur (vide supra). Therefore, the shift differences for the dodecanoate chains which occur upon formation of mixed micelles are to be ascribed exclusively to the inclusion of shorter chains or the replacement of C_{11} chains for shorter ones. Our measurements would probably not distinguish between these phenomena. However, the latter model was postulated by Brady et al.[43] for the aggregation of haloalkanes in *cis*-Decalin. Although the physical conditions for their experiments and ours differ considerably, a certain analogy between the two situations cannot be denied. However, the basic idea of the model presented here is not impaired by the uncertainty regarding inclusion vs. replacement.

The enclosure of hexanoate molecules in dodecanoate micelles causes a clear gradient of shielding along the long chains from the ω_1 methyl group toward the ω_s (i.e., C_6) methylene group. This indicates that changes in van der Waals interactions prevail over conformational changes. A measurable contribution of the latter effect can, however, not be ruled out. This is in contrast with mixed micelles of dodecanoate and heptanoate (or longer chains than the latter). We will return to this matter in more detail in a subsequent article, dealing with mixed micelles of dioctanoyl-L-α-lecithin and *n*-alkyltrimethylammonium bromides of different chain lengths.[11] To explain the shielding gradient comparable to that observed completely in terms of conformational changes, there has to be a large contribution of kinks around the ω_{1-4}–ω_{1-3} carbon–carbon bond, which seems very unlikely from a steric point of view. Furthermore, kinking around the ω_{1-1}–ω_{1-2} carbon–carbon bond would result in a large shielding at the ω_1 methyl group, which has not been observed. The occurence of chain separation between the dodecanoate chains in their mixed micelles is contrary to previously reported results on CTAB/TTAB mixed micelles and solubilization of 1-decanol in octanoate micelles.[17,18]

The values of the C_{11}/C_5 mixed micelles (see Table II) show increased shielding for the dodecanoate chain for the 2:1 through the 1:1 mixing ratio. At smaller mixing ratios the chemical shift differences remain fairly constant. This implies a maximal solubilization of ca. 1 equiv of hexanoate. At higher concentrations of the C_5 amphiphile mixed micelles 1:1 coexist with monomers of the hexanoate anion. Because of increased van der Waals solvent effects[30,42] upon solubilization, the hexanoate surfactants show deshieldings with regard to their reference solution. Deshieldings decrease upon lowering the mixing ratio. In the following scheme the observations are summarized:

$$\underset{\substack{\text{single}\\\text{micelles}}}{C_{11}} + \underset{\substack{\text{mon-}\\\text{omers}}}{aC_5} \xrightarrow{\text{mixing}} \underset{\substack{\text{1:1}\\\text{mixed}\\\text{micelle}}}{C_{11}/C_5} + \underset{\text{monomers}}{(a-1)C_5}$$

Comparing calculated (see Table III) and observed (see Table II) shieldings for the C_{11}/C_6 mixed micelles indeed indicates pronounced contributions of van der Waals solvent effects rather than conformational changes. Consequently, mainly chain separation causes the observed shieldings. Furthermore, the solubilization increases to ca. 2 equiv of the short amphiphile, as can be deduced from Table II. Monte Carlo calculations[44] reveal that the conformational free energy minimum of closely packed alkyl chains is proportional to the alkyl chain length. Under the assumption that head group/solvent and head group/head group interactions in single micelles of dodecanoate are comparable to their mixed micelles, only alkyl interchain interactions are important in the process of mixed-micelle formation. This explains an enhanced solubilization on increasing the alkyl chain length from six to seven carbon atoms. Dodecanoate shielding effects increase from the 2:1 through the 1:2 mixed micelle and reach a constant value at lower mixing ratios. The chemical shift changes of the heptanoate component upon increasing its percentage proceed analogously to those observed for the hexanoate detergents in their mixed micelles. Thus, for lower mixing ratios, it is obvious that 1:2 mixed micelles coexist with heptanoate monomers up to the 1:8 mixing ratio. At this ratio, the remaining heptanoate detergent molecules would form a solution with a concentration exceeding their cmc.[45] Consequently, heptanoate micelles would be formed. The heptanoate fragments would equilibrate between the mixed and the single micelles. For the dodecanoate fragments a new situation might occur, involving a statistical distribution over all available micelles. In this way, heptanoate micelles would be formed with one to two dodecanoate chains included. We like to speculate that for the latter chains the ninth and tenth carbon atoms would presumably be located in the center of the heptanoate micelle. In this region the average distance of both carbon atoms to other ones will be relatively large, causing smaller van der Waals interactions.

The ω_1 methyl effects are almost independent of the *n*-alkyl chain length of the solubilized partner as can be seen from the $\Delta\delta$ values of the mixed surfactants. The intermolecular ω_1 distances apparently depend only on the concentration of solubilized short-chain component. So at equal mixing ratios elongation of the chain length of the short amphiphile decreases the volume of the cavities between the C_{11} chains, as can be deduced from the decreasing shielding effects of the dodecanoate methylenes.

From the deshielding effects of the short-chain surfactants (C_5 up to and including C_9), it is clear that both the dodecanoate and the nonanoate in mixed micelles with C_{11} are in good agreement with previously observed solvent effects.[30,42] The octanoate and the heptanoate are borderline cases, while the hexanoate matches with the deshielding effects of solubilized pentanol in octanoate micelles.[17] These deshieldings are attributable to the extension of the hexanoate molecules as compared with their single-micellar solution.[17] This can be deduced by using the (opposite) values of Table III. Finally, the results of

CTAB/TTAB mixed micelles, studied by Lindman et al.,[18] correspond nicely with those of the 1:1 mixed micelles of decanoate and dodecanoate of this study. In retrospect, the CTAB/TTAB mixed micelles form a special case of the more general situation as presented.

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Mixed Micelles of Dioctanoyl-L-α-lecithin and Hydrocarbon Amphiphiles. Aspects of Fluidization of the Micellar Interior

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^{13}C NMR measurements of dioctanoyl-L-α-lecithin micellar solutions detect an almost complete visibility of the intrinsic magnetic nonequivalent behavior of the two lipid acyl chains. This is an extension of recently published observations. According to the latter, the chemical shift data are interpreted in terms of effectively different lengths of the *sn*-1 and *sn*-2 acyl chains due to a bending near the C_2 carbon atom of the *sn*-2 chain. Mixed micellar systems of DOPC and several *n*-alkyltrimethylammonium bromides show a difference in effective chain lengths of the constituent detergent types. ^{13}C NMR shieldings are observed for *n*-alkyl detergent fragments which are longer than both acyl chains of the lipid molecules. At an effective chain length difference of seven carbon atoms a sizeable contribution of *extra* gauche conformers with respect to their single micelles occur for these *n*-alkyl surfactants. For smaller differences *de*creasing van der Waals interactions (i.e., decreasing molecular packing) participate almost exclusively leading to chain separation. The deshieldings observed for the *n*-alkyl segments situated directly between neighboring lecithin chains indicate conformational changes toward more extended forms, as compared with their single micellar solutions, rather than *in*creasing van der Waals interactions. The lipid molecules do not undergo measurable conformational changes upon mixed micelle formation but are only subject to increased molecular packing. This may indicate that conformational changes are of minor importance for solubilizing micelle bound hydrocarbon-like compounds.

Introduction

The importance of micelle-forming phospholipids in biological membranes has often been stated, for example, as carriers for membrane bound enzymes[1,2] or trans-membrane transport-enhancing constituents within a bilayer membrane or particles stimulating cell division.[2] Conformational and motional behavior of head groups and acyl tails and perhaps also intermolecularly correlated molecular ordering[3] may well be of great interest for these important regulations.

Efforts have been made in the elucidation of the conformational structures of micelles of short-chain lecithins by means of different spectroscopic methods. By ^1H NMR the intrinsic nonequivalence of the *sn*-1 and *sn*-2 acyl chains of dioctanoylphosphatidylcholine and dipalmitoylphosphatidylcholine is visible.[4] In total, four separate α protons were observed; the remaining proton signals either overlapped or were not assigned. The explanation was given in terms of different conformational behaviors of both chains, as suggested earlier by Seelig et al.[6] who studied the gel phase and liquid crystalline phase of dipalmitoylphosphatidylethanolamine and dipalmitoylphosphatidylcholine. In this picture, the *sn*-1 and *sn*-2 chains run parallel to each other except for bending of the *sn*-2 chain near the C-2 carbon atom. This results in different effective chain lengths.[6]

Recently, also ^{13}C NMR spectra were published for dibutyryl-, dihexanoyl-, diheptanoyl-, and dioctanoylphosphatidylcholine.[5] Again, the intrinsic nonequivalent chains resulted in partially resolved spectra. In the present study ^{13}C NMR spectra with considerably better resolution will be presented; for all but two carbons separate signals were observed and assigned to the *sn*-1 and *sn*-2 chains. It will be shown that micelles of dioctanoyl-L-α-lecithin (DOPC) resemble mixed micelles of *n*-alkyl detergents bearing chains of nonequivalent lengths.

Increasing the effective chain length difference upon elongation of the *sn*-1 chain causes fluidization near the apolar middle region of the bilayer. Keough et al.[7] described this fluidization in terms of intermolecular ordering. Stümpel et al.[8] supposed intramolecular contributions like disordering conformational changes. However, van der Waals attractive interactions either were ignored[8]

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