Understanding enzymic binding affinity
Talhout, Reinskje

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CHAPTER 6

Aggregation Behaviour of p-n-Alkylbenzamidinium Chloride Surfactants

The aggregation behaviour of a novel class of surfactants, p-n-alkylbenzamidinium chlorides, has been investigated. The thermodynamics of aggregation of p-n-decylbenzamidinium chloride mixed with cationic and anionic cosurfactants has been studied using isothermal titration calorimetry. For mixtures of p-n-decylbenzamidinium chloride with n-alkyltrimethylammonium chlorides, the aggregation process is enthalpically more favourable than for the pure n-alkyltrimethylammonium chlorides, probably caused by diminished headgroup repulsion due to charge delocalisation in the amidinium headgroup. A critical aggregation concentration between 3 and 4 mM has been extrapolated for p-n-decylbenzamidinium chloride at 40 °C, around two times lower than that of similar surfactants without charge delocalisation in the headgroup and well comparable to that of similar surfactants with charge delocalisation in the headgroup. In mixtures of p-n-decylbenzamidinium chloride with either sodium n-alkylsulfates or sodium dodecylbenzenesulfonate, evidence is found for the formation of bilayer aggregates by the pseudo-double-tailed catanionic surfactants constituted of p-n-decylbenzamidinium and the anionic surfactant. These aggregates are solubilised to mixed micelles by excess free anionic surfactant at the measured cac.

"EINSTWEILN SEIEN HIER EINIGE SEHR GENAUE DATEN ANGEFÜHRT, DIE IM GEGENSATZ ZU DER ANSICHT KRAFFTS UNZWEIFELHAFT BEWEISEN, DASS DIE NORMALE SEIFEN IN KONZENTRIERTER LÖSUNG KEINE KOLLOIDE SIND."


"... THE CONDUCTIVITY CANNOT BE WHOLLY ASCRIBED TO SIMPLE PALMITATE IONS. THE SUGGESTION WE MADE IS THAT WE HAVE A NEW TYPE OF AGGREGATE OR MICELLE THE MOBILITY OF WHICH, ..., IS COMPARABLE WITH THAT OF A TRUE ION."

6.1 Introduction

Surfactants, short for surface active agents, are molecules that contain both hydrophilic and hydrophobic parts, which induces a spatial separation of their solvation properties. Their hydrophilic headgroups tend to be strongly hydrated, whereas their tails are sufficiently hydrophobic to cluster (Section 1.1.6). Therefore, this amphiphilic nature leads to aggregation of surfactants in water above a certain concentration. The type of aggregate that is formed and the concentration at which aggregation starts, the so-called critical aggregation concentration (cac), depend on the specific structural properties of the surfactant, the temperature and the composition of the solution. Often, different types of aggregates are found in different concentration ranges.

The molecular geometry of the surfactant determines to a large extent the type of aggregate that is formed in aqueous solution. An elegant concept, the so-called critical packing parameter \( P \), relating surfactant geometry and aggregate morphology, has been proposed by Ninham and Israelachvili:

\[
P = -\frac{V}{a_0 \cdot l}
\]  

(6.1)

where \( V \) is the volume of the hydrocarbon chain(s) of the surfactant, \( a_0 \) the mean effective cross-sectional headgroup area and \( l \) the length of the hydrocarbon chain in the all-trans conformation. The more bulky the hydrophobic part of a surfactant is in comparison with the effective cross-sectional headgroup area, the larger the packing parameter. The formed aggregate can then have less curvature in order to still be capable to accommodate the surfactants constituting it and will thus have a larger minimal critical radius. Therefore, in general it is the case that single-tailed unbranched surfactants form micelles, whereas double-tailed surfactants form aggregates consisting of bilayers, such as vesicles, depending on the specific structure of the surfactant. Micelles are dynamic, thermodynamically stable aggregates, whereas bilayer aggregates are more rigid and usually thermodynamically metastable, with cac’s typically up to four orders of magnitude lower than those of micelles.

Another phenomenon influencing the aggregation of surfactants is their characteristic solubility behaviour: the solubility is low at low temperatures, but increases dramatically around the Krafft-temperature \( T_K \), the temperature at which the solubility of the surfactant starts to exceed the cac. \( T_K \) is strongly dependent on the type of counterion and within a homologous series of surfactants, it increases with increasing chain length.

The properties of mixed surfactant solutions are often significantly dissimilar from those of the pure surfactant solutions of which they are composed. Whereas nonionic surfactants tend to mix ideally, large departures from ideal behaviour, either synergistically or antagonistically, can be expected for mixtures with specific interactions between the constituent surfactants. Large synergistic effects are encountered in mixtures of cationic and anionic surfactants, where the electrostatic attraction between the headgroups of the different surfactants diminishes the total
headgroup repulsion.\textsuperscript{12,13} This attraction effectively yields a pseudo-double-tailed catanionic surfactant with a much larger packing parameter than its single-tailed components. As a consequence, the morphology of the aggregates formed will be quite different from that of its components and the cac will be dramatically lower;\textsuperscript{11-13} for instance, vesicles may be formed instead of micelles. On the other hand, large antagonistic effects are reported for mixtures of surfactants with hydrocarbon tails and surfactants with fluorocarbon tails, resulting in a much higher cac than either of the constituting surfactants.\textsuperscript{10,11}

The cac of a surfactant mixture can be described by Equation 6.2, that has been derived using regular solution theory in the context of the phase separation model:\textsuperscript{9}

\[
\frac{1}{\text{cac}_{\text{mix}}} = \frac{\alpha}{f_1 \cdot \text{cac}_1} + \frac{(1-\alpha)}{f_2 \cdot \text{cac}_2}
\]  

(6.2)

where cac\textsubscript{mix}, cac\textsubscript{1} and cac\textsubscript{2} are the critical aggregation concentrations of, respectively, the mixture, pure surfactant 1 and pure surfactant 2, \(\alpha\) is the mole fraction of surfactant 1 in the surfactant mixture, and \(f_1\) and \(f_2\) are the micellar activity coefficients of surfactants 1 and 2, respectively. \(f_1\) and \(f_2\) are empirical parameters that are obtained by fitting of the equation to experimental cac data and reflect both specific interactions between surfactants 1 and 2 and the optimal micellar composition of each surfactant. In the ideal case, where specific interactions are absent, \(f_1 = f_2 = 1\), whereas \(f\) will be small for synergistic and large for antagonistic specific interactions.

Mechanistically, the aggregation process is a sum of attractive interactions involving the hydrophobic tails and repulsive interactions between the hydrophilic headgroups. The latter can, in case of ionic surfactants, be separated into an electrostatic and a non-electrostatic contribution.\textsuperscript{5,14} The electrostatic contribution is endothermic and increases the cac compared to nonionic surfactants due to the formation of an electrical double layer.\textsuperscript{14} Counterions are able to screen this electrostatic repulsion to an extent that depends on both the specific type and the concentration of the counterion.\textsuperscript{2} The endothermic non-electrostatic contribution includes the repulsion due to the hydration shell of the headgroup. The hydrophobic contribution is very temperature-dependent, as reflected in a large and negative heat capacity change \(\Delta C_p\) upon aggregation. The temperature at which the enthalpy of aggregation is zero is defined as \(T_H\) and depends strongly on the chain length. \(\Delta \Delta C_p\), the change in heat capacity upon aggregation per methylene group, amounts, depending on the specific system studied, to around \(-50\) J mol\(^{-1}\) K\(^{-1}\).\textsuperscript{5,14-16}

The relation between the different thermodynamic parameters is given by:

\[
\Delta G = \Delta H - T\Delta S = (1 + \beta)RT \ln \text{cac}
\]  

(6.3)

where \(\Delta G\) is the Gibbs energy of aggregation, \(\Delta H\) is the enthalpy of aggregation, \(\Delta S\) is the entropy of aggregation, \(T\) is the temperature in K, \(\beta\) is the degree of counterion binding and the cac is expressed in mole fraction of surfactant. The right hand side of Equation 6.3, that relates the cac and \(\beta\) to \(\Delta G\), can be derived using the equilibrium constant from the mass action model\textsuperscript{3,17} for surfactant aggregation. In the alternative phase separation model,\textsuperscript{3,17} where the aggregate is considered to be a
separate phase consisting of pure surfactant, it is usually assumed that $\beta$ is 1, or, in other words, that 100% of the counterions is bound to the aggregate.

The cac and $\Delta H$ of aggregation can be conveniently determined using isothermal titration calorimetry (ITC) by titrating a concentrated surfactant solution (concentration larger than the cac) in water. The process monitored is the breakdown of the surfactant aggregates until the cac is reached in the measuring cell. The ideal type of enthalpogram is an S-curve where all injections before the cac have an (almost) constant heat effect, and after the cac level off rather quickly to a constant dilution value. In this case, determination of the cac and $\Delta H$ of aggregation is quite straightforward. The cac corresponds to the break in the enthalpogram, which is more easily quantified by plotting cumulative enthalpies against the concentration of surfactant. $\Delta H$ of deaggregation is the difference between the y-values of the horizontal lines that can be drawn through the two horizontal parts of the enthalpogram and $\Delta H$ of aggregation is the opposite of this process.$^{5,17}$

However, this ideal behaviour is only encountered when the observed heat per injection is sufficiently large to mask nonideal effects. If the cac is relatively high or if the measurement is performed around $T_H$, where aggregation is mainly entropy-driven, the observed heat per injection may be only very modest. These circumstances lead to nonideal effects showing up prominently in the resulting enthalpogram, which is then characterised by a positive slope before the break is reached. Although this slope is also present in the ideal-type enthalpogram, in that case it is hardly visible due to the relative small magnitude with respect to the magnitude of the total heat effect.$^5$

$p$-Substituted benzamidinium chlorides in water are hydrotropes.$^{18}$ Hydrotropes are amphiphiles with a hydrophobic moiety too small to induce micelle formation.$^{19,20}$ At high concentrations, self-association does occur to yield aggregates that are probably open and planar instead of the comparatively well-defined, closed structures formed by surfactants. Upon increasing the tail length, a gradual transition occurs between hydrotropes and surfactants.$^{19}$ In this study,$^1$ we investigated the aggregation behaviour of a novel class of surfactants, $p$-$n$-alkylbenzamidinium chlorides, in water. Two surfactants, differing in their tail length, were synthesised as outlined in Scheme 6.1: $p$-$n$-decybenzamidinium chloride ($C_{10}$Benz) and $p$-$n$-dodecybenzamidinium chloride ($C_{12}$Benz). In order to overcome solubility problems, $C_{10}$Benz has been mixed with both cationic and anionic surfactants. In both cases, the cosurfactants were selected for their similarity to $C_{10}$Benz. For these mixtures, the cac and $\Delta H$ were determined with ITC.
6.2 Structural and Physical Properties of \( p-n \)-Alkylbenzamidinium Surfactants

\( p-n \)-Alkylbenzamidinium surfactants possess interesting structural properties that differ from those of conventional cationic surfactants. An angle of 36.6° is reported between the plane of the amidinium group and the plane of the phenyl ring for the crystal structure of solid benzamidinium chloride.\(^{21}\) This angle is supposed to prevent conjugation between the two \( \pi \) systems. Although a molecule in the crystal structure is not the same as one in the aqueous phase, we assume that, due to the reduced conjugation between the amidinium group and the phenyl ring, the phenyl ring of \( \text{C}_{10}\text{Benz} \) is not part of the headgroup, but of the tail.

The phenyl ring in the tail introduces both the possibility of \( \pi-\pi \)-stacking between surfactants and a bending of the tail. It is expected that \( \pi-\pi \)-stacking will decrease the cac, whereas bending of the tail will increase the cac. To understand the influence of the phenyl ring on the cac, the cacs and the tail lengths of surfactants containing a phenyl ring in their tail have been compared to those of their aliphatic counterparts, e.g. \( p-n \)-alkylbenzenesulfonates and \( n \)-alkylsulfonates. Comparison of the cacs yielded the rule of thumb that addition of a phenyl ring to a tail leads to a lowering of the cac corresponding to that for 3.5 methylene units.\(^2\) Comparison of the tail lengths, calculated for several types of surfactants using the ACD/3D program of ACD/Labs\(^{22}\) (results not shown), showed that introduction of a phenyl ring into a tail leads to an increase of the tail length corresponding to three to four methylene groups. Since these considerations show that the cacs of surfactants with
aromatic and aliphatic tails of similar tail lengths are similar, it seems that structural changes occurring upon introducing a phenyl ring into the tail of the surfactant compensate each other with respect to the cac. Therefore, the tail of C\textsubscript{10}Benz may be regarded equivalent to a linear alkyl tail of approximately 13.5 carbon atoms long.

The charge of the amidinium headgroup, formally the nitrogen analogue of a carboxylate group\textsuperscript{23} is delocalised over the amidinium carbon and both amidinium nitrogens. This decreases the charge density in the headgroup as compared to e.g. ammonium\textsuperscript{24} which may also lead to a less extensive hydration of the headgroup. Since headgroup repulsion is largely a combined electrostatic and hydration effect, it may well be that this is diminished in amidinium surfactants, as compared to surfactants were such charge delocalisation in the headgroup is not possible.

The Krafft temperatures of C\textsubscript{10}Benz and C\textsubscript{12}Benz have been measured by monitoring the temperature-dependence of the transmission at 400 nm of a stirred 10 mM aqueous solution. In Figure 6.1, this temperature-dependence upon both heating and cooling is shown for C\textsubscript{12}Benz. The temperatures at which the transmission is 50% are indicated with dotted lines. It is obvious that this temperature is higher upon heating the solution than upon cooling the solution. The temperature at which the transmission is 50% upon heating was taken as the Krafft temperature and amounts to 64 °C for C\textsubscript{12}Benz and to 54 °C for C\textsubscript{10}Benz.

![Figure 6.1. Temperature-dependence of the transmission at 400 nm upon heating and cooling of a 10 mM aqueous solution of C\textsubscript{12}Benz.](image-url)
Unfortunately, these temperatures are, from a practical point of view, unconveniently high, especially in case of C_{12}Benz. Therefore we decided to only study the thermodynamics of aggregation of C_{10}Benz. As the Krafft temperature of C_{10}Benz is 54 °C, and, on cooling, precipitation will start around 49 °C, measurements can only be performed above the latter temperature. Also, due to the practical reason that the injection syringe of the Microcal titration calorimeter is not thermostatted but adopts the temperature of the surroundings, it was not possible to perform titrations at this minimal required temperature of 49 °C or higher, because crystallisation would occur in the syringe in that case. Therefore, isothermal titration calorimetry measurements on pure C_{10}Benz, are, due to practical problems, not feasible at any temperature. To retrieve calorimetric information on this surfactant, we decided to study the properties of mixed systems of C_{10}Benz with both cationic and anionic cosurfactants.

6.3 Thermodynamics of Aggregation of Mixtures of \( p-n \)-Decylbenzamidinium Chloride with Cationic Surfactants

The properties of mixed systems of C_{10}Benz with cationic cosurfactants were studied. First, mixtures of C_{10}Benz and \( n \)-alkyltrimethylammonium chlorides were examined. In order to find out which \( n \)-alkyltrimethylammonium chloride (C\( _n \)TAC) is, with respect to tail length, similar to C_{10}Benz, the structures of these surfactants were geometry-optimised with the ACD/3D program of ACD/Labs\(^{22} \) and the following distances, corresponding to the labels in Scheme 6.2, were calculated (Table 6.1): \( C_\alpha -C_\omega \), \( N^+ -C_\omega \), \( C^+ -C_\omega \), \( N_1 -C_\omega \) and \( N_2 -C_\omega \). Since the charge of the C_{10}Benz amidinium group is delocalised over the amidinium carbon and both amidinium nitrogens, both \( C^+ -C_\omega \) and \( N_1 -C_\omega /N_2 -C_\omega \) are taken into account. It was found that the length of the C_{10}Benz tail is in between the tails of \( n \)-tridecytrimethylammonium chloride (C_{13}TAC) and \( n \)-tetradecyltrimethylammonium chloride (C_{14}TAC).\(^{25} \)

![Scheme 6.2. Structures of C\( _n \)TAC\(^+ \) (left hand side) and C_{10}Benz\(^+ \) (right hand side), with labels to define the distances mentioned in the text and listed in Table 6.1.](image)
Table 6.1. Distances, corresponding to the labels in Scheme 6.2, as calculated with ACD/3D, in C\textsubscript{13}TAC, C\textsubscript{10}Benz and C\textsubscript{14}TAC.

<table>
<thead>
<tr>
<th>distance (Å) between</th>
<th>C\textsubscript{13}TAC</th>
<th>C\textsubscript{10}Benz</th>
<th>C\textsubscript{14}TAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>C\textsubscript{α}-C\textsubscript{ω}</td>
<td>14.98</td>
<td>14.99</td>
<td>16.23</td>
</tr>
<tr>
<td>N\textsuperscript{+}-C\textsubscript{ω}</td>
<td>16.24</td>
<td>-</td>
<td>17.48</td>
</tr>
<tr>
<td>C\textsuperscript{+}-C\textsubscript{ω}</td>
<td>-</td>
<td>16.43</td>
<td>-</td>
</tr>
<tr>
<td>N\textsubscript{1}-C\textsubscript{ω}</td>
<td>-</td>
<td>16.15</td>
<td>-</td>
</tr>
<tr>
<td>N\textsubscript{2}-C\textsubscript{ω}</td>
<td>-</td>
<td>17.03</td>
<td>-</td>
</tr>
</tbody>
</table>

In order to visualise the similarity in tail length, but differences in headgroup and bending of the tail, 3D pictures of C\textsubscript{13}TAC, C\textsubscript{10}Benz and C\textsubscript{14}TAC are shown in Figure 6.2. Since n-tridecyltrimethylammonium is not commercially available with any counterion, C\textsubscript{14}TAC was chosen as a cosurfactant. The tail of this surfactant is slightly longer than that of C\textsubscript{10}Benz. The fraction of C\textsubscript{14}TAC in the surfactant mixture, α(C\textsubscript{14}TAC), ranged from 0.7 to 1; at lower ratios, C\textsubscript{10}Benz could not be fully solubilised.

Figure 6.2. 3D structures of C\textsubscript{14}TAC (left hand side), C\textsubscript{10}Benz (middle) and C\textsubscript{13}TAC (right hand side), generated with ACD/3D.
Titration of C\textsubscript{14}TAC into water yields an unusual form of the raw data and the enthalpogram. Figure 6.3A shows the raw data for titration of C\textsubscript{14}TAC into water at 25 °C. The first five injections yield exothermic raw data peaks, followed by five injections were the raw data peaks of each single injection change from endothermic to exothermic within the same peak; all following peaks are completely endothermic. Figure 6.3B shows the accompanying enthalpogram, where the heat effect changes from exothermic to endothermic with increasing concentration of C\textsubscript{14}TAC.

In contrast, titration of \textit{n}-tetradecyltrimethylammonium bromide (C\textsubscript{14}TAB, results not shown) into water at 25 °C yielded an ideal endothermic S-curve, indicating that the counter ion effect is very strong in the thermodynamics of aggregation of tetradecylammonium salts. To the best of our knowledge, a titration calorimetry study has never been performed with C\textsubscript{14}TAC. However, titrations of \textit{n}-dodecyltrimethylammonium chloride (C\textsubscript{12}TAC) and \textit{n}-dodecyltrimethylammonium bromide (C\textsubscript{12}TAB) into water at 25 and 40 °C also show a very strong counterion effect.\textsuperscript{26,27} At both temperatures, the enthalpy of aggregation is more exothermic for C\textsubscript{12}TAB than for C\textsubscript{12}TAC. From the reported enthalpies of aggregation it can be calculated that the heat capacity change upon aggregation is stronger negative for C\textsubscript{12}TAC than for C\textsubscript{12}TAB.

Since the the main contribution to a negative value of the heat capacity change upon aggregation stems from the burial of nonpolar surface area from water (Section 1.1.6), this effect can be attributed to a less extensive surfactant tail dehydration in case of micelle formation by C\textsubscript{12}TAC.
H-NMR and $^{13}$C-NMR measurements on the downfield shift of the first two methylene groups of the surfactant tail indeed showed that the core of micelles formed by C$_{12}$TAB is more extensively hydrated than that of those formed by C$_{12}$TAC, whereas their monomers are hydrated to a similar extent.$^{26,27}$

The form of the enthalpogram in Figure 6.3 can be rationalised as follows. For titration experiments characterised by a relatively small heat effect per injection, the resulting enthalpogram will be characterised by a visible slope before the break due to nonideal effects showing up prominently (Section 6.1). Enthalpograms of the type depicted in Figure 6.3 have also been reported for a temperature-dependent study of the titration of $n$-decylpyridinium chloride and $n$-dodecylpyridinium chloride into water at temperatures around $T_{\text{H}}$. The authors discuss this type of plot in terms of an endothermic maximum in the region of the cac. This maximum is found at a concentration lower than the cac when the cac is relatively high, as in case of $n$-decylpyridinium chloride with a cac of 80 mM at 45 °C and at a concentration higher than the cac when the cac is relatively low, as in case of $n$-dodecylpyridinium chloride with a cac of 12.4 mM at 30 °C. This endothermic maximum implies that aggregation becomes progressively more favourable when the surfactant concentration in the cell increases, since deaggregation becomes progressively less favourable.

Interestingly, when $n$-decylpyridinium chloride and $n$-dodecylpyridinium chloride are titrated into a 100 mM sodium chloride solution, the heat effect per injection remains the same. However, the endothermic maximum is found at a lower concentration, and, in case of $n$-dodecylpyridinium chloride, even shifts to below the cac. Because of the headgroup screening due to increased counterion binding, the cacs are lowered to respectively 62.5 and 6.5 mM. It is therefore tempting to conclude that the endothermic maximum results from a more effective screening of the headgroup charge by the chloride ions due to the increased ionic strength upon increasing the surfactant concentration in the cell. When approaching the cac, the repulsion between the headgroups becomes progressively more compensated by the attraction between the tails and therefore the enthalpy of aggregation becomes progressively more favourable. The observation that this maximum is found at a concentration lower than the cac when the cac is relatively high and at a concentration higher than the cac when the cac is relatively low, can perhaps be explained by the fact that in case of a high cac, the ionic strength of Cl$^-$ at the cac is higher than for surfactants with lower cacs. This indicates that the maximum headgroup charge screening has already been reached below the cac. In case of a low cac, the ionic strength of Cl$^-$ necessary for maximum headgroup screening has not yet been reached at the cac.

In conclusion, Figure 6.3 is characterised by a small heat effect, which leads to nonideality effects being prominently visible. The first few injections are exothermic, but due to the slope before the cac a crossing between exo- and endothermicity is encountered. The effect that within one injection, the resulting raw data peak changes from endothermic to exothermic, is an effect often encountered for peaks on the boundary between a crossing from an exothermic to an endothermic effect or vice versa.$^{28-30}$ Since the cac is relatively low, namely 6.5 mM, the endothermic maximum is observed at a concentration higher than the cac, namely at approximately 7.5 mM.
Although efforts have been made to design equations to fit these nonideal enthalpograms, they remain difficult to interpret in comparison to enthalpograms corresponding to deaggregations accompanied by a larger heat effect, where nonideal effects are masked. In Figure 6.4, showing the enthalpograms of titrations of C$_{14}$TAC into water at 25, 30 and 40 °C, it is clear that the titration performed at 25 °C is around $T_H$. Deaggregation is characterised by a large, positive heat capacity change due to the strong hydrophobic interactions between the surfactant tails. Therefore, deaggregation is more endothermic at higher temperatures; at 40 °C, the enthalpogram is very close to the ideal type. Since we are primarily interested in comparing the values of the cac and $\Delta H$ for the different ratios of C$_{14}$TAC and C$_{10}$Benz, we decided to perform titration experiments at 40 °C.

The measured cac and $\Delta H$ of the mixtures, as well as the $\Delta G$ and $T\Delta S$ calculated from these data using Equation 6.3, are listed in Table 6.2. For the calculation of $\Delta G$, a value for $\beta$ of 1, corresponding to 100% counterion binding, was assumed according to the phase separation model. This value is, most probably, too high, yielding an absolute value for $\Delta G$ that is too large, but within this mixture series, assuming not too large differences between the values of $\beta$ for the different ratios, the trend in $\Delta G$ will be meaningful.
Table 6.2. Thermodynamic parameters of aggregation of C_{14}TAC/C_{10}Benz mixtures at 40 °C.

<table>
<thead>
<tr>
<th>α(C_{14}TAC)</th>
<th>cac (mM)</th>
<th>ΔG (kJ mol^{-1})</th>
<th>ΔH (kJ mol^{-1})</th>
<th>TΔS (kJ mol^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.35</td>
<td>-47.3</td>
<td>-7.61</td>
<td>39.6</td>
</tr>
<tr>
<td>0.897</td>
<td>5.9</td>
<td>-47.6</td>
<td>-8.3</td>
<td>39.4</td>
</tr>
<tr>
<td>0.799</td>
<td>5.7</td>
<td>-47.8</td>
<td>-9.5</td>
<td>38.4</td>
</tr>
<tr>
<td>0.752</td>
<td>5.5</td>
<td>-48.0</td>
<td>-10.2</td>
<td>37.8</td>
</tr>
<tr>
<td>0.695</td>
<td>4.9</td>
<td>-48.6</td>
<td>-11.4</td>
<td>37.2</td>
</tr>
</tbody>
</table>

It is remarkable that upon addition of C_{10}Benz, a surfactant with a shorter tail length than C_{14}TAC, the cac of the mixture is lowered in comparison to that of pure C_{14}TAC (Table 6.2). In Figure 6.5, the cac of the mixture is plotted against the fraction of C_{14}TAC in the surfactant mixture, α(C_{14}TAC). Because C_{10}Benz and C_{14}TAC are both cationic surfactants with an linear alkyl tail of similar length (Table 6.1), strong specific interactions between both surfactants are not likely in these mixtures and therefore large departures from ideal mixing behaviour are not expected. Thus, despite the long extrapolation, a reasonable approximation to fit the data in Figure 6.5 is the ideal case of Equation 6.2, with both $f_1$ and $f_2$ equal to 1; this fit yields the cac for $α(C_{14}TAC) = 0$.

Figure 6.5. Plot of cmc mix against $α(C_{14}TAC)$ at 40 °C. The lines are fitted using Equation 6.2; the solid line is obtained with the data point $α(C_{14}TAC) = 0.695$ excluded, the dotted line with this point included.
Since the data point for $\alpha(C_{14}TAC) = 0.695$ is not in line with the trend of the other data points, probably due to the fact that this fraction of $C_{14}TAC$ is close to the amount necessary to solubilise $C_{10}Benz$, two different fits were performed. The dotted line in Figure 6.5 represents the fit including the data point $\alpha(C_{14}TAC) = 0.695$, yielding a value for the cac of 3.7 mM for $\alpha(C_{14}TAC) = 0$, whereas the solid line represents the fit excluding this data point, yielding a value of 3.9 mM. The latter seems to fit the data points reasonably, thereby validating the approximation of ideal mixing behaviour. Although the fitted cac's for $\alpha(C_{14}TAC) = 0$ do not correspond to a real physical situation, since precipitation occurs in solutions with $\alpha(C_{14}TAC) < 0.7$ due to the high Krafft temperature of $C_{10}Benz$, it does give some indication of the interactions occurring in a hypothetical aggregate consisting of pure $C_{10}Benz$ at 40 °C and an aggregate at temperatures above the Krafft temperature.

In order to compare this cac to those of similar surfactants with a phenyl group between the headgroup and the tail, one has to turn to anionic surfactants, since, to the best of our knowledge, information on the cac of that type of cationic surfactants is not available. Perhaps the best comparison between $C_{10}Benz$ and an anionic surfactant is that with sodium $p-n$-decylbenzoate. Although the cac of this compound has not been reported in literature, those of $p-n$-hexyl- and $p-n$-octylbenzoate have been reported$^{32}$ and amount to, respectively, 48 mM at 25 °C and 13 mM at 35 °C. The cacs for aliphatic, linear chain sodium alkanoates $RCOO\cdot Na^+$ at 60 °C for R is 9, 10, 11, 12, 13 and 14, amount to, respectively, 106, 38, 31, 12, 9 and 3.8 mM.$^{33}$ When these values are compared to the cacs of sodium $p-n$-hexyl- and $p-n$-octylbenzoate stated above, it is clear that, for alkanoates, regarding the cac, the phenyl group is equivalent to slightly less than four methylene units. This is in accord with the rule of thumb mentioned in the introduction. Following this trend, a value of approximately 4 mM can be expected for the cac of sodium $p-n$-decylbenzoate. Another anionic surfactant to which $C_{10}Benz$ could be compared is sodium $p-n$-decylbenzenesulfonate, for which a cac of 3.98 mM at 50 °C has been reported.$^{8}$ Both values are similar to the value found for $C_{10}Benz$.

It is interesting to compare the cacs of these surfactants with the possibility of charge delocalisation over the headgroup to the cacs of surfactants without this possibility, such as $n$-alkyltrimethylammonium chlorides. The length of the $C_{10}Benz$ chain is in between that of $C_{14}TAC$ and $C_{13}TAC$ (Table 6.1). The cac of $C_{14}TAC$ is 6.35 mM (Table 6.2) and that of $C_{12}TAC$ is 21 mM$^{26,27}$ the cac of $C_{13}TAC$ (no literature value found), will be in between these values. These values are significantly higher than those of the surfactants described above for which headgroup charge delocalisation is possible. Therefore, it seems likely that headgroup charge delocalisation is a structural factor that decreases the cac of a surfactant.

In Figure 6.6, $\Delta H$ and $-T\Delta S$ are plotted against $\alpha(C_{14}TAC)$. The lowering of the cac upon addition of $C_{10}Benz$, reflected in a more favourable $\Delta G$ of aggregation, is an enthalpic effect. The more favourable enthalpy of aggregation is partly compensated by a less favourable entropy of aggregation. By applying a linear fit to the data points, with the deviant data point $\alpha(C_{14}TAC) = 0.695$ included in the dotted line and excluded in the solid line, values for $\Delta H$ for $\alpha(C_{14}TAC) = 0$ of, respectively, $-19.5$ and $-17.8$ kJ mol$^{-1}$, and of $T\Delta S$ for $\alpha(C_{14}TAC) = 0$ of, respectively, 31.7 and 32.5 kJ mol$^{-1}$ were obtained.
The lowering of the cac by a more exothermic $\Delta H$ upon addition of C$_{10}$Benz to C$_{14}$TAC could be caused by the charge delocalisation in the headgroup of C$_{10}$Benz. As argued in Section 6.2, this might reduce the endothermic headgroup repulsion. The entropy simultaneously becomes less favourable because of enthalpy-entropy compensation,\textsuperscript{34-36} a phenomenon that has been explained in detail in Section 1.1.7.

In order to study the influence of a longer tail, $n$-hexadecyltrimethylammonium chloride (C$_{16}$TAC) was studied as cosurfactant. In Table 6.3, the thermodynamic parameters of aggregation of pure $n$-hexadecyltrimethylammonium chloride (C$_{16}$TAC) and of a mixture of C$_{16}$TAC and C$_{10}$Benz are listed. The addition of C$_{10}$Benz to C$_{16}$TAC slightly increases the cac due to the fact that C$_{10}$Benz has a higher cac than C$_{16}$TAC. As was also the case for C$_{14}$TAC, $\Delta H$ is more favourable in the mixture, but for C$_{16}$TAC this is outweighed by a less favourable $T\Delta S$.

\begin{table}[h]
\centering
\caption{Thermodynamic parameters of aggregation of C$_{16}$TAC/C$_{10}$Benz mixtures at 40 °C.}
\begin{tabular}{cccc}
\hline
$\alpha$(C$_{16}$TAC) & cac & $\Delta G$ & $\Delta H$ & $T\Delta S$ \\
& (mM) & (kJ mol$^{-1}$) & (kJ mol$^{-1}$) & (kJ mol$^{-1}$) \\
\hline
1 & 1.59 & -54.5 & -11.6 & 42.9 \\
0.701 & 1.85 & -53.7 & -12.8 & 40.9 \\
\hline
\end{tabular}
\end{table}
In conclusion, addition of C_{10}Benz as a cosurfactant to both C_{14}TAC and C_{16}TAC makes the aggregation process enthalpically more favourable. In case of addition to C_{14}TAC, a surfactant of similar tail length, this outweighs the less favourable entropy, resulting in a more favourable Gibbs energy of aggregation. On the other hand, in case of addition to the longer-tailed C_{16}TAC, the less favourable entropy outweighs the more favourable enthalpy, resulting in a less favourable Gibbs energy of aggregation.

6.4 Thermodynamics of Aggregation of Mixtures of p-n-Decylbenzamidinium Chloride with Anionic Surfactants

The properties of mixed systems of C_{10}Benz with anionic cosurfactants were studied as well. Because the amidinium headgroup is the nitrogen analogue of a carboxylate group, both having the same type of charge delocalisation, it was first tried to mix C_{10}Benz with alkanoates. Tetradecanoate is, with respect to chain length, most similar to C_{10}Benz (calculated with ACD/Labs). Since sodium tetradecanoate has a Krafft temperature of 43.9 °C, which makes it unsuitable for use as cosurfactant for C_{10}Benz, other counterions were tried. From tetradecanoic acid, different tetradecanoate salts in solution were prepared by adding hydroxide solutions containing the appropriate counterion. Whereas the lithium salt has a higher T_K than the sodium salt, the potassium and the cesium salt have a lower T_K. In the latter cases, a T_K below room temperature can be achieved if excess salt is added to increase the pH to, respectively, 12 and 10. In mixtures with C_{10}Benz, these values for the pH result in a small fraction of deprotonated C_{10}Benz. However, when 10 mol% of C_{10}Benz was added to the cesium tetradecanoate solution at pH 12, C_{10}Benz was not solubilised, even when more CeOH was added to increase the pH and further lower the T_K. Since the T_K of sodium p-n-decylbenzoate will be around 40 °C, it was decided, based on the results of sodium tetradecanoate, not to try this commercially available, but very expensive close analogue of C_{10}Benz.

In order to circumvent the Krafft temperature problems, the shorter tail length surfactant dodecanoate was tried, for which the sodium salt has a T_K of 28.1 °C. The cesium salt was prepared from dodecanoic acid and was found to have a T_K below room temperature without the necessity of adding excess of CeOH. However, 10 mol% C_{10}Benz could not be solubilised, even upon addition of excess of CeOH. It could be that in this case the problem is not the solubility of the anionic, but the solubilising potential of this shorter-tailed surfactant. In conclusion, alkanoates are not suitable as cosurfactants for C_{10}Benz.
Next, two sodium \( n \)-alkylsulfates (Na\( C_n \)SO\(_4\)), namely sodium \( n \)-dodecylsulfate (Na\( C_{12} \)SO\(_4\)) and sodium \( n \)-tridecylsulfate (Na\( C_{13} \)SO\(_4\)) were mixed with C\(_{10}\)Benz. Again, the structures of these surfactants were geometry-optimised using the ACD/3D program of ACD/Labs and the following distances, corresponding to the labels in Scheme 6.3, were calculated: \( C_{\alpha}-C_{\omega} \), \( S-C_{\omega} \), \( O-C_{\omega} \), \( O_1-C_{\omega} \), \( O_2-C_{\omega} \), \( O_3-C_{\omega} \), \( C^+ -C_{\omega} \), \( N_1-C_{\omega} \) and \( N_2-C_{\omega} \). These distances are listed in Table 6.4 and show that Na\( C_{12} \)SO\(_4\) is shorter than C\(_{10}\)Benz and Na\( C_{13} \)SO\(_4\) is of very similar tail length as C\(_{10}\)Benz.

### Table 6.4. Distances, corresponding to the labels in Scheme 6.3, as calculated with ACD/3D, in C\(_{10}\)Benz, Na\( C_{12} \)SO\(_4\) and Na\( C_{13} \)SO\(_4\).

<table>
<thead>
<tr>
<th>distance (Å) between</th>
<th>C(_{10})Benz</th>
<th>Na( C_{12} )SO(_4)</th>
<th>Na( C_{13} )SO(_4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( C_{\alpha}-C_{\omega} )</td>
<td>14.99</td>
<td>13.77</td>
<td>14.99</td>
</tr>
<tr>
<td>( C^+ -C_{\omega} )</td>
<td>16.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( O-C_{\omega} )</td>
<td>14.91</td>
<td>16.16</td>
<td></td>
</tr>
<tr>
<td>( S-C_{\omega} )</td>
<td>16.28</td>
<td>17.50</td>
<td></td>
</tr>
<tr>
<td>( N_1-C_{\omega} )</td>
<td>16.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( N_2-C_{\omega} )</td>
<td>17.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( O_1-C_{\omega} )</td>
<td>16.04</td>
<td>17.19</td>
<td></td>
</tr>
<tr>
<td>( O_2-C_{\omega} )</td>
<td>16.91</td>
<td>18.14</td>
<td></td>
</tr>
<tr>
<td>( O_3-C_{\omega} )</td>
<td>17.40</td>
<td>18.62</td>
<td></td>
</tr>
</tbody>
</table>
In Table 6.5, the thermodynamic parameters of deaggregation of NaC\textsubscript{12}SO\textsubscript{4}/C\textsubscript{10}Benz mixtures are listed; $\alpha$(NaC\textsubscript{12}SO\textsubscript{4}) = 0.9 was the lowest fraction where NaC\textsubscript{12}SO\textsubscript{4} could still solubilise C\textsubscript{10}Benz. The addition of C\textsubscript{10}Benz to NaC\textsubscript{12}SO\textsubscript{4} slightly increases the cac due to a less favourable $\Delta H$ that is not completely compensated by a more favourable $T\Delta S$. This is somewhat counterintuitive, since the added C\textsubscript{10}Benz has a lower cac than pure NaC\textsubscript{12}SO\textsubscript{4}.

Interestingly, the mixed surfactant solution is bluish below the observed cac, whereas it is clear above the cac. In line with previous observations on mixtures of cationic and anionic surfactants,\textsuperscript{13} we therefore propose that aggregates, most likely vesicles, are formed at low concentrations (micromolar range) by the catanionic surfactant constituted of one C\textsubscript{10}Benz and one C\textsubscript{12}SO\textsubscript{4-} surfactant molecule. The presence of these aggregates gives the solution its turbid appearance below the cac. At the cac, the aggregates are solubilised by the excess of NaC\textsubscript{12}SO\textsubscript{4} present in solution, yielding mixed micelles of C\textsubscript{10}Benz and NaC\textsubscript{12}SO\textsubscript{4} and therefore a clear solution.

Indeed, for NaC\textsubscript{13}SO\textsubscript{4}/C\textsubscript{10}Benz mixtures, cryo-electron microscopy showed the presence of several types of bilayer aggregates at concentrations below the cac (see below).

Since the fraction of excess NaC\textsubscript{12}SO\textsubscript{4}, $\alpha$(NaC\textsubscript{12}SO\textsubscript{4})\textsubscript{free}, which is the fraction of NaC\textsubscript{12}SO\textsubscript{4} that does not have an oppositely charged C\textsubscript{10}Benz counterpart in solution, is responsible for the solubilisation process studied, the observed data have to be corrected using this fraction. The data in Table 6.5 printed in \textit{italics} are corrected for the amount of $\alpha$(NaC\textsubscript{12}SO\textsubscript{4})\textsubscript{free} present in solution. In that case, the corrected cac is obtained by multiplying the observed cac with $\alpha$(NaC\textsubscript{12}SO\textsubscript{4})\textsubscript{free} and the corrected $\Delta H$ by dividing the observed $\Delta H$ by $\alpha$(NaC\textsubscript{12}SO\textsubscript{4})\textsubscript{free}. Having performed this correction, we observe that the cac corresponding to $\alpha$(NaC\textsubscript{12}SO\textsubscript{4})\textsubscript{free} = 0.798 is \textit{lowered} in comparison to pure NaC\textsubscript{12}SO\textsubscript{4}. This stabilisation is entropy-driven; the enthalpy is slightly less favourable than in pure NaC\textsubscript{12}SO\textsubscript{4}. As stated in the introduction, mixtures of cationic and anionic surfactants show large departures from ideal mixing; therefore, the cac of C\textsubscript{10}Benz cannot be estimated using Equation 6.3 with $f_1 = f_2 = 1$. 

### Table 6.5. Thermodynamic parameters of aggregation of NaC\textsubscript{12}SO\textsubscript{4}/C\textsubscript{10}Benz mixtures at 40 °C.

<table>
<thead>
<tr>
<th>$\alpha$(NaC\textsubscript{12}SO\textsubscript{4})</th>
<th>cac (mM)</th>
<th>$\Delta G$ (kJ mol$^{-1}$)</th>
<th>$\Delta H$ (kJ mol$^{-1}$)</th>
<th>$T\Delta S$ (kJ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.70</td>
<td>-45.0</td>
<td>-8.36</td>
<td>36.7</td>
</tr>
<tr>
<td>0.899</td>
<td>10.2</td>
<td>-44.8</td>
<td>-6.4</td>
<td>38.4</td>
</tr>
<tr>
<td>0.798</td>
<td>8.1</td>
<td>-46.0</td>
<td>-8.0</td>
<td>38.0</td>
</tr>
</tbody>
</table>
Table 6.6. Thermodynamic parameters of aggregation of NaC₁₃SO₄/C₁₀Benz mixtures at 40 °C.

<table>
<thead>
<tr>
<th>α(NaC₁₃SO₄)</th>
<th>cac (mM)</th>
<th>ΔG (kJ mol⁻¹)</th>
<th>ΔH (kJ mol⁻¹)</th>
<th>ΔS (kJ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.39</td>
<td>-47.2</td>
<td>-9.25</td>
<td>38.0</td>
</tr>
<tr>
<td>0.901</td>
<td>6.2</td>
<td>-47.4</td>
<td>-8.3</td>
<td>39.1</td>
</tr>
<tr>
<td>0.802</td>
<td>5.0</td>
<td>-48.5</td>
<td>-10.4</td>
<td>38.1</td>
</tr>
<tr>
<td>0.801</td>
<td>5.90</td>
<td>-47.6</td>
<td>-8.09</td>
<td>39.5</td>
</tr>
<tr>
<td>0.603</td>
<td>3.55</td>
<td>-50.3</td>
<td>-13.4</td>
<td>36.9</td>
</tr>
</tbody>
</table>

In Table 6.6, the thermodynamic parameters of aggregation of NaC₁₃SO₄/C₁₀Benz mixtures are listed, as observed and, in italics, corrected for the amount of free NaC₁₃SO₄ present; α(NaC₁₃SO₄) = 0.8 was the lowest fraction where NaC₁₃SO₄ could still solubilise C₁₀Benz. Again, the mixed solutions are turbid below and clear above the cac. Observing the corrected data, the lowering of the cac upon increasing the amount of C₁₀Benz in the mixture is enthalpy-driven.

For the NaC₁₃SO₄/C₁₀Benz 8/2 mixture, a bluish, visco-elastic solution, cryo-electron microscopy was performed at 2 mM total surfactant concentration, a concentration well below the cac at which solubilisation to clear, mixed micelle solutions occurs. No special care was taken to prevent evaporation of water during sample preparation, since the surfactant concentration was already necessary rather low (see above) and a certain minimum concentration is required in order to be able to find some vesicles on the grids. Therefore, it is expected that the concentration on the grid is higher than 2 mM. A large variety of bilayer aggregates was observed, of which some representative structures are shown in Figure 6.7. In the upper two micrographs, examples of multilamellar vesicles of ca. 200 nm are shown, some of which are still intact (left hand side), while others are not (right hand side), probably being already partly solubilised by excess NaC₁₃SO₄. Predominantly, long, straight tubular multilamellar aggregates of ca. 40 nm wide and some extending over 3 µm, were observed, examples of which are shown in the lower micrograph of Figure 6.7. These long aggregates are responsible for the visco-elastic character of the solution. Thus, the hypothesis that bilayer aggregates are formed at concentrations below the cac that has been observed with ITC, has been verified.
Figure 6.7. Cryo electron micrographs of bilayer aggregates formed in a mixture of NaC\textsubscript{13}SO\textsubscript{4}/C\textsubscript{10}Benz 8/2 at 2 mM total surfactant concentration. Top left: intact vesicle, top right: partly solubilised vesicle, bottom: tubular, multilamellar aggregates. The bar represents 100 nm.
Table 6.7. Thermodynamic parameters of aggregation of NaDoBS/C\textsubscript{10}Benz mixtures at 40 °C.

<table>
<thead>
<tr>
<th>α(NaDoBS)</th>
<th>cac (mM)</th>
<th>ΔG (kJ mol(^{-1}))</th>
<th>ΔH (kJ mol(^{-1}))</th>
<th>TΔS (kJ mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.96</td>
<td>-47.6</td>
<td>-7.67</td>
<td>39.9</td>
</tr>
<tr>
<td>0.899</td>
<td>7.32</td>
<td>-46.5</td>
<td>-5.33</td>
<td>14.2</td>
</tr>
<tr>
<td>0.798</td>
<td>5.85</td>
<td>-47.7</td>
<td>-6.68</td>
<td>41.0</td>
</tr>
<tr>
<td>0.793</td>
<td>8.1</td>
<td>-46.0</td>
<td>-5.02</td>
<td>41.0</td>
</tr>
<tr>
<td>0.586</td>
<td>4.7</td>
<td>-48.8</td>
<td>-8.57</td>
<td>40.2</td>
</tr>
</tbody>
</table>

Since \(p\)-alkylbenzenesulphonates, like \(p\)-\(n\)-alkylbenzamidiniums, have a phenyl group adjoining the headgroup, this class of amphiphiles was studied as cosurfactants as well. First, \(p\)-\(n\)-octylbenzenesulphonate was tried. Neither sodium \(p\)-\(n\)-octylbenzenesulphonate, with a \(T_K\) of 18.5 °C, nor cesium \(p\)-\(n\)-octylbenzenesulphonate, with a \(T_K\) expected to be lower than that of the sodium salt, could solubilise 5 mol% of C\textsubscript{10}Benz. Probably, surfactants with longer tails are required to act as cosurfactants. Since \(p\)-\(n\)-alkylbenzenesulphonates with suitable tail lengths have rather high \(T_K\)'s, the commercial surfactant sodium dodecylbenzenesulfonate (NaDoBS) was used. This polydisperse surfactant has a branched alkyl tail of, on average, twelve carbon atoms and a \(T_K\) below room temperature. The lowest fraction for which NaDoBS could still solubilise C\textsubscript{10}Benz was \(α\) (NaDoBS) = 0.8. These mixtures are turbid below the cac and turbid and viscous, like a liquid detergent solution, above the cac. In Table 6.7, the thermodynamic parameters of aggregation of pure NaDoBS and mixtures of NaDoBS and C\textsubscript{10}Benz are listed, as observed and, in italics, corrected for the amount of free NaDoBS present. The interpretation of these data is not straightforward: the corrected data do not show a trend similar to that for the C\textsubscript{10}Benz/C\textsubscript{14}SO\textsubscript{4}Na mixtures and no other explainable trend appears to be apparent.

6.5 Conclusions

The novel class of \(p\)-\(n\)-alkylbenzamidinium chloride surfactants shows interesting thermodynamics of aggregation in mixtures with cationic and anionic surfactants. From the measurements in mixed solutions of C\textsubscript{14}TAC/C\textsubscript{10}Benz, it could be deduced that at 40 °C a hypothetical aggregate consisting of pure C\textsubscript{10}Benz has a cac between 3 and 4 mM, approximately twice as low as comparable surfactants without the possibility of charge delocalisation in the headgroup, such as C\textsubscript{14}TAC. This cac is well comparable to the cacs of around 4 mM of sodium \(p\)-\(n\)-decylbenzoate and sodium \(p\)-\(n\)-decylbenzenesulfonate, both surfactants with the possibility of charge delocalisation in the headgroup. The lowering of the cac in comparison to C\textsubscript{14}TAC is enthalpically driven and opposed by a less favourable entropy; in a C\textsubscript{16}TAC/C\textsubscript{10}Benz mixture, the enthalpy was also found to be more
favourable than in pure C_{10}TAC. It is proposed that this more favourable enthalpy is due to reduced headgroup repulsion in the mixed aggregate. In mixtures of C_{10}Benz with some anionic surfactants, evidence has been found for the formation of bilayer aggregates consisting of catanionic surfactants, which are solubilised at the cac of the C_{10}Benz/anionic mixed micellar aggregate.

### 6.6 Acknowledgments

Dipl. Chem. Thorsten Stafforst is acknowledged for synthesising the *p*-n-alkylbenzamidinium chloride surfactants. Dr. Marc Stuart is acknowledged for performing cryo electron microscopy experiments.

### 6.7 Experimental Section

**General remarks.**

The starting materials and the palladium-catalyst for the syntheses were purchased from Aldrich (*p*-n-decylbenzaniline, *p*-n-dodecylbenzaniline, tetrakis[triphenylphosphine]palladium(0)). The other chemicals were purchased from Acros (n-tetradecyltrimethylammonium bromide and cesium hydroxide), Aldrich (n-hexadecyltrimethylammonium chloride, sodium dodecysulphate and n-tetradecanoic acid), Fluka (n-dodecanoic acid), BHD Chemicals (sodium n-dodecysulphate), Lancaster (sodium *p*-n-octylbenzenesulphonate and sodium n-tridecysulphate), Merck (lithium hydroxide, potassium hydroxide, and sodium hydroxide). 1H-NMR spectra were recorded on Varian Gemini 200 (200 MHz) and VRX 300 (300 MHz) spectrometers. Elemental analyses were performed in the analytical department of our laboratory by Mr. Harm Draaijer, Mr. Jan Ebels and Mr. Jannes Hommes. Concentrated mixed surfactant solutions (concentration >> cac) were prepared by adding a solution of the cosurfactant to a suspension of *p*-n-decylbenzamidinium chloride, followed by sonication of the mixture to solubilise all C_{10}Benz.

**p-n-Decyliodobenzene.** A solution of 1.1 g (4.5 mmole) of *p*-n-decylbenzaniline in 18 ml of glacial acetic acid was slowly added to an ice-cold solution of 0.44 g (6.4 mmole) of well-powdered sodium nitrite in 4 ml of concentrated sulphuric acid and stirred for 10 minutes.\(^\text{40}\) Next, a solution of 4.0 g (24.1 mmole) of KI in 4 ml of water was quickly added.\(^\text{41}\) When nitrogen gas evaluation had ceased, the reaction mixture was heated slowly to 80 °C and stirred for 45 min. After the mixture cooled down to room temperature, it was extracted three times with 10 ml of dichloromethane. The combined organic layers were washed with 1 M KOH solution to neutralise the acid, washed with sodium monohydrogen sulphite to destroy formed iodide, washed with brine and dried over anhydrous sodium sulphate. After filtration, the solvent was evaporated to obtain 1.2 g of crude product, which was purified by column chromatography (silica gel, pentane) to obtain 0.83 g (2.4
mmole, 53%) of \( p-n \)-decyliodobenzene.\(^{42} \) \(^1\)H-NMR (200 MHz, CDCl\(_3\), ppm): 7.59 (d, 2 H, J = 5.9 Hz), 6.93 (d, 2 H, J = 6.0 Hz), 2.53 (t, 2 H, J = 7.8 Hz), 1.57 (m, 2 H), 1.25 (m, 14 H), 0.88 (t, 3 H, J = 6.8 Hz).

\( p-n \)-Dodecyliodobenzene\(^{43} \) was synthesised analogously using \( p-n \)-dodecylbenzaniline. \(^1\)H-NMR (200 MHz, CDCl\(_3\), ppm): 7.57 (d, 2 H, J = 8.4 Hz), 6.92 (d, 2 H, J = 8.4 Hz), 2.54 (t, 2 H, J = 7.2 Hz), 1.57 (m, 2 H), 1.25 (m, 18 H), 0.88 (t, 3 H, J = 6.8 Hz).

\( p-n \)-Decylbenzonitrile was synthesised using an adapted literature procedure.\(^{44} \) 0.17 g (1.5 mmol) of \( p-n \)-decyliodobenzene in 4 ml of dry DMF under a \( N_2 \) atmosphere; the yellow slurry was refluxed for 1.5 h. Next, the solution was cooled down to room temperature and 50 ml of toluene was added. The solution was washed with 50 ml of 2M ammonium hydroxide twice, washed with 20 ml of brine and dried over anhydrous sodium sulphate. After filtration, the solvent was evaporated to yield 0.52 g (2.1 mmole, 90%) of \( p-n \)-decylbenzonitrile.\(^{45} \) \(^1\)H-NMR (200 MHz, CDCl\(_3\), ppm): 7.56 (d, 2 H, J = 8.2 Hz), 7.27 (d, 2 H, J = 8.4 Hz), 2.65 (t, 2 H, J = 7.8 Hz), 1.60 (m, 2 H), 1.25 (m, 8 H), 0.88 (t, 3 H, J = 6.8 Hz).

\( p-n \)-Dodecylbenzonitrile\(^{45} \) was synthesised analogously using \( p-n \)-dodecyliodobenzene. \(^1\)H-NMR (200 MHz, CDCl\(_3\), ppm): 7.56 (d, 2 H, J = 8.2 Hz), 7.27 (d, 2 H, J = 8.4 Hz), 2.65 (t, 2 H, J = 7.8 Hz), 1.60 (m, 2 H), 1.25 (m, 8 H), 0.88 (t, 3 H, J = 6.8 Hz).

\( p-n \)-Decylbenzamidinium chloride was synthesised using a modified Pinner reaction.\(^{46} \) A solution of 0.52 g (2.1 mmole) of \( p-n \)-decylbenzonitrile in 2.5 ml of dry ethanol and 5 ml of dry ether was saturated with dry gaseous hydrogen chloride at 0 °C, stirred for 3 h at that temperature and for 6 h at room temperature. The solvent was evaporated and a solution of the imido-ether in 10 ml of dry ethanol and 20 ml of dry ether was saturated with dry gaseous ammonia at 0 °C and stirred for 2 h at that temperature and for 2 days at room temperature. The solvent was evaporated and organic by-products were removed by extraction with ether in a Soxhlet apparatus to yield 0.50 g of crude product still containing ammonium chloride. This mixture was added to 1.7 g of \( i \)-propanol, stirred overnight, filtered and dried under reduced pressure over \( P_2O_5 \) to yield 200 mg (6.14 mmole, 29%) of \( p-n \)-decylbenzamidinium chloride, m.p. 149-151 °C (dec., recrystallises around 118 °C). \(^1\)H-NMR (200 MHz, DMSO, ppm): 9.29 (s, broad, 2H, amidinium), 9.04 (s, broad, 2 H, amidinium), 7.75 (d, 2H, J = 8.0 Hz), 7.45(d, 2H, J = 8.0 Hz), 2.68 (t, 2H, J = 8.0 Hz), 1.60 (m, 2 H), 1.25 (m, 14 H), 0.86 (t, 3 H, J = 6.6 Hz). Elemental Analysis: calc: C 68.78% H 9.85% N 9.44% Cl 11.94%, found: C 66.97% H 9.79% N 9.77% Cl 13.56% (consistent with 2.63% ammonium chloride: calc C 66.97% H 9.79% N 9.88% Cl 13.37%).

\( p-n \)-Dodecylbenzamidinium chloride\(^{45} \) was synthesised analogously using \( p-n \)-dodecyliodobenzene. The product was further purified by recrystallisation from water and subsequently freeze-dried from 1M HCl. m.p. 149-151 °C (dec., recrystallises around 118 °C). \(^1\)H-NMR (200 MHz, DMSO, ppm): 9.32 (s, broad, 2H, amidinium), 9.04 (s, broad, 2 H, amidinium), 7.75 (d, 2H, J = 8.0 Hz), 7.45(d, 2H, J = 8.0 Hz), 2.68 (t, 2H, J = 8.0 Hz), 1.60 (m, 2 H), 1.25 (m, 14 H), 0.86 (t, 3 H, J = 6.6 Hz). Elemental Analysis: calc: C 68.78% H 9.85% N 9.44% Cl 11.94%, found: C 66.97% H 9.79% N 9.77% Cl 13.56% (consistent with 2.63% ammonium chloride: calc C 66.97% H 9.79% N 9.88% Cl 13.37%).

\( n \)-Tetradecyltrimethylammonium chloride. An ion-exchange column, prepared with Dowex 1x8 200-400 mesh, trimethylammonium type, chloride-form (Fluka), was washed with methanol. A solution of 1.0 g of \( n \)-tetradecyltrimethylammonium bromide in methanol was introduced on the
column and fractionally collected in 20 ml tubes. The solvent in the combined tubes containing product (indicated by TLC) was evaporated and the product was freeze-dried from water to yield 0.81 g of \(n\)-tetradecyltrimethylammonium chloride, mp 233-235 °C. Since this surfactant is strongly hygroscopic, it was not possible to remove all (crystal) water. \(^1\text{H-NMR (300 MHz, CDCl}_3\text{, ppm): 3.46 (m, 2H), 3.40 (s, 9 H), 1.68 (s, broad, 2H + H}_2\text{O), 1.31 (s, broad, 2H), 1.20 (s, broad, 20H), 0.82 (t, 3 H, J = 6.9 Hz). Elemental Analysis: calc: C 69.94% H 13.12% N 4.80% Cl 12.14% Br 0%, found: C 69.44% H 13.20% N 4.77% Cl 12.00% Br < 0.1% (consistent with 0.71% H\(_2\)O: calc C 69.44% H 13.11% N 4.77% Cl 12.05%).

**Isothermal Titration Calorimetry.**

Titration experiments were performed with an Omega Isothermal Titration Calorimeter, coupled to a nanovolt preamplifier in order to improve the signal to noise ratio (Microcal, Inc., Northampton, MA) and connected to a Haake N3 waterbath for temperature control. The instrument was calibrated using standard electrical pulses. Concentrated surfactant solutions (concentration >> cac, typically ca. 10 times the cac) were titrated into the stirred (350 rpm) cell (1.3249 ml) containing degassed (ca. 10 min.) water after a stable baseline (rms noise < 0.0050) was achieved. The injection sequence consisted of an initial injection of 1 µl to prevent artifacts arising from the filling of the syringe (not used in data analysis), followed by injections of 5 µl each at 300 s intervals until the region well beyond the cac was reached. The enthalpograms were created using Origin Software (Microcal, Inc.). Data were analysed by the method of van Os et al.\(^{(17)}\) that yields \(\Delta H\) (enthalpy of aggregation) and cac (critical aggregation concentration). Measurements were performed at least in duplo; for pure surfactants, the cac and \(\Delta H\) were reproducible to within 1% and for mixtures the cac was reproducible to within 5% and \(\Delta H\) was reproducible to within 4%.

**Cryo Electron Microscopy.**

The surfactant solution was brought on a holey carbon coated grid, and a thin film was obtained by gentle blotting with filter paper. The samples were vitrified by rapid plunging into liquid ethane. The grids were quickly transferred to a Gatan model 626 cryo-holder and examined at ca. −170 °C in a CM12 microscope (Philips) operating at 120 kV. Micrographs were recorded under low dose conditions.

**Krafft Temperature Determination.**

Krafft temperatures were determined by monitoring the temperature-dependence of the absorbance of a stirred 10 mM solution of the surfactant in water at 400 nm on a Perkin Elmer \(\lambda_5\) spectrophotometer coupled to a water bath for temperature control. The heating and cooling rates were ca. 1 °C/min.
6.8 References and Notes

(1) Part of this work has been submitted for publication: Talhout, R.; Stafforst, T.; Engberts, J. B. F. N.


(25) As discussed in section 6.2, it is assumed that the phenyl ring of C_{10}Benz is not part of the headgroup of C_{10}Benz, but contributes, with respect to the cac, an equivalent of 3 to 4 methylene units to the tail. If this assumption is not correct, the actual tail length of C_{10}Benz is shorter than reported above, since then the phenyl ring does not contribute to the tail but is part of the headgroup.


Since the concentration of the surfactant solutions was approximately 100 mM in each case and the solubility limit of CeCl is 9.6M (Handbook of Chemistry and Physics; Weast, R. C., ed. CRC Press: Cleveland, Ohio, 1977), the precipitate cannot be CeCl.

The O in of the NaC$_n$SO$_4$ in Scheme 6.3 is considered to be part of the headgroup.


