Carbohydrate-derived surfactants containing an N-Acylated amine functionality
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Chapter 5

Bis(1-amino-1-deoxy-D-glucityl)alkanes and
Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes

5.1 Introduction

As outlined in Chapter 1, gemini or dimeric surfactants (surfactants comprising two hydrophilic headgroups and two hydrophobic chains linked by a rigid or flexible spacer) are a new class of surface-active compounds displaying interesting behavior, such as: lower CMCs, larger surface tension reduction, lower Krafft temperatures and better solubility in water than conventional surfactants, synergism in surface-active properties with conventional surfactants\(^1\) and good (oil) solubilization properties.\(^1\)

Almost all gemini surfactants described in the literature have ionic headgroups. Extensive studies have not been carried out on the structure-property relationships of nonionic geminis. Therefore, we prepared a small series of nonionic gemini surfactants based on carbohydrates and investigated their aggregation behavior. Application of the same synthetic routes as described in Chapter 2 for the \(N\)-alkyl-1-amino-1-deoxy-D-alditols with use of \(\alpha,\omega\)-diamino alkanes instead of alkyl amines led to intermediate bolaamphiphiles (bis(1-amino-1-deoxy-D-glucityl)alkanes). The nonionic gemini surfactants (bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes) were obtained by acylation of the bolaamphiphiles with anhydrides, in this case tetradecanoic anhydride.

This Chapter summarizes the history and properties of gemini surfactants described in the literature. Subsequently, the results obtained for the aggregation of carbohydrate-derived gemini surfactants are discussed.\(^10\) We studied the aggregation behavior by optical polarization and electron microscopy\(^10\) and determined the rheology of one of the compounds (bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)hexane).

In Chapter 6, two more series of gemini surfactants (bis(N-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes and bis(N-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes) are described.

5.2 History of gemini surfactants

The name gemini surfactant was introduced by Menger in 1991, as outlined in Chapter 1. The first gemini surfactants, however, had already been prepared twenty years before by Bunton et al. The compounds (Figure 1a and 1b) were initially termed "dicationic detergents". Bunton intended to combine micellar catalysis and polyelectrolyte catalysis of nucleophilic substitutions by preparing these "dicationic detergents". Polyelectrolyte catalysis is often more effective than micellar catalysis, but suffers from the reduced mobility of polyelectrolytes. The new dimeric surfactant combined both features. Bunton et al. found that some of the gemini surfactants were catalytically more active than cetyltrimethylammonium bromide. They also found that the CMCs of the gemini surfactants were much lower than those of the monomeric surfactants. The first evaluation of the properties of (anionic) gemini surfactants was described by Okahara et al. in 1988 (Figure 1c). For this type of gemini surfactants, they noted the general features of these surfactants: low Krafft temperatures, good water solubility, low CMCs and a low surface tension at the CMC.

Figure 1. a: Alkanediyl-α,ω-bis(dimethylalkylammonium) bromide surfactants (abbreviated as m-s-m, 2Br⁻), b: alkanediyl-α,ω-bis(dimethyl-2-butyn-aminonium) bromide surfactants, c: disodium 1,8-bis(alkoxymethyl)-3,6-dioxaoctane-1,8-disulfates and d: disodium 5,12-bis(alkoxymethyl)-4,7,10,13-tetraoxahexadecane-1,16-disulfonates.
To date, the most extensively studied gemini surfactants are the alkanediyl-α-ω-bis(dimethylalkylammonium halide) surfactants (Figure 1a). They are abbreviated as m-s-m, 2X-, where m denotes the number of carbon atoms in the chains, s the number of carbon atoms in the alkyl spacer, and X the counterion.

### 5.2.1 Adsorption at the air-water interface and critical micelle concentrations

Like conventional surfactants, gemini surfactants adsorb at the air-water interface. By measuring the surface area per surfactant molecule at the air-water interface, it was established that when the spacer is rigid (Figure 2b), the entire gemini surfactant (spacer and alkyl chains) lies flat at the air-water interface.\(^{11,17}\) Only sufficient film pressure reorients the chains towards the air.

For the series 12-s-12, 2Br\(^-\) (Figure 1a), a maximum in the surface area is observed at s = 10 - 12.\(^{18,19}\) This maximum was ascribed to a change of location of the spacer. Spacers with s > 10 - 12 are too hydrophobic to remain in contact with water and are flexible enough to attain a looped conformation at the air-water interface, pointing towards the air side.\(^{20,21}\) When the spacer is smaller than 10, the gemini surfactant remains flat at the interface.\(^{21}\)

Generally, dimeric or gemini surfactants form micelles at a lower concentration than the corresponding monomeric surfactants. In solutions of dimeric surfactants, two alkyl chains are transferred from water into the aggregate. The standard Gibbs energy of micellization per CH\(_2\) group of dimeric surfactants with short spacer lengths is about the same as that of the corresponding monomeric surfactants \((\Delta_{\text{mic}}G^\circ = -3.2 \pm 0.3 \text{ kJ mol}^{-1})\), resulting in a nearly standard double Gibbs energy of aggregation, and thus in lower CMCs.\(^{18,22}\) For longer spacers, the standard Gibbs energy of micellization per chain may be slightly less favorable than that.
for the monomeric surfactants, but as there are two alkyl chains, the total Gibbs energy of micellization for the gemini surfactants remains more favorable and consequently, the CMCs are lower.\textsuperscript{18,22-24}

Alkanediyl-α,ω-bis(dimethylalkylammonium bromide) geminis (m-6-m) show a linear decrease in log CMC with increasing tail lengths, as for conventional surfactants.\textsuperscript{7,18,22,25,26} When the tails have a fixed length (between 10 and 16) and the spacer length is varied, a maximum in the CMC is observed for \( s = 5 \).\textsuperscript{7,26,27} This maximum has been attributed to a possible change of conformation of the surfactants with \( s \) increasing from 2 to 5 towards a preferential \textit{cis} conformation.\textsuperscript{26} It has been proposed that in this \textit{cis} conformation, the chains would already experience contact, resulting in a lower, slightly less favorable \( \Delta G \) per CH, group and higher CMCs.\textsuperscript{26} When \( s > 10 \), the spacer progressively penetrates into the micellar core, behaving almost like additional tails and hence the log CMC decreases linearly with increasing spacer length.\textsuperscript{18,26,28}

Bis(quaternary ammonium halide) geminis with a flexible hydrophilic spacer (Rosen et al.\textsuperscript{29}: \( s = -\text{CH}_2\text{CHOHCHOHCH}_2- \)) have even lower CMCs than the alkanediyl-α,ω-bis(dimethylalkylammonium halide) surfactants. The spacer possibly bends into the aqueous phase, forming hydrogen bonds with water molecules, thus facilitating micellization.\textsuperscript{29,30}

For geminis with a rigid hydrophobic spacer (Figure 2), the CMC decreases with increasing chain lengths up to \( m = 16 \), when \( m = 16-20 \), the CMC increases with increasing chain lengths.\textsuperscript{26} This unexpected behavior has been ascribed to the formation of submicellar aggregates. The same behavior has been observed with the flexible hydrophilic spacers.\textsuperscript{31}

Di-n-dodecyl α,ω-alkyl biphosphate surfactants prepared by Duivenvoorde et al.\textsuperscript{32} show a decrease in CMC on going from 6 to 12, as for the bis(quaternary ammonium halide) gemini surfactants.

Maiti et al.\textsuperscript{33} performed Monte Carlo simulations on micellar aggregates of model gemini surfactants in which they varied the length of the spacer (from 2 to 20 at a fixed tail length), the length of the tail (5 or 15), and the nature of the headgroups (either ionic or nonionic). For ionic surfactants, a maximum for the CMC is observed at a certain spacer length, as was experimentally observed. The length of the spacer at which the CMC reaches a maximum is higher in the simulations: about 12 compared to 5 obtained from the experimental results. For nonionic geminis, the simulations show a decrease in the CMC with increasing spacer length. This trend has not been verified experimentally, as there are no data available for nonionic geminis.
5.2.2 Aggregate morphology

In the case of short spacers, dimerization leads to reduced curvature of the aggregates formed in aqueous solution compared to the monomeric surfactants. The \(12-s-12, 2Br\) series of the \textit{bis}(quaternary ammonium bromide) gemini surfactants show the following sequence of aggregates upon increasing \(s\) (observed by cryo transmission electron microscopy): thread-like micelles \((s = 2, 3)\) → spheroidal micelles \((s = 4-12)\) → vesicles \((s = 16, 20)\).\(^{34-40}\) For spacer lengths 2 and 3, the aggregation number rapidly increases upon increasing concentration. \(12-2-12\) already forms (strongly entangled) thread-like micelles at a concentration of 2%. Due to these entangled thread-like micelles, the solution shows viscoelastic behavior.\(^{18,36}\)

The spheroidal micelles of \(12-3-12\), formed initially, grow to thread-like micelles at a concentration of 7%; the threads are shorter than for \(s = 2\).\(^{18,36,41}\) It is not surprising that spacers with \(s = 4-8\) form spheroidal micelles: the distances between the polar heads in these gemini surfactants are about 0.6 to 1.1 nm, which is close to the average distance between polar heads of spherical or spheroidal micelles.\(^{18,35,36}\)

For the \(16-s-16, 2Br\) series the sequence is as follows: vesicles and thread-like micelles \((s = 3)\) → entangled thread-like micelles and spheroidal micelles \((s = 4)\) → spherical or slightly elongated micelles \((s = 6)\) → spheroidal micelles \((s = 8)\).\(^{18,28,36}\) Thus, when the alkyl chain length is increased, the spacer length at which a significant change of aggregate morphology is observed, becomes larger.\(^{18,36}\)

Di-n-dodecyl \(a,\omega\)-alkyl biphosphate surfactants with \(s = 6, 8, 12\) form micellar structures in water. When \(s = 18\) or 24\(^b\) vesicles are observed by means of electron microscopy.\(^{32}\)

Karaborni \textit{et al.},\(^{42}\) using molecular dynamics simulations on a model water-gemini surfactant system, found that gemini surfactants with spacer = 1 form linear thread-like micelles at low concentrations and tree-like micelles at higher concentrations. Gemini surfactants with spacers \(\geq 2\) form a mixture of spheroids and tree-like micelles. There is, however, no experimental evidence that tree-like micelles exist.

The Monte Carlo simulations performed by Maiti \textit{et al.}\(^{33}\) show that the gemini surfactants with a spacer length of 2 and chain lengths 15 form long, thread-like and entangled micelles. Gemini surfactants with the same chain lengths (15), but spacer length 16, form shorter, rod-like micelles.\(^{33}\) No differences in aggregation morphologies between gemini surfactants with ionic and with nonionic headgroups were observed. A more detailed study by Maiti is underway.\(^{43}\)

\(b\) The surfactant 12-24-12 is at the borderline between a bolaamphiphile and a gemini surfactant. As no clear distinction has been made in literature between these two types of surfactants, we consider the surfactants to be bolaamphiphiles when \(2m \leq s\) and gemini surfactants when \(2m > s\), on the presumption that when \(2m \leq s\) a linear conformation is possible where the two headgroups are on opposite sides of the surfactant layer or membrane (membrane overspanning).
5.3 Synthesis and physical constants of bis(1-amino-1-deoxy-D-glucityl)alkanes and bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes

Bis(1-amino-1-deoxy-D-glucityl)alkanes can be prepared by reaction of two mole equivalents of glucose with one mole equivalent of an \textit{\textalpha;\omega;}-diamino alkane in the presence of sodium borohydride. A more elegant route involves the reductive amination of glucose using Pd/C (5\%) under hydrogen pressure in a one-pot synthesis (Scheme 1). The product formed is the intermediate bolaamphiphile (a surfactant which has headgroups at both ends of a hydrophobic chain). If the appropriate methanol/water ratio is chosen, the bolaamphiphiles crystallize from the reaction mixture upon cooling (after the Pd/C has been filtered off). We used \textit{diaminohexane}, -octane, and -decane; the corresponding compounds are abbreviated as bola-6, bola-8, and bola-10.

Scheme 1. The synthesis of bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes via acylation of bis(1-amino-1-deoxy-D-glucityl)alkanes.
The gemini surfactants, the bis(N-tetradecanoyl-l-amino-l-deoxy-D-glucityl)alkanes, can be prepared from the bolaamphiphiles by acylation of the amine functionality using an acid anhydride (in this case tetradecanoic anhydride). The use of acyl halides leads to low yields and undesired side products (hydrolysis of the acyl halide and corresponding salt formation). The compounds are abbreviated as 14-6-14, 14-8-14, and 14-10-14.

Table 1 shows the melting points and Krafft temperatures (the Krafft temperature may be viewed as the melting point in an aqueous environment), and the melting enthalpies of the bolaamphiphiles and gemini surfactants. In the solid state, the hydrogen bonds and the London dispersion forces are much stronger in the tightly packed linear bolaamphiphiles than in the gemini surfactants, where close packing is hampered by the presence of two bulky acyl side chains. This results in lower Krafft temperatures as well as in lower melting points (and melting enthalpies) for the gemini surfactants (Table 1). For the bolaamphiphiles, the spacer length has little influence on the melting points and the enthalpy of melting; this suggests that the packing of these compounds in the solid state is similar and is determined predominantly by interactions involving the carbohydrate headgroup.

Table 1. Physical properties of bis(l-amino-l-deoxy-D-glucityl)alkanes and bis(N-tetradecanoyl-l-amino-l-deoxy-D-glucityl)alkanes.

<table>
<thead>
<tr>
<th>compound</th>
<th>mp (°C)</th>
<th>ΔH_{melt} (kJ mol⁻¹)</th>
<th>T_{Krafft} (°C)</th>
<th>ΔH_{Krafft} (kJ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>bola-6</td>
<td>151.4-153.4</td>
<td>112.8</td>
<td>53</td>
<td>28.0</td>
</tr>
<tr>
<td>bola-8</td>
<td>151.9-154.2</td>
<td>116.0</td>
<td>74</td>
<td>55.0</td>
</tr>
<tr>
<td>bola-10</td>
<td>150.0-152.0</td>
<td>116.5</td>
<td>90</td>
<td>81.4</td>
</tr>
<tr>
<td>14-6-14</td>
<td>76.8-82.2ᵃ</td>
<td>57.4</td>
<td>32</td>
<td>45.5</td>
</tr>
<tr>
<td>14-8-14</td>
<td>94.4-96.9ᵇ</td>
<td>83.7</td>
<td>43</td>
<td>63.7</td>
</tr>
<tr>
<td>14-10-14</td>
<td>83.1-87.6</td>
<td>63.9</td>
<td>38</td>
<td>50.7</td>
</tr>
</tbody>
</table>

ᵃ Broad transition.ᵇ Clearing point 135.2°C (smectic A phase).ᶜ Monotropic smectic A, clearing point upon cooling 44.5°C.⁴⁵,⁵⁰
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5.4 Aggregation behavior

5.4.1 Aggregation behavior of bis(1-amino-1-deoxy-D-glucityl)alkanes and bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes studied by the penetration technique

The penetration technique provides an initial insight into the aggregation behavior of the bolaamphiphiles and the gemini surfactants (compare section 3.2). When water penetrates a crystalline amphiphilic compound, one or more lyotropic mesophases are often formed as bands around the anhydrous bulk of the sample, and consequently the entire concentration range from pure water to anhydrous compound is present. These lyotropic mesophases provide an indication of the kind of aggregates formed when the compound is dissolved in water. Unfortunately, the bolaamphiphiles dissolve in water only at high temperatures and do not form lyotropic mesophases. The gemini surfactants, on the other hand, show intriguing properties upon hydration. Gemini 14-10-14 displays myelin formation (a kind of L\textsubscript{o} phase) in the temperature range from 40°C to about 60°C (Figure 3), which suggests that vesicles will be formed in dilute solution. By contrast, 14-6-14 and 14-8-14 show two cubic phases and a lamellar phase, the latter being observed at higher surfactant concentrations (Figure 4). In the cases of 14-6-14 and 14-8-14, the penetration technique does not give a clear indication of the type of aggregates that can be expected upon dissolving these compounds in water.

Figure 3. Formation of lyotropic mesophases in a contact preparation of water and 14-10-14, 45°C; from top to bottom, water-myelin figures-1-compound.
since the exact relationship between cubic phases and the corresponding aggregates in aqueous solution is unclear in most cases.

5.4.2 Aggregation behavior of bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)-alkanes studied by electron microscopy

When the gemini surfactants 14-6-14, 14-8-14, and 14-10-14 (5 mM in water) were sonicated at 55°C, large spheres were formed, as could easily be demonstrated using a light microscope. These spheres are not an indication of aggregate formation: due to the poor solubility in water, a phase separation between hydrated surfactant and bulk water occurred. Therefore, 5 mole percent of an anionic surfactant (sodium dodecylbenzenesulfonate) was added to increase the solubility of the gemini surfactants. These mixed surfactant solutions were examined using electron microscopy. Two different techniques were applied, negative staining and cryo-transmission electron microscopy. When cryo-transmission electron microscopy is applied, the solution is cooled rapidly in liquid ethane. Cryo-transmission electron microscopy generally provides a more realistic view of samples under investigation, since negative staining may give rise to staining and drying artefacts.

Electron microscopy confirmed that the length of the spacer of the gemini surfactants has a dramatic influence on the morphology of the aggregates formed. Electron micrographs of negatively stained samples (Figure 5) show that 14-10-14, with a spacer length of ten
methylene groups, forms vesicles (as predicted by the penetration technique). The vesicles formed are unilamellar and the size distribution is nonuniform. The size of the vesicles is in the range of 20 to 200 nm.

Figure 5. Negatively stained (2% PTA) electron micrograph of 14-10-14 shows vesicles. The bar represents 100 nm.

Compounds 14-6-14 and 14-8-14 with spacer lengths of six and eight methylene groups, respectively, display long thread-like micelles (Figure 6). The thickness of the threads is about 60-70 Å, which is approximately twice the length of the alkyl chains plus the headgroups. This thickness is the cross section of the micellar cylinder. The long threads are strongly entangled. Some toroidal micelles (closed loops) are also observed. Almgren et al. argued that closing of the micelles probably occurs either when they are confined to a plane, or when the aggregates have a preference for the air/solution interface. Trimeric surfactants 12-3-12-3-12, 3Bi form branched thread-like micelles. Thread-like micelles formed by carbohydrate-derived geminis 14-6-14 and 14-8-14 do not show clear branching points. Nearly all junctions seem to result from overlap of micelles.

The cryo-TEM experiments were performed on compounds 14-6-14 and 14-10-14. For 14-10-14 vesicles were observed again. Compound 14-6-14 displayed thread-like micelles, in addition to sheets and vesicles (Figure 7).

Thread-like micelles can also be formed by conventional surfactants upon increasing concentration, addition of salts, or addition of certain strongly binding counterions such as salicylate. In the latter cases, a specific higher counterion binding permits the surfactant monomers to pack more tightly, resulting in an increase in the packing parameter (Chapter 1) and the formation of less curved, thread-like micelles.
As described in paragraph 5.2.2, thread-like micelles have also been observed for the cationic gemini series $m$-$s$-$m$, $2Br$ with short spacer lengths. The packing parameter calculated for this series also indicates the formation of elongated micelles ($\frac{1}{6} < P < \frac{1}{2}$). If $s < 4$, the equally charged headgroups are closer than the optimal distance. The thread-like micelles are...
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observed up to the point where the distance between the ammonium headgroups is the normal distance between the headgroups in spheroidal micelles, and consequently, spheroidal micelles are observed. The spacer can penetrate into the core of the aggregate when $s \geq 10$.

As the optimal surface areas of the carbohydrate-derived gemini surfactants have not been determined, the packing parameter cannot be calculated, but it is likely to be positioned between $1/3$ and 1. In case of the carbohydrate-derived surfactants, there is no electrostatic repulsion between the headgroups, resulting in a shorter equilibrium distance between the headgroups. The spacer can probably already fold back when $s = 6$. When the spacer folds back, the area of the headgroup ($a_c$) is reduced, which leads to a larger value for the packing parameter ($p = v \cdot (a_c \cdot 1)^{1/3}$; Chapter 1) and renders the formation of vesicles more likely.

5.5 Viscoelastic behavior of the carbohydrate-derived gemini surfactants

Simultaneously with the results for the aggregation behavior obtained by electron microscopy, we observed that the solution of 14-6-14 is clear when prepared at 55°C and becomes blueish after half an hour in an oven at 60°C. The blueish solution remains stable for at least 24 hours and turns clear again when cooled to room temperature. The ultimate clear solution is viscoelastic and much more viscous than water (the initial clear solution is not viscoelastic). This behavior can be observed visually. When a viscoelastic solution in a glass vessel is rotated for a few seconds, trapped air bubbles recoil when the motion is stopped. We contend that this viscoelasticity is due to the conversion of vesicles into thread-like micelles. Entanglement of threads is the cause of the viscoelastic behavior. The clear, viscous solution remains stable for about a day.

The solution prepared from 14-8-14 is blueish at room temperature and becomes clear and viscoelastic when placed in the refrigerator. For both compounds, this process is reversible. The solution of 14-10-14 remains blueish at all temperatures, is not viscous, and does not display viscoelastic behavior. Hence, vesicles formed by these gemini surfactants become more stable when the spacer length is increased.

The shorter spacer lengths are probably flexible enough to penetrate into the core of the aggregate at high temperature, thus facilitating the formation of vesicles. However, flexibility of the spacer decreases with decreasing temperature leading to a preferred formation of thread-like micelles at lower temperatures and hence to viscoelastic behavior.

The results from (cryo-transmission) electron microscopy and the viscoelastic behavior are summarized in Table 2.
Table 2. Aggregation behavior of the *(gemi)n* surfactants based on carbohydrates.

<table>
<thead>
<tr>
<th>Compound</th>
<th>EM (negative staining)</th>
<th>cryo-TEM</th>
<th>viscoelastic behavior</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-6-14</td>
<td>thread-like micelles</td>
<td>threads, sheets, vesicles</td>
<td>at room temperature</td>
</tr>
<tr>
<td>14-8-14</td>
<td>thread-like micelles</td>
<td>not determined</td>
<td>at 4°C</td>
</tr>
<tr>
<td>14-10-14</td>
<td>vesicles</td>
<td>vesicles</td>
<td>no viscoelasticity observed</td>
</tr>
</tbody>
</table>

### 5.6 Introduction to rheology

The rheology of a solid, liquid, or gas describes its deformation when strained. The deformation of an ideal solid is elastic: the energy required for the deformation is fully recovered when the strain is removed. For ideal fluids (gasses, liquids) the energy required for the deformation is dissipated in the fluid as heat: the deformation is irreversible, fluids "flow". The resistance of a fluid against flowing is called viscosity.

The elastic and viscous properties of a system can be measured simultaneously by applying a small, oscillating strain. The measurement is performed using a rheometer, in which the sample is brought between, e.g., two parallel platens. A sinoidal oscillating strain ($\gamma = \gamma_0 \cdot \sin(\omega \cdot t)$) with angular velocity $\omega$ and maximum strain $\gamma$ is applied to the lower platen. Due to the moving lower platen, the solution exerts a stress on the upper platen. This stress is balanced by the rheometer, such that the upper platen remains at its original position. The stress to strain ratio is expressed by the complex modulus, $G^*(\omega)$:

$$G^*(\omega) = G'(\omega) + i G''(\omega)$$

Herein:
- $G'$ = $G^* \cos \delta$, the elastic or storage modulus
- $G''$ = $G^* \sin \delta$, the viscous or loss modulus
- $\delta$ is the phase shift angle
- $\omega$ is the angular velocity

When the stress is in-phase with the strain (i.e., when the strain applied is at a maximum, so is the stress), $\delta = 0$ and $\cos \delta = 1$: the response is called elastic. A response that is $90^\circ$ out-of-phase is called viscous ($\delta = 90^\circ$, $\sin \delta = 1$). A system is viscoelastic if $0 < \delta < 90^\circ$.

Long-chain molecules such as polymers (or in our case long aggregates) in solution (also for polymers in the melt) can loop and entangle with other long-chain molecules (or long aggregates). When a force is applied, the molecules or aggregates cannot flow freely, as they

\[i = (-1)^h\]
are held back by the entanglements and interloops. A deformation therefore causes the molecules or aggregates to stretch in the direction of the force applied. Stretching raises the energy state of the molecules or aggregates. When the force is removed, the molecules or aggregates try to relax and return to the unstretched (lower energy) state. Part of the deforming energy is recovered during the relaxation phase. This partially retracts molecules and leads to a microflow in the direction opposite to the original flow; finally, the molecules or aggregates will disentangle and the fluid will flow continuously. Such a pronounced example of viscoelastic behavior was also observed for solutions of compounds 14-6-14 at 25°C and for 14-8-14 at 4°C. Of course, thread-like micelles differ from polymers in that they have a more dynamic structure, which breaks and reforms reversibly.67,70,74

5.6.1 Rheology of a solution of bis(N-tetradecanoyl-l-amino-l-deoxy-D-glucityl)hexane

A 5 mM solution of gemini surfactant 14-6-14 containing 5 mol% NaLAS was subjected to a rheological study at temperatures between 60°C and 7.5°C. At high temperatures the solution was as thin as water, but interesting behavior was observed at 7.5°C. Figure 8 shows G' and G" as a function of time at 7.5°C. After about an hour, G' >> G". This is indicative for a gel phase.75 According to Hoffmann et al., the Encyclopedia Britannica describes a gel as
Bis(1-amino-1-deoxy-D-glucityl)alkanes and Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes

"an elastic coherent mass consisting of a liquid in which ultramicroscopic particles are either dispersed or arranged in a fine network extending throughout the mass". A gel clearly combines viscous and elastic properties.

When the strain (expressed as percentage deformation) is increased at 7.5°C, the elastic modulus $G'$ remains linear up to 0.5% strain, Figure 9 (ignoring the first point). This pattern indicates that the solution of the gemini surfactant is a weak gel, which is disrupted at deformations $>0.5%$.

![Figure 9. Dynamic properties of a 5 mM solution of 14-6-14 as a function of strain $\gamma$ ($\omega = 1 \text{ rad s}^{-1}, 7.5^\circ\text{C}$).](image)

When an oscillating deformation of 0.5% is imposed on the solution at varying frequencies, the elastic and viscous moduli show only a slight frequency dependence and $G' > G''$ over the whole range of frequencies (Figure 10) which is typical for a gel phase. From the fact that the dependence of $G'$ on the frequency is rather flat from 0.1 to 100 rad s$^{-1}$, it follows that the linkages in the gel have a life-time exceeding at least 10 seconds.

In our case, the solution was put between parallel platens. A better reproducibility could have been obtained if a concentric cylinder had been used. When the solution is put in a cylinder, the surface to which the strain is applied is larger, but much more material is needed. Despite the low reproducability of the exact values for $G'$ and $G''$, the trend was the same in all measurements. Therefore, we conclude that a 5 mM solution of gemini surfactant 14-6-14 shows viscoelastic behavior and forms a weak gel at 7.5°C. The concentration used was low (0.4%). The strength of the gel might be improved by increasing the concentration of the solution.
5.7 Conclusions

The nonionic carbohydrate-derived germini surfactants show interesting aggregation behavior. When the spacer length is decreased from ten to six methylene groups, the vesicles formed by these surfactants become less stable and turn into thread-like micelles upon cooling, thus giving the solution a viscous and viscoelastic character. This process is reversible.

Rheology showed that at 7.5°C, a 5 mM solution of the germini surfactant 14-6-14 forms a weak gel.

5.8 Experimental

Characterization. 'H- and 13C-NMR spectra were recorded on a Varian VXR 300 spectrometer at 50°C. Melting points, Krafft temperatures and the corresponding enthalpies were determined by differential scanning calorimetry on a Perkin-Elmer DSC7 PC Series apparatus (heating/cooling rates 5 K min⁻¹). The lyotropic mesophase textures were studied by polarizing optical microscopy using a Nikon polarizing microscope equipped with a Mettler FP82 hot-stage (linked to a Mettler FP80 temperature controller) and a Minolta 7000 camera. Elemental analyses were performed at the Microanalytical Department of this laboratory by Mr. H. Draaijer, Mr. J. Ebels, and Mr. J. Hommes.
Bis(1-amino-1-deoxy-D-glucityl)alkanes and Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes

Vesicle preparation. Vesicles were prepared either with a Branson cell disruptor (2 min, 40 W, pulsed, 55°C) or with an MSE sonicator (6 cycles of 20 s sonication with a 5 s rest period in between, amplitude 19 microns). 5 mM solutions were prepared (5 ml) and sonicated for two minutes. 50 µL of a 25 mM aqueous solution of sodium dodecyl benzenesulfonate was added and the solution was sonicated again for 2 minutes.

Electron Microscopy. Aliquots of 5 mM solutions of 14-6-14, 14-8-14, 14-10-14 were applied on carbon-coated formvar grids, negatively stained with a 2% (w/v) solution of sodium phosphotungstate (PTA, pH 7.2) and examined in a Philips 201 electron microscope (operating at 100 kV). For cryo-transmission-electron microscopy, aliquots of 14-6-14 and 14-10-14 were absorbed onto holey carbon grids which were plunged into liquid ethane and then observed in a Philips CM120 electron microscope at about -170°C using a Gatan-626 cryo-holder. Observations were made under low dose conditions, at 120 kV.

Rheology. The rheology of a 5 mM solution of gemini surfactant 14-6-14 was measured using a constant strain rheometer (Rheometrics Fluids Spectrometer RFS II). The dynamic time sweep was run at a frequency of 1 rad s⁻¹ (γ = 0.5%). Subsequently, the strain sweep (ω = 1 rad s⁻¹; γ = 0.15-0.5%) and the frequency sweep (ω = 0.1 - 100 rad s⁻¹, γ = 0.5%) were measured.

Bis(1-amino-1-deoxy-D-glucityl)alkanes. A slight excess of D-glucose (0.085 mol) was added to a solution of 0.04 mol of the appropriate diaminoalkane in methanol (750 mL). The solution was stirred for 24-48 h at room temperature, and additionally sonicated for three hours to obtain a clear solution. Subsequently, the solution was cooled to 0°C and NaBH₄ (0.085 mol) was added over a period of two days. The solution was stirred for another 24 h. The solution was acidified with concentrated HCl (pH 2-3), the bolaamphiphile precipitated as its HCl salt. The solution was centrifuged (3500 rpm, 5°C, 30 min), the precipitate was washed with MeOH and centrifuged again. Residual amounts of solvent and borate esters were removed by trituration with EtOH. The HCl salt of the bolaamphiphile was stirred in MeOH with an excess of NaOMe and subsequently refluxed or sonicated to remove all HCl salt. The suspension was centrifuged twice. The bolaamphiphiles were crystallized from water/methanol. Elemental analyses are shown in Table 3.

A more elegant route to prepare bis(1-amino-1-deoxy-D-glucityl)alkanes is described in Chapter 6.

Bis(1-amino-1-deoxy-D-glucityl)hexane (bola-6): m.p. 151.4-153.4 (Table 1). ¹H-NMR (DMSO-d₆, ppm): 1.14 (m, 4H), 1.26 (m, 4H), 2.36 (m, 8H), 3.39 (m, 12H), 3.51 (m, 8H). ¹³C-NMR (DMSO-d₆, ppm): 26.66, 29.31 (C₁, C₂), 49.17, 50.97 (C₃, C₄), 63.67 (C₅), 70.76, 70.86, 71.12, 71.36 (C₆-C₈).

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes. The corresponding geminis (14-6-14, 14-8-14, and 14-10-14) were obtained by acylation of the bolaamphiphiles with tetradecanoic anhydride (2.5-3 mol equivalents) in ethanol. The solution was neutralized with Dowex OH⁻ (Sigma). The products were crystallized from ethanol (14-6-14, 65%), ethyl acetate (14-8-14, 73%), or
extracted with hexane (14-10-14, 78%, to remove excess fatty acid). Elemental analyses are shown in Table 3.

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)hexane (14-6-14): \(^1\)H-NMR (CD\(_2\)OD, ppm): alkyl chain 0.97 (t, 6H), 1.37 (s, 44H), 1.67 (m, 8H), 2.48 (dt, 4H), sugar moiety 3.56 (m, 18H), 4.04 (m, 2H), 4.73 (s, 10H), \(^13\)C-NMR (CD\(_3\)OD, ppm): 14.66 (C\(_{6}\), 23.92, 26.91, 27.01, 27.81, 27.89, 28.45, 30.04, 30.65, 30.77, 30.85, 30.98, 33.28, 34.33, 34.60 (C\(_2\)-C\(_3\)), 47.65, 51.02, 51.99 (C\(_1\), C\(_2\)), 65.10 (C\(_6\)), 71.67, 72.03, 73.11, 73.43, 73.55, 73.63, 74.10, 74.57 (C\(_2\)-C\(_3\)), 176.67, 176.79, 176.85 (C\(_4\)). Note: double or triple resonances are due to the presence of rotamers caused by the amide bonds (Chapter 2).

Table 3. Elemental analyses of the bis(1-amino-1-deoxy-D-glucityl)alkanes and bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% C</td>
<td>% H</td>
<td>% N</td>
</tr>
<tr>
<td>bola-6</td>
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<tr>
<td>bola-10</td>
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<td>9.66</td>
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<td>14-6-14</td>
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<td>10.72</td>
</tr>
<tr>
<td>14-8-14</td>
<td>C(<em>{40})H(</em>{92})N(<em>2)O(</em>{12})</td>
<td>64.54</td>
<td>10.83</td>
</tr>
<tr>
<td>14-10-14*</td>
<td>C(<em>{50})H(</em>{100})N(<em>2)O(</em>{12})</td>
<td>65.18</td>
<td>10.94</td>
</tr>
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</table>

Due to problems with the crystallization no fully satisfactory analysis could be obtained.

Acknowledgements. We gratefully acknowledge the assistance of Ronald Terpstra (HLO trainee, Netherlands Institute for Carbohydrate Research) who prepared the gemini surfactants described in this chapter. Dr. Marc Stuart (Department of Biophysical Chemistry, University of Groningen) kindly performed the cryo-transmission electron microscopic experiments. We very much appreciated the hospitality in Prof. Alain Brisson's laboratory. We sincerely thank Albert Woortman (TNO Nutrition and Food Research Institute, Groningen) for performing the rheology experiments.

5.9 References

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As opposed to their monomeric counterparts, the alkanediyl-a,o-bis(dimethylalkylammonium) surfactants do not exhibit thermotropic liquid crystalline behavior, probably due to geometrical constraints (ref. 21).
Bis(1-amino-1-deoxy-D-glucityl)alkanes and Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes


