Nonionic Bolaamphiphiles and Gemini Surfactants Based on Carbohydrates

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Introduction

Bolaamphiphiles (also known as bolaform surfactants, bolaphiles, or ωω-type surfactants) are molecules that have a hydrophilic group at both ends of a (long) hydrophobic chain.1-3 Compared to the case for the single-headed amphiphiles, the introduction of a second headgroup generally induces a higher solubility in water, an increase in the critical micelle concentration (cmc), and a decrease in the aggregation number.1 The aggregate morphologies of bolaamphiphiles include spheres, large cylinders, small and large disks, and vesicles.1

Gemini surfactants consist of two hydrophobic chains and two hydrophilic headgroups, linked by a relatively short (rigid or flexible) spacer.4,5 The gemini surfactants reported thus far all possess ionic headgroups.6 This class of compounds shows intriguing properties, including higher cmc’s for geminis with two long chains (16-20 carbon atoms) than for the shorter-chain analogs, submicellar aggregation, markedly low surface tensions, good oil solubilization properties, and the formation of thread-like micelles.4,10

The interest in nonionic bolaamphiphiles based on carbohydrates is increasing.11-18 Recently, patents on carbohydrate-based gemini surfactants have been granted,19,20 but to our knowledge, nonionic (carbohydrate-based) geminis have not been reported in the open literature.6 Herein we report novel nonionic bolaamphiphiles 1, prepared directly from 1-glucose, and aωω-diaminoalkanes and nonionic gemini surfactants 2, obtained by acylation of 1 (Figure 1). A preliminary study of their aggregation behavior has been made.

Experimental Section

Materials. Starting materials and solvents were purchased from any of the large chemical suppliers.

Characterization. 1H- and 13C-NMR spectra were run 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 polarized 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.

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 µm). Solutions (5 mM) were prepared (5mL) and sonicated for 2 min. A 25 mM aqueous solution of sodium dodecylbenzenesulfonate (50 µL) was added, and the solution was sonicated again for 2 min.

Electron Microscopy. Aliquots of solutions of 2a-2c 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 CM120 electron microscope (operating at 100 kV). For cryo-electron microscopy, aliquots of 2a and 2c 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.

Bis[1-amino-1-deoxy-α-glucityl]alkanes (1). These bolaamphiphiles were prepared in yields up to 75% by catalytic hydrogenation at elevated pressure (40 bar, 40 °C, 24 h) of 2 mol equiv of D-glucose and the appropriate aωω-diaminoalkane in the presence of 5% palladium on carbon. The products could be recrystallized from their reaction mixtures (methanol/water) after the Pd/C had been filtered off.

Bis[1-amino-1-deoxy-α-glucityl]hexane (1a). 1H-NMR (DMSO-d₆, ppm): 1.14 (m, 4H), 1.26 (m, 4H), 2.36 (m, 8H), 3.39

Figure 1. Structures of bis[1-amino-1-deoxy-α-glucityl]alkanes 1. R = H; 1a, n = 6; 1b, n = 8; 1c, n = 10) and bis[1-(N-tetradecanoyl)-1-amino-1-deoxy-α-glucityl]alkanes (2, R = C(O)-C₁₄H₂₉; 2a, n = 6; 2b, n = 8; 2c, n = 10).

Notes

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(m, 12H), 3.51 (m, 8H). $^{13}$C-NMR (DMSO-$d_6$, ppm): 26.66, 29.31 (C$_2$, C$_3$), 49.17, 50.97 (C$_1$, C$_1'$), 63.67 (C$_6$), 70.76, 70.86, 71.12, 71.36 (C$_2$–C$_5$).

Anal. Calcd for C$_{18}$H$_{40}$N$_2$O$_{10}$: C, 48.64; H, 9.07; N, 6.30. Found: C, 48.68; H, 8.99; N, 6.31.

Bis(1-amino-1-deoxy-D-glucityl)octane (1b). Anal. Calcd for C$_{20}$H$_{44}$N$_2$O$_{10}$: C, 50.83; H, 9.38; N, 5.93. Found: C, 50.88; H, 9.35; N, 5.84.

Bis(1-amino-1-deoxy-D-glucityl)decane (1c). Anal. Calcd for C$_{22}$H$_{48}$N$_2$O$_{10}$: C, 52.78; H, 9.66; N, 5.60. Found: C, 52.55; H, 9.39; N, 5.48.

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)-alkanes (2). The corresponding geminis (2a–c, Figure 1) were obtained by acylation of the bolaamphiphiles with a small excess of tetradecanoic anhydride in ethanol. The solution was neutralized with Dowex OH$^-$ (Sigma). The products were crystallized from hexane (2a, 78%, to remove excess fatty acid).

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)hexane (2a). $^1$H-NMR (CD$_3$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$_{14}$′′), 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$_3$′), C$_{14}$′′–C$_{13}$′′, 47.65, 51.02, 51.99 (C$_1$, C$_1'$), 65.10 (C$_6$), 71.67, 72.03, 73.11, 73.43, 73.55, 73.63, 74.10, 74.57 (C$_2$–C$_5$), 176.67, 176.79, 176.85 (C$_{14}$′′). Note: double or triple resonances are due to the presence of rotamers caused by the amide bonds. Anal. Calcd for C$_{46}$H$_{92}$N$_2$O$_{12}$: C, 63.89; H, 10.72; N, 3.24. Found: C, 63.56; H, 10.55; N, 3.32.

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)octane (2b). Anal. Calcd for C$_{48}$H$_{96}$N$_2$O$_{12}$: C, 64.54; H, 10.83; N, 3.14. Found: C, 64.57; H, 10.79; N, 3.21.

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)decane (2c). Anal. Calcd for C$_{50}$H$_{100}$N$_2$O$_{12}$: C, 65.18; H, 10.94; N, 3.04. Found: C, 65.60; H, 10.75; N, 3.07. Due to problems with the crystallization no fully satisfactory analysis could be obtained.

Table 1. Physical Properties of Bis(1-amino-1-deoxy-o-glucityl)alkanes (1) and Bis(N-tetradecanoyl-1-amino-1-deoxy-o-glucityl)alkanes (2)

<table>
<thead>
<tr>
<th>compd</th>
<th>mp (°C)</th>
<th>$\Delta H_{melt}$ (kJ mol$^{-1}$)</th>
<th>$T_{Krafft,a}$ (°C)</th>
<th>$\Delta H_{Krafft,a}$ (kJ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>151.4–153.4</td>
<td>112.8</td>
<td>53</td>
<td>28.0</td>
</tr>
<tr>
<td>1b</td>
<td>151.9–154.2</td>
<td>116.0</td>
<td>74</td>
<td>55.0</td>
</tr>
<tr>
<td>1c</td>
<td>150.0–152.0</td>
<td>116.5</td>
<td>90</td>
<td>81.4</td>
</tr>
<tr>
<td>2a</td>
<td>76.8–82.2$^b$</td>
<td>57.4</td>
<td>32</td>
<td>45.5</td>
</tr>
<tr>
<td>2b</td>
<td>94.4–96.9$^c$</td>
<td>83.7</td>
<td>43</td>
<td>63.7</td>
</tr>
<tr>
<td>2c</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.

Results and Discussion

The aggregation behavior of the bolaamphiphiles and the gemini surfactants was studied by means of the contact preparation method. When water penetrates an amphiphilic sample, 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.\(^2\)

Theselyotropicmesophasesareanindicationofthekindofaggregatesformedwhenthecompoundisdissolvedinwater. Unfortunately, the bolaamphiphiles 1a–1c 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 2c displays myel information in the temperature range from 45 °C to about 65 °C (Figure 2), which suggests that vesicles will be formed in dilute solution.\(^2\)\(^1\)\(^2\) By contrast, geminis 2a and 2b show cubic and lamellar phases, the latter being observed at higher surfactant concentrations.

The Krafft temperature of a surfactant may be viewed as its melting point in an aqueous environment.\(^2\)\(^2\) In the solid state, the hydrogen bonds and the London dispersion forces are much stronger in the tightly packed linear structure.
bolaamphiphiles than in the gemini surfactants, where close packing is hampered by the presence of two bulky acyl sidechains. 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 determined predominantly by the carbohydrate headgroup.17

Solutions of the geminis were prepared by sonicating 5 mM turbid solutions of compounds 2a–2c at 55 °C; it was necessary to add 5 mol % of an anionic surfactant (sodium dodecylbenzenesulfonate) to increase the solubility of the gemini surfactants. 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 3) show that 2c, with a spacer length of ten methylene groups, forms vesicles (as predicted), whereas compounds 2a and 2b with spacer lengths of six and eight methylene groups, respectively, display threadlike micelles (Figure 3a). Since negative staining is known to give rise to staining and drying artifacts,23 we also performed cryoelectron microscopy experiments on compounds 2a and 2c which provide a more realistic view of the samples under investigation.24 For 2c again vesicles were observed. Compound 2a displayed sheets and both vesicles and threadlike micelles (Figure 4). We simultaneously observed that the solution of 2a is clear when prepared at 55 °C and then becomes bluish after 0.5 h in an oven at 60 °C and turns clear again when cooled down to room temperature. The ultimate clear solution is viscoelastic and much more viscous than water (the initial clear solution is not viscoelastic). We contend that this viscoelasticity is due to the conversion of vesicles into threadlike micelles. The clear, viscous solution remains stable for about 1 day. The solution prepared from 2b is bluish at room temperature and becomes clear and viscoelastic when placed in the refrigerator. For both compounds, this process is reversible. The solution of 2c remains bluish at all temperatures, is not viscous, and does not display viscoelastic behavior. This indicates that the vesicles formed by the gemini surfactants become more stable when the spacer length is increased.

Conclusions

A series of nonionic bolaamphiphiles and gemini surfactants was synthesized. The gemini surfactants show interesting aggregation behavior. When the spacer length

Figure 3. Negatively stained (2% PTA) electron micrographs of (a) 2a (presence of threadlike micelles) and (b) vesicles formed by 2c. The bars represent 100 nm.

Figure 4. Cryo-transmission electron micrograph showing sheets, vesicles, and threadlike micelles formed by 2a. The bar represents 100 nm.
is decreased from 10 to 6 methylene groups, the vesicles formed by these surfactants become less stable and turn into threadlike micelles upon cooling, thus giving the solution a viscous and viscoelastic character. This process is reversible.

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