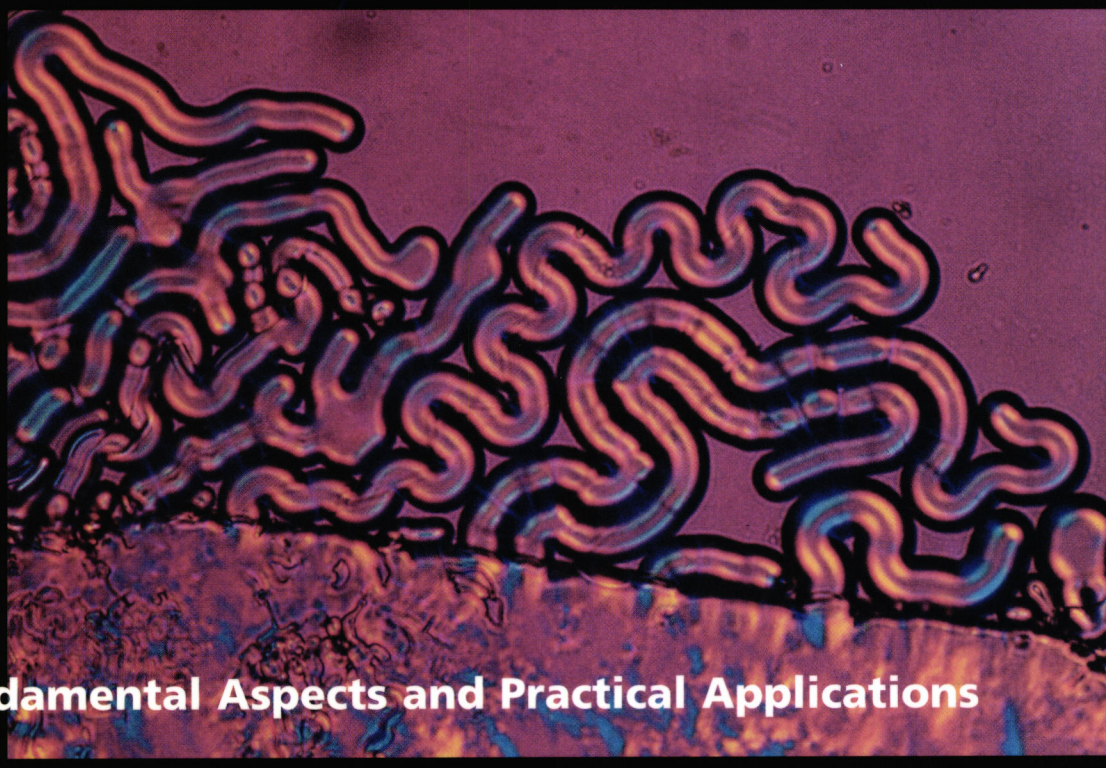
Carbohydrate-Derived Surfactants Containing an *N*-Acylated Amine Functionality

Monique Pestman



Fundamental Aspects and Practical Applications

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Fundamental Aspects and Practical Applications

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RIJKSUNIVERSITEIT GRONINGEN

Carbohydrate-Derived Surfactants Containing an *N*-Acylated Amine Functionality

Fundamental Aspects and Practical Applications

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Promotores: Prof. dr. J. B. F. N. Engberts

Prof. dr. R. M. Kellogg

Referent: Dr. H. A. van Doren

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Voorwoord

Nu het boekje "druk-klaar" is rest mij nog een leuke taak, namelijk degenen bedanken die mij de afgelopen vier jaar begeleid en geholpen hebben.

Gedurende mijn vier jaar durend promotieonderzoek was ik gedetacheerd op het Nederlands Instituut voor Koolhydraat Onderzoek (NIKO-TNO), thans TNO Voeding Groningen. Hierdoor was ik verder verwijderd van mijn promotores, professor Jan Engberts en professor Dick Kellogg, dan de meeste promovendi: een half uur fietsen. Ik heb deze afstand nooit hinderlijk gevonden. Vragen die ik had werden altijd meteen via de telefoon of per e-mail beantwoord. Bovendien lieten ze me duidelijk weten dat ik altijd langs kon komen als er iets was. Ik wil jullie hier hartelijk voor bedanken.

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aan de microscoop te wennen, ik zat er maar een aantal weken achter en dan weer een hele tijd niet. Wilma Bergsma en Jan van Breemen schoten altijd meteen te hulp als ik weer eens niets zag, zoals ze ook deden toen ik tijdens mijn hoofdvak EM-experimenten uitvoerde.

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Monique

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Chapter 1

Nonionic Carbohydrate-Derived Surfactants and their Use in Industry

1.1 Aim of the research: surfactants from renewable sources

The name surfactant is a contraction of the term "surface-active agent". Surfactants are adsorbed at interfaces and change the properties of those interfaces; thus they are surface active.[1] They have a dualistic character; they possess a headgroup, which by itself would be highly soluble in water, and a hydrophobic tail that tends to minimize water contact. The headgroup can be anionic (*e.g.,* sulphate, sulfonate, phosphate, carboxylate), cationic (*e.g.,* ammonium, alkyl substituted ammonium, pyridinium), zwitterionic (*e.g.,* betain), or nonionic (polyglycol ether, carbohydrate).[2] The tail consists of one or more alkyl chains which can be branched or unbranched and may be saturated or unsaturated.

Surfactants are large volume chemicals: their annual production exceeds 5 million tons worldwide.[3] They are primarily used as cleaning agents in laundry and dish-washing applications. Surfactants are also applied in cosmetics and pharmaceuticals, in manufacturing textiles and fibers, in the food industry, in paints and plastics, in the paper industry, in pesticides, and in the oil production process. Their intrinsic interest, the large production, and their application justifies research into the structures, properties, and performance of surfactants as well as their impact on the environment (synthetic process, toxicity, and biodegradability).

Classic types of surfactants are produced from petrochemical raw materials. In the long term, fossil feedstocks will be exhausted and products based on renewable materials will become more important. Growing consumer demands for "natural" products have also directed the search for new surfactants towards renewable sources.[4]

Therefore, our aim was to synthesize new surfactants based on renewables. We based our surfactants on carbohydrates, amines (which can be prepared from fatty acids), and acetic anhydride (which is prepared from natural acetic acid) or propionic anhydride. The surfactants should preferably be readily biodegradable and non-toxic and the syntheses should be possible on a large scale.

An additional benefit of applying carbohydrates is the creation of a new market for abundant agricultural products, such as starch. For the work described in this thesis glucose and lactose have been used. The former is prepared on a large scale by enzymatic hydrolysis of starch, whereas the latter is a unique carbohydrate only found in mammalian milk. The principle source of lactose is whey, the liquid that is a by-product in the production of cheese.

1.2 Aggregation behavior of surfactants

In water, surfactants adsorb at the air-water interface. At a certain concentration (the critical aggregation concentration), the surfactants form aggregates in water. The polar headgroups points towards water and the apolar alkyl chains stick together. This behavior arises from their dualistic character. Although water is the primary solvent in surfactant studies and applications, aggregation behavior is not restricted to water. There are also examples of the formation of aggregates in polar hydrogen-bonding solvents such as hydrazine, formamide, ethylene glycol, and ethyl ammonium nitrate.[5]

In apolar solvents, the situation is reversed. The apolar alkyl chain is readily soluble and the polar headgroup is insoluble in apolar solvents. The surfactants do not adsorb at the air-apolar solvent interface as air is also apolar. However, in solution a reversed aggregation to inverted micelles is possible, but the process is much less cooperative than that in water. The headgroups stick together with traces of water in the inner core of the inverted micelles to avoid contact with the solvent. The alkyl chains point towards the apolar solvent and keep the aggregates in solution.[2] Electrostatic interactions within the core provide the main driving force for the reversed aggregation. The size and structure of the inverted micelles depend on the nature of the surfactants and the apolar solvent. The amount of water present in the system is also an important factor and its presence may even be a prerequisite for the aggregation process.[6]

The driving force for aggregation in water is related to the formation of a hydrophobic hydration shell around the hydrophobic moiety of the surfactant. Traditionally, it was thought that water undergoes a structural enhancement in the hydrophobic hydration shell which is expressed in the formation of stronger and/or more hydrogen bonds per unit volume. Upon aggregation, these shells overlap and structured water is released; this process is accompanied by a gain in entropy. A novel view is that in order not to sacrifice hydrogen bonds compared to bulk water, the hydrogen bonds of water in the hydrophobic hydration shells adjacent to the apolar moiety are predominantly oriented tangentially to the apolar surface.[5] This leads to a loss of entropy. This tangential alignment does not lead to an appreciable enhancement of the three dimensional hydrogen bond structure. At a certain surfactant concentration, the number of water molecules is not sufficient to form a complete hydrophobic hydration shell, which leads to interference and mutual obstruction of hydration shells.[7] Hydrogen bonds are sacrificed and an increasing number of O-H bonds point towards the apolar surface. As a result, the tendency to form aggregates increases rapidly.[5] Subsequently, the lost entropy upon formation of the tangentially oriented hydrogen bonds is regained.

Additional factors such as headgroup effects also play a role. Headgroups of ionic surfactants are equally charged and repel each other. Furthermore, an ionic headgroup will partially break down the hydrophobic hydration shell of the hydrophobic tail by its presence

(and thus decrease the inclination to aggregate). Aggregation is also influenced by the counterions of ionic surfactants. By binding to the surfactant assembly counterions minimize headgroup repulsion. Nonionic surfactants aggregate at lower concentrations than ionic surfactants due to smaller headgroup repulsion. Repulsion between uncharged headgroups is due to hydration shell overlap and mainly of steric nature. Furthermore, in the case of nonionic surfactants, no counterions are involved.

Many techniques are available to determine the critical aggregation concentrations: surface tension, electrical conductivity in the case of ionic surfactants, NMR, and microcalorimetry. These techniques are all based upon a clear break near the CMC in the plot of a particular physical property versus the surfactant concentration. Extrapolation of the results at high and low concentration provides an intersection point, the CMC.

1.3 Surfactant types

Conventional surfactants contain one headgroup and one or two alkyl chains[8] (types a and b in Figure 1).[9] There are further interesting types of surfactants: bolaform and gemini surfactants.

Bolaamphiphiles (types c and d in Figure 1) are molecules which have a hydrophilic headgroup at both ends of a (long) hydrophobic chain.[10-12] Compared to the case for single-headed surfactants, introduction of a second headgroup generally induces better solubilization in water, an increase in the critical aggregation concentration, and a decrease in aggregation number.[10]

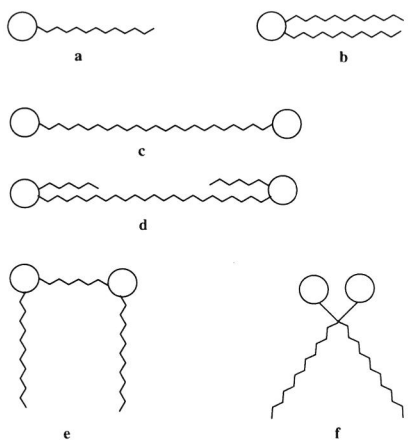


Figure 1. A single-chained surfactant (a), a double-chained surfactant (b), bolaamphiphiles (c and d) and gemini surfactants (e and f).

Menger[13,14] introduced the term gemini surfactants in 1991 to describe surfactants possessing, in sequence, a long hydrocarbon chain, an ionic group, a rigid spacer, a second ionic group, and another hydrocarbon tail. Rosen extended the meaning of the word to all such "double-surfactants" regardless of the spacer (Figure 1, type e).[15] Currently, all surfactants having two hydrophilic groups and two hydrophobic tails and a mirror plane or a C-2 axis are termed gemini surfactants, even if no spacer is present (Figure 1, type f).[16] The majority of gemini surfactants reported so far possess ionic headgroups. This class of surfactants shows intriguing properties, including low CMCs, submicellar aggregation, markedly low surface tensions, good oil solubilization properties, and the formation of thread-like micelles.[14,15,16-21]

1.4 Types of aggregates

Surfactants can form various types of aggregates (Figure 2).[21] The type of aggregate that is

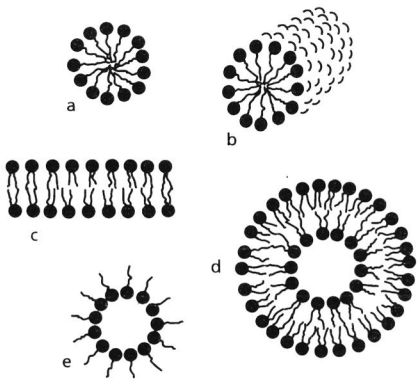


Figure 2. Various aggregate morphologies: a micelle (a), cylindrical micelle (b), bilayer (c), vesicle (d), and inverted micelle (e).

preferred by a specific surfactant in water depends on its geometry and is described in the packing parameter:[22-24]

$$P = v \cdot (a_0 \cdot l_c)^{-1} \quad (1)$$

v is the volume of the hydrophobic tail, l_c is the critical chain length (which is slightly less than the length of the fully extended, *all-trans*, chain) and a_0 is the optimal cross-sectional

surface area of the headgroup.[a] This cross-sectional area is an effective area and also includes electrical repulsion between ionic headgroups.[25] Table 1 shows the relationship between the packing parameter of surfactants and the aggregates preferably formed in aqueous solution.

Table 1. The relation between surfactant geometry and preferred structure.

Packing parameter $v \cdot (a_0 \cdot l_c)^{-1}$	< ⅓	⅓ - ½	½ - 1	~ 1	> 1
effective shape of surfactant molecule	cone	truncated cone	truncated cone	cylinder	inverted truncated cone
preferred structure	spherical micelles	cylindrical micelles[b]	flexible bilayers, vesicles	planar, bilayers	inverted micelles

A rough prediction for the type of aggregates (primarily valid for ionic surfactants) is that surfactants having a single alkyl chain form micelles and surfactants containing two alkyl chains form bilayers or vesicles (closed bilayers) in water.

The aggregate morphologies of bolaamphiphiles include spheres, large cylinders, small and large disks, and vesicles.[10] Inside these aggregates, the hydrophobic tail can be either folded or fully stretched.

The packing parameter has also been used to predict the aggregate morphologies of gemini surfactants. Generally, aggregates formed by dimeric (gemini) surfactants with short spacer lengths are less curved than those formed from the corresponding monomeric surfactants.[21] Aggregates formed by gemini surfactants include o.a. (long) thread-like micelles, spheroidal micelles and vesicles.[21]

1.5 Conventional nonionic surfactants versus carbohydrate-derived surfactants

In petrochemical-based nonionic surfactants, the hydrophilic moiety is usually built from ethylene oxide.[26] Synthesis of polyoxyethylene alkyl ethers is relatively easy and inexpensive and these surfactants find many large-scale applications in *e.g.* detergents. In the future, the availability of petroleum will decrease and consequently, the price of petrochemical products such as ethylene oxide, the precursor of the hydrophilic part of the conventional nonionic surfactants, and fatty alcohols and substituted phenols, the main hydrophobic ingredients, will

[a] The packing parameter approach has been criticized, and, as pointed out by Nagarajan, a_0 and l_c are not independent.[24]

[b] Cylindrical micelles have been given various names, *e.g.*, worm-like micelles, rod-like micelles, elongated micelles, and thread-like micelles. We use the term thread-like micelles only for reasonably long cylindrical micelles.

rise. More important in the short term is the growing demand of consumers for natural products. Therefore, the detergent industry is considering the replacement of classical petrochemicals by natural-based products. Of all detergent ingredients, 50 to 75% could be replaced by, *e.g.*, starch-derived products.[27]

Available and (relatively) cheap carbohydrates that can be used as raw material for surfactants include glucose, fructose, sucrose, maltose, cellobiose, and lactose. The atom that connects the carbohydrate-moiety and the hydrophobic chain can be either oxygen (ether, ester),[28-44] or nitrogen (amine, amide).[45-56] In principle, all hydroxyl groups of the carbohydrates can be linked to an alkyl chain, but the alkyl chain is mainly linked to the anomeric centre. Less common due to tedious synthetic routes are surfactants in which the alkyl chain and the carbohydrate moiety are connected through either a carbon-carbon bond[57] or a sulfur link.[58-62] Ames[63] reviewed carbohydrate-derived surfactants in 1960. Miethchen and Peters[57] updated this review in 1987.

Polyethylene oxide surfactants and carbohydrate-derived surfactants also differ in some physical and chemical properties. For example, the saturation concentration of conventional polyethylene oxide surfactants in lipophilic media is fairly high, which means that relatively high concentrations are needed for, *e.g.*, solubilization, emulsification, and detergency.[26]

Polyethylene oxide surfactants possess a cloud point.[26] When aqueous solutions of these nonionic surfactants are heated, they suddenly become turbid. The temperature at which this occurs is called the cloud point. At a somewhat higher temperature, the solutions separate into two phases. One phase contains a very low concentration of surfactant approximately equal to the CMC. The other phase is surfactant-rich.[64] The solubility gap of these systems is usually ascribed to partial dehydration of the headgroups. Carbohydrate-derived surfactants do not show this clouding phenomenon. The less sensitive phase behavior of the carbohydrate-based surfactants may result from the much stronger hydrophilicity of the glycoside moiety compared to that of the ethylene oxide units.[26] Hence, the oxyethylene type of surfactants are suitable for technical processes which require change of emulsion types. Solutions of carbohydrate-derived surfactants are insignificantly affected by increasing the temperature, which makes them attractive for formulation work.

However, the solubility of carbohydrate-derived surfactants might cause a problem. These solubilities depend on the sizes of the headgroups and the tails. Carbohydrate-derived surfactants may display an unfavorable Krafft temperature. Below this temperature spontaneous crystallization of the solution occurs. (T_{Krafft} may also be described as the temperature at which the CMC equals the solubility of the surfactant).[65]

Carbohydrate-derived surfactants are extensively used in protein extraction from membranes.[66-69]

1.6 Commercially produced carbohydrate-derived surfactants

Nonionic surfactants with a carbohydrate-derived headgroup are interesting because they are readily biodegradabe, non-toxic, mild to the skin, and have synergistic effects in combinations with anionic surfactants.[70,71] Applications are growing in the areas of foods, pharmaceuticals, cosmetics, and detergents.

Table 2. Application fields of industrially produced and used carbohydrate-derived surfactants.

application field	sorbitan esters	sucrose esters	glucamides	APGs[a]
detergents			X	X
cosmetics	X	X		X
food	X	X		
other non-food	X			

[a] Alkyl polyglucosides.

Carbohydrate-derived surfactants produced and used on an industrial scale are (ethoxylated) sorbitan and sucrose fatty acid esters, fatty acid glucamides, and alkyl polyglucosides; Figure 3. Table 2 shows their application fields. An advantageous property of glucosides and amides over esters is that they are less sensitive to hydrolysis under alkaline conditions.

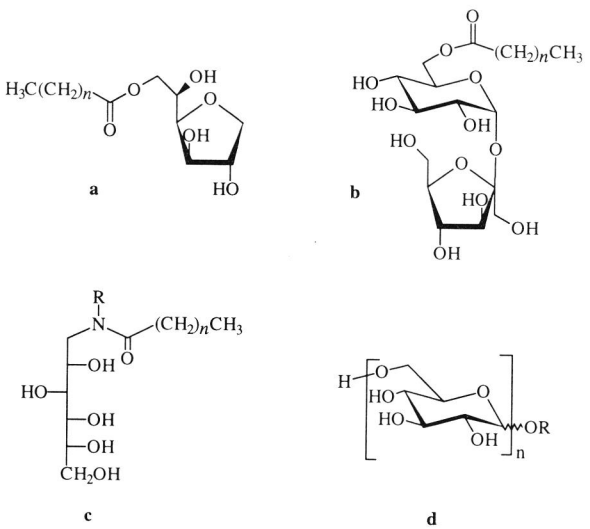


Figure 3. Commercially produced carbohydrate-based surfactants: sorbitan fatty acid ester (a), sucrose fatty acid ester (b), fatty acid glucamide (c), and alkyl polyglucoside (d).

1.6.1 Alkyl glucosides

Alkyl glucosides are the simplest carbohydrate-derived surfactants (Figure 4).[72-83] They are well-studied and are the most important ingredients of the sugar-based surfactants with the largest worldwide production capacity, the alkyl polyglucosides. Depending on the synthetic route, the configuration at the anomeric center can either be α or β (Figure 4).[84] The glycosilation reactions used to synthesize specific alkyl glucosides (Koenigs-Knorr syntheses and modifications thereof) require expensive reagents and are rather time-consuming. They are, however, a necessary tool for the analytical description of the alkyl glucosides.[84,85]

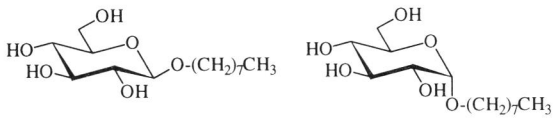


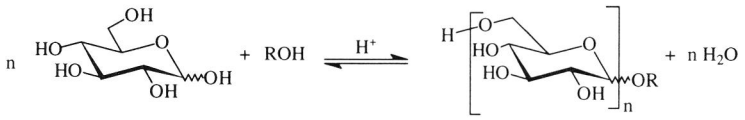
Figure 4. β-1-*n*-octyl-D-glucopyranoside (a) and α-1-*n*-octyl-D-glucopyranoside (b).

The physicochemical properties of both types of surfactants differ.[73,75,76,86] For example, β-1-*n*-octyl-D-glucopyranoside is readily soluble in water and has a critical micelle concentration of $1.9 \cdot 10^{-2}$ M. By contrast, the α-1-*n*-octyl-D-glucopyranoside is only sparingly soluble and has a CMC of $6.3 \cdot 10^{-3}$ M.[75] Furthermore, β-1-*n*-octyl-D-glucopyranoside forms micelles in solution whereas α-1-*n*-octyl-D-glucopyranoside forms very large, nonspherical assemblies.[75] Molecular dynamic simulations on monolayers of β-1-*n*-decyl-D-glucopyranoside and α-1-*n*-decyl-D-glucopyranoside show that the β compound forms a significantly larger number of hydrogen bonds between glucose units, whereas the α compound compensates the smaller number of intersurfactant bonds by a larger number of hydrogen bonds to water.[79] The tails of the β-1-*n*-decyl-D-glucopyranoside are able to pack more densely than those of the α counterpart due to the different orientation of the headgroups with respect to the tails.[79]

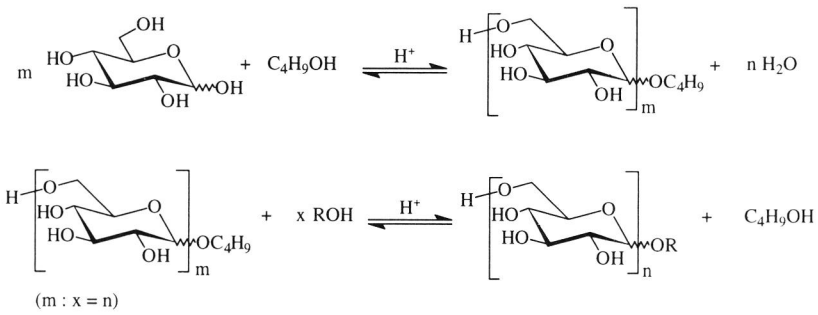
β-1-*n*-Octyl-D-glucopyranoside is widely used in biomembrane research for the extraction of water-insoluble membrane proteins without denaturation. It is preferred over other nonionic surfactants such as polyethylene glycol alkyl ethers because it has a very high CMC. Hence, it can easily be separated from the proteins by dialysis.[78]

On an industrial scale, alkyl polyglucosides (APGs) are synthesized by the Fischer synthesis (Scheme 1). The reaction is a specific acid-catalyzed acetalization. There are two variants. One is the direct synthesis, in which dry glucose is allowed to react with a fatty alcohol. The solubility of glucose in alcohols declines sharply with increasing hydrocarbon chain length and for higher alcohols, the reaction mixture separates into two phases. The second variant overcomes this problem. The synthesis starts from glucose syrup, which is

Direct synthesis:



Two step synthesis:



Scheme 1. Direct and two step Fischer synthesis.

allowed to react with a low boiling alcohol such as *n*-butanol in the presence of an acidic catalyst to form butyl glucoside. Although the solubility of glucose syrup in butanol amounts to only a few percent, the solubility is greatly enhanced by the presence of butyl glucoside. In the second step, butylglucoside is *trans*-glycosylized with the fatty alcohol.[84] The APGs produced are slightly colored and hence need final refining steps to meet application requirements.

The isolated product is a mixture of mono-, di-, and oligoglucosides (< 10% of tri- and higher oligoglucosides). The α-configuration is favored thermodynamically, but considerable amounts of β-product are also formed. Furthermore, the glucose moieties exist predominantly in the pyranose form, but appreciable amounts of furanosides (3-8%) are also found.[87] The saccharide moieties are predominantly (1→4) and (1→6) linked. Most industrially prepared APGs have an average degree of polymerization (number of monosaccharide units) between 1.2 and 1.6.[88] Although the common name for the products is alkyl polyglucosides, they are actually alkyl oligoglucosides.

Although the compounds had long been known, real interest was shown in the early 1980s, first by Procter and Gamble, soon followed by Kao (Japan), SEPPIC, Hüls AG, and Henkel.[89-95] The first commercial production of $APGs_{12-14}$ started in 1989 (Horizon). Today, the worldwide production capacity is estimated at 70,000 - 80,000 tons per year. Currently, APGs are by far the most important carbohydrate-derived surfactant.[95]

Advantageous properties of APGs, such as being well tolerated by the skin, their high synergism with anionic surfactants, and their foam-stabilizing properties make them particularly beneficial for use in manual dishwashing detergents.[87,96] Furthermore, they have a low toxicity and are completely biodegradable. Because they are non-toxic and tolerated well by the skin, APGs also have potential for use in cosmetics.[87, 88,96-98]

Up to now, APGs have found limited applications in laundry detergent compositions due to their relatively high prices compared to linear alkylbenzene sulfonates (ionic) and nonionic alcohol ethoxylates.[87,96]

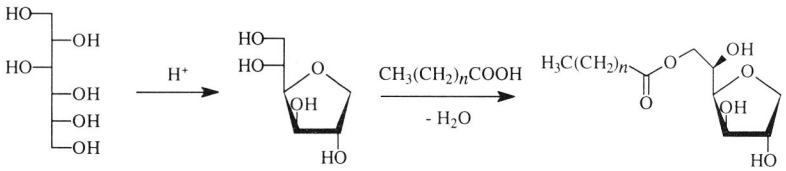
1.6.2 Sucrose esters

Carbohydrate-derived esters have a much older industrial tradition than APGs and glucamides. Sucrose fatty acid esters are prepared by transesterification of fatty acid methyl esters or triglycerides and sucrose, in aprotic solvents such as DMSO and DMF.[70] The use of methyl esters is advantageous because the equilibrium can be forced towards the sucrose ester by distilling off the methanol as it is formed. Disadvantages of the process are the cost of the solvents and their high boiling points which makes them difficult to remove. The products obtained are complex mixtures and since only the monoesters show favorable surface active properties, elaborate purification steps are necessary.[88]

Due to their tedious preparation and relatively high price, sucrose fatty acid esters have only been used as specialty surfactants in cosmetics, food, and pharmacy where dermatological and toxicological criteria are stringent.[99] The annual world production is only about 2,000 tons.[88]

1.6.3 Sorbitan esters

Sorbitan (anhydro sorbitol) esters are prepared by esterification of sorbitol with fatty acids under acidic conditions (Scheme 2). The cyclic ether structures are formed *in situ* by loss of water from sorbitol during the industrial esterification process, under the influence of heat or acidic reagents or both.[100] The annual world production of sorbitan esters exceeds 10,000 tons. These products are known as "Spans" and are used as emulsifiers and solubilizers in food, cosmetics, and pharmaceuticals. The Spans become more water-soluble when polyoxyethylene chains are grafted onto the cyclic moiety. These products are known as Tweens or polysorbates and have found applications in the same fields.



Scheme 2. Synthesis of sorbitan esters.

1.6.4 Glucamides

The Mega compounds, short for *N*-alkanoyl-*N*-methylglucamine, have a linear headgroup derived from D-glucitol which is coupled via an amide linkage to an alkyl chain (Figure 5). They are synthesized by the reaction of *N*-methyl-D-(-)glucamine with a fatty acid.[101,102] Megas are polyols, but like the alkyl glucosides, they do not show a cloud point.[103,104] The

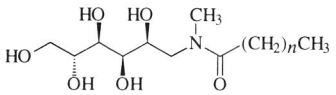


Figure 5. *N*-alkanoyl-*N*-methylglucamide (Mega).

nomenclature of these compounds is quite confusing. They have been called *N*-alkanoyl-*N*-methylglucamides, *N*-alkanoyl-*N*-methylglucamines, *N*-methyl-*N*-D-glucalkanamide, and 1-(alkanoylmethyl amino)-1-deoxy-D-glucitols.[102,103,104-107] Aggregation properties of a number of Megas have been described in the literature.[102,103,104,105,106,108] Recently, oleoyl-*N*-methylglucamide was synthesized enzymatically.[109]

The Megas are part of the industrially produced fatty acid glucamides; in the latter, the alkyl group on the nitrogen is not restricted to methyl.[110-120] Like APGs, glucamides show synergistic effects with other types of surfactants and due to their polyol structure, they have a low irritation potential. A disadvantage of glucamides is their affinity towards calcium ions. They always have to be formulated with sequestering agents in order to avoid precipitation. *N*-Methyllauroylglucamine is applied in dish-washing compositions.[88,121] The annual world production is about 5,000 tons per year. However, if *N*-methylglucamine is present either as a residue from the synthesis or as a metabolism product during biodegradation, *N*-Methyllauroylglucamine may form an *N*-nitrosoamine which is suspected to be carcinogenic. Therefore, its toxicological properties have not yet been satisfactorily defined.[88]

1.6.5 Aldo(bio)namides

An aldonamide (*e.g.*, gluconamide, Figure 6a) is the amide of an aldonic acid (a carbohydrate in which the anomeric aldehyde functionality has been oxidized to a carboxylic acid). An aldonamide based on a disaccharide is often called aldobionamide (*e.g.*, lactobionamide, Figure 6b, or maltobionamide). The alkylgluconamides are less soluble in

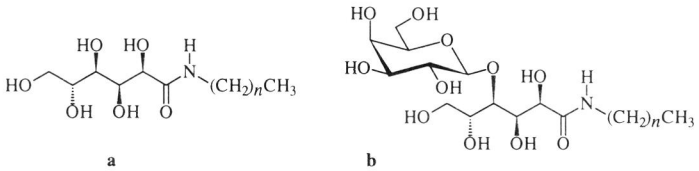


Figure 6. A gluconamide (a) and a lactobionamide (b).

water than β-1-*n*-alkyl-D-glucopyranosides. Pfannemüller *et al.*[122,123] showed that upon cooling a hot solution, *n*-alkyl gluconamides form gels in water at a concentration of only a few percent. Gel formation is favored by strong intermolecular hydrogen bonds between the carbohydrate residues. The gels consist of rope-like fibrillar structures with a right-handed helical twist.[124,125] The helical growth is probably induced by the hydrogen bonds between the amide linkages in combination with one or several chiral centres of the carbohydrate-moiety. On standing at room temperature, water is continuously expelled from the gel and crystalline needles start to grow; the gel is thus a metastable state. The molecular conformations of the gluconamide headgroups and the alkyl chains in the helical micellar fibres (all-*anti*) were elucidated.[126-132] Due to the methylation on nitrogen, Megas are much less prone to gel formation.

Micelle formation by some aldo(bio)namides has also been studied.[133-136] Although applications of aldonamides in detergents have been claimed in patents, these compounds are not (yet) produced on an industrial scale.[137-139]

The carbohydrate-derived surfactants under study in this thesis also contain an amide functionality. Structures and relevant references are given in section 1.9.

1.7 Bolaamphiphiles and gemini surfactants based on carbohydrates

Interest in nonionic bolaamphiphiles[140-156] and gemini surfactants based on carbohydrates is increasing. Some bolaamphiphiles based on carbohydrates that have been described in the literature are shown in Figure 7. The structures clearly resemble monomeric carbohydrate-derived surfactants. Much attention has been paid to the way the amide containing

bolaamphiphiles pack in the crystal lattice.[145,146,147,151,152,153,154] The packing is strongly stabilized by inter- and intramolecular hydrogen bonds between the carbohydrate moieties and the amide functionalities. Some aggregation properties of these bolaamphiphiles were also examined; they tend to aggregate when the structures contain a certain number of methylene groups in the hydrophobic moiety.[145,147]

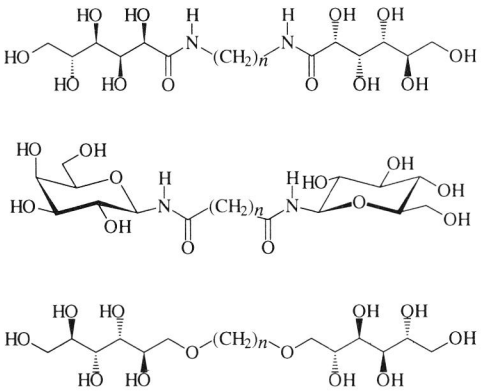


Figure 7. From top to bottom: "bis-gluconamide", "1-glucosamide bolaamphiphile", and α,ω-di-(1-*O*-D-mannityl)-alkane.

"1-D-glucamide bolaamphiphiles" (*N,N'*-bis(β-D-galactopyranosyl)alkane-α,ω-dicarboxamide) produce solid-like fibrous assemblies upon cooling a hot aqueous solution. The nature of the assemblies strongly depends on whether the hydrocarbon chain has an odd or an even number of methylene groups.[152]

Generally, bolaform surfactants are less effective surfactants than conventional surfactants, but they often display biological activity and some drugs are, in fact, bolaform surfactants.[157] Bolaamphiphiles can span a membrane, having one headgroup on the outside of the membrane and one on the inside. The membranes of extremophiles (bacteria that live under extreme temperature and pH conditions), are stabilized in this way.[158] The potential applications of bolaamphiphiles include the formation of ultrathin monolayer membranes, inclusion of functionalities into membranes, and disruption of biological membranes.[159]

As already mentioned, the field of gemini surfactants (or dimeric surfactants) is quite new. Most reported physico-chemical results on gemini surfactants concern bisquaternary ammonium surfactants of the alkanediyl-α,ω-bis(dimethylalkylammonium halide) type. They are referred to as *m-s-m*, $2X^-$; *s* is the number of carbon atoms in the spacer and *m* is the number of carbon atoms in the alkyl chains, X stands for the counterion.

Recently, the first nonionic gemini surfactants were described by Castro *et al.*[156] and by our group (Figure 8).[160] The gemini surfactants reported by Castro possess very short alkyl chains. The gemini surfactants that we have prepared had not appeared in the nonpatent literature.

However, they have been described in a number of patents by Procter & Gamble in which they are claimed as components in laundry, cleaning, fabric, and personal care compositions.[161-165]

Some other gemini surfactants have also been claimed in the same fields,[166-169] but in general, it is not yet clear what the added value of gemini surfactants will be and in what fields they can be applied. However, industry is closely monitoring the research that is being undertaken in this subject.

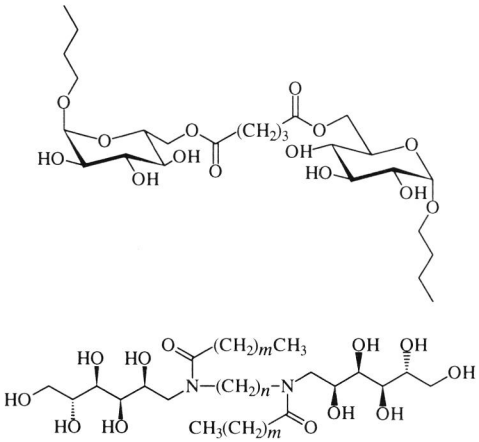


Figure 8. 1,5-Bis[6-*O*-(n-butyl α-D-glucopyranoside)] glutarate prepared by Castro *et al.*[156] (above) and the bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)alkanes prepared by our group.

1.8 Brief outline of the thesis

Following this introductory chapter, Chapter 2 describes the syntheses and physical properties of extensive series of carbohydrate-derived surfactants, namely *N*-acyl,*N*-alkyl-β-D-aldosylamines and *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols (Figure 9).[170-182]

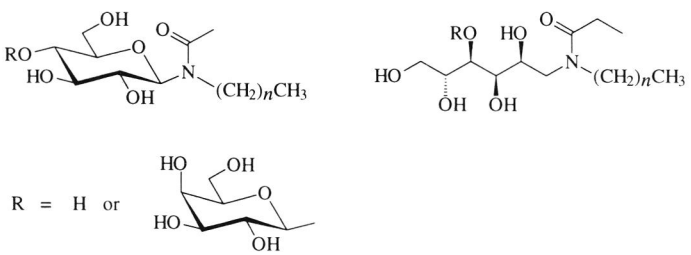


Figure 9. Structures of the monomeric surfactants under study in this thesis (Chapter 2 - 4).

Aggregation of these surfactants is described in Chapter 3. The lyotropic behavior of these *N*-acyl,*N*-alkyl-β-D-aldosylamines and *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols is a first indication of their properties in aqueous solutions. Critical micelle concentrations have been determined both by drop tensiometry and microcalorimetry. Drop tensiometry not only yields the CMCs, but also the surface tension at the CMC. Furthermore, the size of the headgroups at the air-water interface can be calculated. Microcalorimetry also offers insight into the thermodynamics of micellization.

In Chapter 4, the applicability of *N*-acyl,*N*-alkyl-β-D-aldosylamines and *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols as cosurfactants in laundry detergent systems is demonstrated by measurements of the increase in performance of a benchmark powder upon addition of 2.5% of our carbohydrate-derived surfactants in mini-bottle tests. Other important parameters are also commented on, such as the foaming power of the surfactants. Environmental issues are also dealt with, such as biodegradation and biotoxicity.

In Chapter 5, a series of nonionic gemini surfactants based on carbohydrates (Figure 8) is described. The gemini surfactants have tetradecanoyl chain lengths and spacers containing 6, 8, or 10 carbon atoms. Their aggregation is studied using electron microscopy. Furthermore, the rheological behavior of one of the gemini surfactants has been examined.

Chapter 6 deals with two other series of gemini surfactants. In one series, the geminis have decanoyl chains and a spacer length varying from 2 to 12 carbon atoms. In the other series, the spacer has a fixed length of 10 methylene groups. The alkanoyl chains range from pentanoyl to hexadecanoyl. Their aggregation is studied using electron microscopy. Their oil solubilization capacities are determined by measuring the amount of hexane and toluene that can be solubilized by the gemini aggregates in water.

In the final chapter, we estimate the costs of these surfactants were they to be prepared on an industrial scale.

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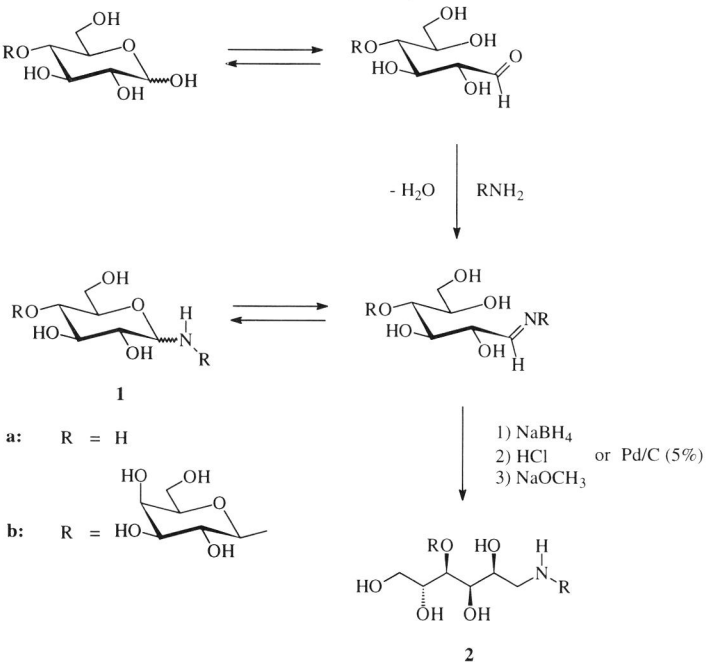
Chapter 2

Synthesis and Physical Properties of *N*-Acyl,*N*-alkyl-β-D-aldosylamines and *N*-Acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols

2.1 Introduction

As noted in Chapter 1, we have prepared several homologous series of carbohydrate-derived surfactants in which the alkyl chain is linked through an *N*-acylated amine bond (Figure 1). The carbohydrate, in our case either D-glucose or D-lactose, is first allowed to react with *n*-octyl-, decyl, or dodecylamine (Scheme 1), leading to *N*-alkyl-α,β-D-gluco-pyranosylamines and *N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]amines. These *N*-alkyl-α,β-D-aldosylamines can be reduced to the *N*-alkyl-1-amino-1-deoxy-D-alditols.



1

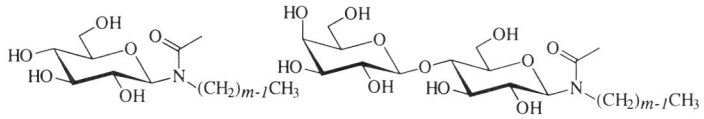
a: R = H

b: R = HO-

2

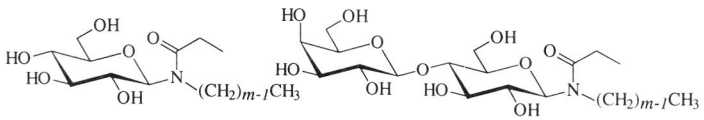
Scheme 1. The formation of *N*-alkyl-α,β-D-glucopyranosylamines (1a), *N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]amines (1b), *N*-alkyl-1-amino-1-deoxy-D-glucitols (2a), and *N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols (2b).

Acylation of the *N*-alkyl-α,β-D-aldosylamines and *N*-alkyl-1-amino-1-deoxy-D-alditols gave the compounds displayed in Figure 1. With these acylated compounds, we can easily vary the carbohydrate headgroup, the length of the acyl group and the length of the alkyl chain. The opportunity of introducing small structural changes should provide us with insights into the structure-property relationships, which are relevant for designing tailor-made materials.



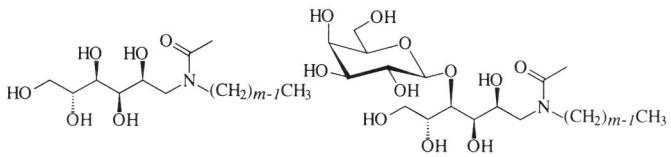
m = 8: NC_2nC_8 glucose
m = 10: NC_2nC_{10} glucose
m = 12: NC_2nC_{12} glucose

m = 8: NC_2nC_8 lactose
m = 10: NC_2nC_{10} lactose
m = 12: NC_2nC_{12} lactose



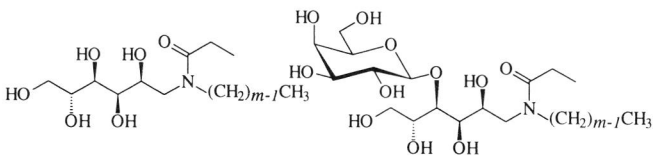
m = 8: NC_3nC_8 glucose
m = 10: NC_3nC_{10} glucose
m = 12: NC_3nC_{12} glucose

m = 8: NC_3nC_8 lactose
m = 10: NC_3nC_{10} lactose
m = 12: NC_3nC_{12} lactose



m = 8: NC_2nC_8 glucitol
m = 10: NC_2nC_{10} glucitol
m = 12: NC_2nC_{12} glucitol

m = 8: NC_2nC_8 lactitol
m = 10: NC_2nC_{10} lactitol
m = 12: NC_2nC_{12} lactitol



m = 8: NC_3nC_8 glucitol
m = 10: NC_3nC_{10} glucitol
m = 12: NC_3nC_{12} glucitol

m = 8: NC_3nC_8 lactitol
m = 10: NC_3nC_{10} lactitol
m = 12: NC_3nC_{12} lactitol

Figure 1. Structures and abbreviated names of the compounds synthesized.

2.2 Historical background

About a century ago, in 1893, Lobry de Bruyn reacted methanolic ammonia with glucose and obtained β-D-glucopyranosylamine.[1] At that time, the structure of the compound was not known. Other researchers, like Irvine[2] in 1913, not only used ammonia, but also performed reactions with ethylamine. About twenty years later, in 1934, Votoček[3] reported reactions of a number of monosaccharides with alkylamines (methyl to heptylamine) and solved their structure. The *N*-alkyl-α,β-D-glucopyranosylamines descibed in this thesis (the *n*-octyl, decyl, and dodecyl derivatives) were synthesized by Pigman *et al.*[4] in 1951, together with the lactose derivative *N*-dodecyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]amine.

Synthesis involving reduction of the intermediate imine was patented in the United States in 1935.[5] The aim of this project was to develop a relatively simple practical method for the preparation of otherwise relatively inaccessible amino alcohols. The reduction was performed using a metal catalyst under pressure in a hydrogen atmosphere. Applications were mentioned, such as dye assistants, ingredients of wetting agents for viscose, and textile lubricants in mineral oil emulsions. Mitts *et al.*[6] also reduced some *N*-alkyl-α,β-D-glucopyranosylamines to the glucitol derivatives by hydrogenation in a Parr type bomb using Raney nickel (1944). He observed that the compounds, especially those from amines of intermediate molecular weight, lower the surface tension and are good wetting agents. Karrer *et al.*[7] described the catalytic reductive amination of carbohydrates with aliphatic amines (the catalyst being nickel or palladium on carbon). Reductions can also be performed stoichiometrically. Hoagland,[8] for example, performed some reductive aminations with lactose using sodium cyanoborohydride in boiling methanol in the presence of a weak organic acid such as propionic or benzoic acid. He obtained the propionate or benzoate salts of the *N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols. Van Dam *et al.*[9] performed the reduction with $NaCNBH_3$ under alkaline conditions. Syntheses of 1-amino-1-deoxy-D-alditols by means of $NaBH_4$/$NaBH_3CN$ provide a useful alternative for the catalytic hydrogenation. The work-up procedure, however, is more laborious.

In 1990 and 1995, van Doren *et al.*[10-12] described the thermotropic and lyotropic liquid crystalline behavior of a number of *N*-alkyl-1-amino-1-deoxy-D-glucitols and *N*-acetyl,*N*-alkyl-1-amino-1-deoxy-D-glucitols.

In 1991 and 1992 Rico-Lattes *et al.*[13-15] patented the *N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols, *N*-acyl,*N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols, *N*-acyl,*N*-alkyl-β-D-glucopyranosylamines, and *N*-acyl,*N*-alkyl-[4-*O*-(β-D-galacto-pyranosyl)-β-D-glucopyranosyl]amines[16] and published a paper describing the syntheses and critical micelle concentrations of some *N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols. Later, they reported several NMR and X-ray diffraction studies on these compounds.[17-20] Some *N*-acetyl,*N*-alkyl-1-amino-1-deoxy-D-glucitols and *N*-acyl,*N*-alkyl-4-*O*-

(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols with long acyl chains (6 to 16 carbon atoms) were described by the same group in 1995 and 1997.[21,22]

Rico-Lattes *et al.*[22] showed some of these compounds can have potential pharmaceutical, biochemical, and medicinal applications. *N*-Nonyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitol showed promising behavior in the extraction of certain proteins from frog brain.[23] *N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols (with an optimum for the dodecyl analog) and *N*-hexadecanoyl,*N*-nonyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitol possess marked anti-HIV activity.[24,25] Patients with AIDS frequently develop infections due to filamentous fungi (*Aspergillus* series) for which there are few effective treatments. Particularly *N*-octadecanoyl,*N*-nonyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitol showed activity against *Aspergillus fumigatus*.[24] Rico-Lattes *et al.*[22] are currently optimizing the structures in order to maximize the ability to extract proteins and to obtain maximal antiviral and antifungal activities.

We prepared several series of these compounds (using slightly different routes) and investigated their thermodynamic properties with respect to micellization (Chapter 3) and their potential as co-surfactants in detergent systems (Chapter 4). This chapter elaborates the syntheses and purfications of the carbohydrate-derived surfactants.

2.3 Syntheses

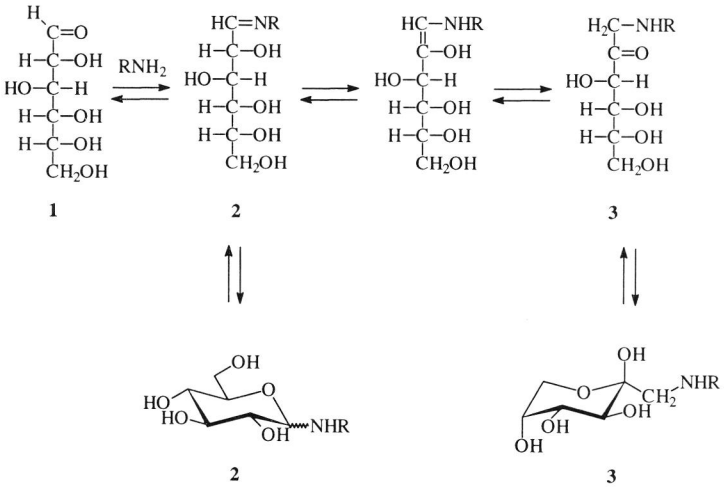
2.3.1 *N*-Alkyl-α,β-D-glucopyranosylamines and *N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]amines

The reactions of D-glucose and D-lactose with alkylamines lead to the formation of *N*-alkyl-α,β-D-glucopyranosylamines and *N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]-amines. The compounds are mixtures of both α (minor product) and β (major product) anomers.

The *N*-alkyl-α,β-D-aldosylamines are unstable. They are susceptible to hydrolysis when dissolved in water and on heating, the solution becomes yellow and, after prolonged heating, brown. This color change is due to the Amadori rearrangement of the aldosylamines.[26,27]

The Amadori rearrangement (Scheme 2) is the transformation of the aldosylamine (a Schiff base) into the more stable 1-amino-1-deoxy-2-ketose.[26,27] This initial rearrangement leads to a whole chain of reactions, called the Maillard reaction.[27] At high temperature, such as during food preparation (*e.g.* roasting or baking), Maillard reactions of amino acids or proteins with sugars give rise to the characteristic appearance and aroma of baked and roasted food.[28] The Maillard reaction is favored at pH 4-7 and at temperatures > 50°C.[28] Although the reaction mixture in our case was alkaline (pH 10-11), the solutions became yellow if the thermal

conditions were too severe.



Scheme 2. Mechanism of the formation of an Amadori product (3) from glucose (1) via glucosylamine (2).

In case of the *N*-alkyl-α,β-D-glucopyranosylamines, methanol was preferred as the reaction medium over ethanol. Small residual amounts of glucose dissolve better in methanol and thus precipitate less easily than from ethanol. As the product precipitated from the reaction mixture, co-precipitation of glucose was not desirable. The *N*-alkyl-α,β-D-glucopyranosylamines were crystallized from methanol and yielded white crystals. The yields increased with increasing chain length. Integration of the anomeric proton signal in ^{1}H-NMR (CD_3OD) showed that about 90% of each glucosylamine exists in the β-configuration and about 10% in the α-configuration.

In an initial attempt to synthesize the *N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]amines, the same route was used as for the glucose derivatives. However, large quantities of methanol had to be used and it was difficult to remove small amounts of residual lactose. Therefore, we used the method developed by Erickson,[13,29] in which a water-*i*-propanol mixture is the solvent. The disaccharide derivatives also displayed coloration upon prolonged heating, but the process is slower than for the monosaccharide derivatives. The products were finally crystallized from ethanol and isolated as white crystals.

Integration of the anomeric proton signal in ^{1}H-NMR (DMSO-d_6) showed that about 75% of each lactosylamine exists in the β-configuration and about 25% in the α-configuration. This ratio is in agreement with the values found by Rico-Lattes *et al.*.[17]

2.3.2 *N*-Alkyl-1-amino-1-deoxy-D-glucitols and *N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols

N-alkyl-α,β-D-aldosylamines can be reduced to alditol derivatives with $NaBH_4$[10,13,30] or $NaCNBH_3$,[8,9,31] or with metal catalysts, *e.g.*, palladium on carbon[14,30,32] or Raney nickel,[14] which is more attractive for large-scale synthesis. *N*-alkyl-1-amino-1-deoxy-D-alditols are not susceptible to hydrolysis and also more stable to heat than *N*-alkyl-α,β-D-aldosylamines.

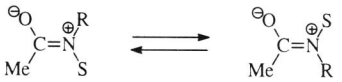
N-alkyl-α,β-D-glucopyranosylamines were reduced to glucitol derivatives with either $NaBH_4$[10] or with palladium on carbon (Scheme 1) in a Parr apparatus under hydrogen pressure. The products crystallized from ethanol.

N-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols can be synthesized via the same routes. Since the disaccharide is less prone to the Maillard reaction, the reaction temperature can be higher than that used for the monosaccharide. Purification by crystallization was more troublesome than for the glucitol derivatives. A wide range of organic solvents and mixtures of solvents (for example, ethanol, methanol, and mixtures of these alcohols with acetonitrile or acetone, 2-propanol, and water/acetone mixtures) were used in attempts to crystallize the compounds. The surfactants solidified in a mixture of methanol/acetonitrile (about 4 : 1) in the form of "structured gels".

2.4 Acylation

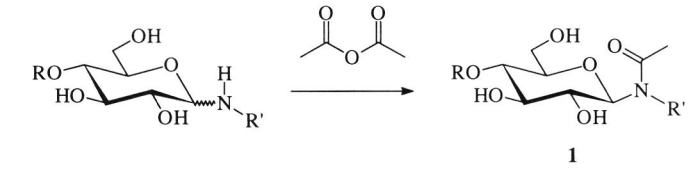
Since *N*-alkyl-α,β-D-aldosylamines and *N*-alkyl-1-amino-1-deoxy-D-alditols contain a secondary amino functionality there is a danger of formation of *N*-nitrosoamines, which are suspected to be carcinogenic. Acylation of the amine functionality (Scheme 3) eliminates the potential risk of nitrosoamine formation and also increases the solubility of the products in water.

Before acylation, *N*-alkyl-α,β-D-aldosylamines are a mixture of α- and β-anomers. The equilibrium between α- and β-configuration is still present when the compounds react with an acid anhydride to form *N*-acyl,*N*-alkyl-β-D-aldosylamines. *N*-acyl,*N*-alkyl-D-aldosylamines exist exclusively as the β-anomers as confirmed by the large coupling constants of the *E*-, *Z*-



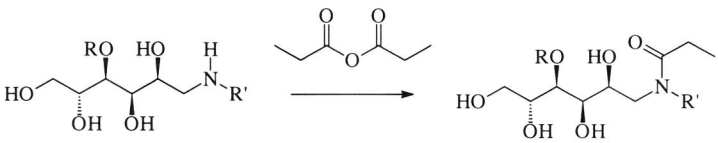
E-conformer *Z*-conformer

Scheme 4. *E*, *Z* conformers of the amide bond (S = sugar).



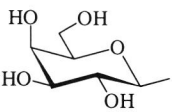
α and β anomers **exclusively β configuration**

1



2

a: R = H

b: R = 

R' = n-alkyl

Scheme 3. Acylation of the *N*-alkyl-α,β-D-aldosylamines and *N*-alkyl-1-amino-1-deoxy-D-alditols. Formation of *N*-acyl,*N*-alkyl-β-D-glucopyranosylamines (1a), *N*-acyl,*N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]amines (1b), *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-glucitols (2a), and *N*-acyl,*N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols (2b).

conformers (Scheme 4) of the amide functionality (δ 4.92 and 5.46 ppm, $^{3}J_{HH}$ = 8-9 Hz). Thus formation of the β-anomer of the *N*-acyl,*N*-alkyl-β-D-aldosylamines is kinetically favored. As the reaction proceeds, the equilibrium between α- and β-anomers of the *N*-alkyl-α,β-D-aldosylamine is maintained and *N*-alkyl-α-D-aldosylamine is transformed into the β-anomer which reacts with the anhydride leading to a β-configuration of the *N*-acyl,*N*-alkyl-D-aldosylamines. According to calculations performed by Rico-Lattes *et al.*[18] the β-configuration of *N*-acyl,*N*-alkyl-D-aldosylamines is also favored thermodynamically.

NMR spectra of the acylated carbohydrate-derived surfactants show that for *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols, the ratio of the *E*-, *Z*-conformers is 1 : 1. For *N*-acyl,*N*-alkyl-β-D-aldosylamines Rico-Lattes *et al.*[18] also found a conformer ratio of 1 : 1 (DMSO-d_6). However, we found ratios of about 15 : 85 for *N*-acyl,*N*-alkyl-β-D-glucopyranosylamines and 25 : 75 for *N*-acyl,*N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]amines (CD_3OD). The *Z*-conformer probably predominates due to possible hydrogen-bond formation

of the primary hydroxyl group of the glucopyranosyl part of the headgroup and the oxygen of the carbonyl functionality (Figure 2).[33] In the case of the reduced carbohydrate headgroups, the glucopyranosyl ring is not intact and the primary hydroxyl group is not available for hydrogen bond formation with the carbonyl oxygen. Indeed, the *E*/*Z* ratio is now 1 : 1.

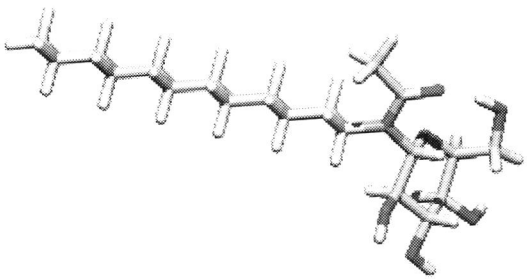


Figure 2. Frame model of the *Z*-conformer of *N*-acetyl,*N*-dodecyl-β-D-glucopyranosylamine (CHARMM program). Hydrogen-bond formation between the hydroxyl group of the primary alcohol functionality of the glucopyranoside headgroup and the carbonyl of the amide functionality is anticipated. Hydrogen-bond formation between C_6-OH and the oxygen in the ring is also possible.

Acylations were performed using acetic anhydride or propionic anhydride. The reactions proceeded quantitatively but during the work-up procedure some product was lost, leading to isolated yields in the range of 85-95%. The purity of the crude product was about 95%, which would suffice for many industrial applications. However, examination of the structure-property relationships require higher purities. The purification of these compounds from 95% purity to the point of satisfactory elemental analyses proved to be a challenge. Column chromatography did not lead to satisfactory results. On a silica gel column a mixture of chloroform and methanol could be used as the eluent, but the amount of methanol required (at least 10%) considerably deactivated the column material. Moreover, the yields were low (30-50%).[15] Other column materials (aluminium oxide, anion and cation exchangers[34]) did not lead to pure compounds.

For large scale syntheses, column chromatography is not desirable and crystallizations are favored. Although crystallization was not easy for the majority of the synthesized compounds, we nevertheless succeeded in finding reasonable to good solvents for crystallization and obtained satisfactory elemental analyses.

Glucose derivatives (*N*-acyl,*N*-alkyl-β-D-glucopyranosylamines) gave the most severe

purification problems. Crude products were slightly yellow. In acetonitrile the yellow impurity precipitated first, and the pure product could be obtained from the clear supernatant. The products were very hygroscopic.

Lactose derivatives (*N*-acyl,*N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]-amines) formed "geolids" from ethanol. The word geolid indicates intermediate structures between a gel and a solid. The precipitates had the appearance of a gel, but they could be separated from the solution by filtration; the geolid remained on the Büchner funnel as a waxy solid. The compounds were then freeze-dried to provide white fluffy solids, which contain one mole of water per mole of product.

The only compounds which did not have crystallization problems were glucitol derivatives (*N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-glucitols). Depending on chain length, they formed nice crystals from ethanol/ether, ethyl acetate, or acetonitrile.

Lactitol derivatives (*N*-acyl,*N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols) were dissolved in methanol. Acetonitrile was added just to the point of precipitation. Upon evaporation, the lactitol derivatives formed white solidified material, the closest physical description is "pimples".

2.5 Physical properties

Melting points of the compounds were determined using differential scanning calorimetry (DSC), Table 1. *N*-acyl,*N*-alkyl-β-D-glucopyranosylamines were very hygroscopic and their melting points could not be determined. No melting peaks were observed either for the fluffy, freeze-dried *N*-acyl,*N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]amines.

C_{10} and C_{12} chain analogs exhibit enantiotropic liquid-crystalline behavior and thus show both "melting" peaks and clearing peaks in a heating run. This phenomenon is described in the next section.

The relatively large difference between the clearing points obtained upon heating and cooling in the cases of NC_2nC_{10} lactitol, NC_3nC_{10} lactitol, and NC_3nC_{12} lactitol (the abbreviations are explained in Figure 1) may indicate initiation of the decomposition of these compounds.

Table 1. Melting points and clearing points of *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-glucitols,[10] *N*-acyl,*N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols, and *N*-acyl,*N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]amines.

Compound	mp (°C)	ΔH (kJ mol^{-1})	cp (°C)	ΔH (kJ mol^{-1})
NC_2nC_8 glucitol	51.3-59.6	24.1	-	-
NC_2nC_{10} glucitol	56.8-62.6	28.2	77.6 (75.5)	0.7 (-1.0)
NC_2nC_{12} glucitol	62.1-66.2	36.2	119.8 (118.6)	1.2 (-1.1)
NC_3nC_8 glucitol	94.0-96.1	47.5	-	-
NC_3nC_{10} glucitol	87.0-88.6	39.0	- (21.9)	(-0.6)
NC_3nC_{12} glucitol	92.4-98.1	63.0	- (66.4)	(-1.1)
NC_2nC_8 lactitol	-[a]	-	-	-
NC_2nC_{10} lactitol	54.9-62.3	22.7	132 (115.4)	0.8 (-0.2)
NC_2nC_{12} lactitol	~50-59.6	25.7	182.3 (168.3)	0.7 (-0.2)
NC_3nC_8 lactitol	93.5-100.9	30.7	-	-
NC_3nC_{10} lactitol	89.9-95.8	37.2	138.8 (134.2)	1.0 (-1.0)
NC_3nC_{12} lactitol	57.4-91.4[b]	-[c]	181.9 (160.7)	1.6 (-0.8)
NC_2nC_{12} lactose	-[d]	-[d]	140.3 (137.7)	0.3 (-0.3)
NC_3nC_{12} lactose	-[d]	-[d]	145.9 (143.4)	1.2 (-1.3)

[a] The compound was solid, but not very structured. [b] Two broad peaks. [c] Could not be detected. [d] The freeze-dried *N*-acyl,*N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]amines did not show melting peaks in the DSC.

2.6 Liquid-crystalline behavior[35]

In the crystalline form, carbohydrate-derived surfactants are packed in bimolecular layers, with the sugar moieties arranged head-to-head and with fully interdigitized alkyl chains.[36] When the crystals are heated, the alkyl chains start to melt, whereas the carbohydrate sheets which are held together by hydrogen bonds remain intact. At this stage, the compound is in an intermediate phase (a mesophase) between the liquid and the crystalline phase. If heating is continued, the hydrogen bonds between the sheets break down and, at the clearing point, an isotropic liquid is formed. This thermal behavior is called thermotropic liquid crystalline behavior. Generally, clearing points are higher for longer chain lengths.

Mesophases formed by amphiphilic carbohydrate-derived liquid crystals fall into two main

categories: (1) compounds with one alkyl chain (generally with an *n*-hexyl chain or longer) form smectic A (S_A) phases; (2) compounds with two or more alkyl chains usually form hexagonal columnar phases.[10,37-40] The compounds we synthesized fall into the first category, because the second chain is very short (C_2 or C_3): the compounds (generally with a chain containing 10 or 12 carbon atoms) display smectic A phases.[10,41] In the smectic (Greek for soap) phase the molecules are aligned more or less parallel and there is also some positional order of the molecules, resulting in a layered structure.

When a clearing point exists both upon heating and cooling, compounds are said to be enantiotropic. NC_3nC_{10} glucitol and NC_3nC_{12} glucitol are monotropic, and hence only show a mesophase upon cooling, due to supercooling of the isotropic phase.[42]

Carbohydrate-derived surfactants not only show liquid-crystalline behavior upon heating (thermotropic liquid-crystalline behavior), but also when a solvent is added (lyotropic liquid-crystalline behavior). The lyotropic mesophases displayed by these compounds are discussed in Chapter 3.

2.7 Conclusions

The synthetic routes we used to prepare carbohydrate-based surfactants are straightforward and have high yields. The final purifications from ~95% purity to satisfactory elemental analyses are rather troublesome, but we have found appropriate solvent mixtures to obtain high purities by crystallization. The syntheses are applicable on a large scale, especially when taking into account that for most industrial applications a 95% purity suffices. For industrial purposes, the palladium on carbon used to prepare the *N*-acyl,*N*-alkyl-1-aminoalditols can be replaced by the economically more attractive Raney nickel.

The syntheses are not restricted to glucose and lactose; other mono- (*e.g.* galactose) and disaccharides (such as maltose) can also be used.

2.8 Experimental

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

General Methods. Quantitative thermal analyses were performed using a Perkin Elmer PC Series DSC 7 (heating rate 5 °C min^{-1}). Thermomicroscopy used a Mettler FP 800 system, the hot stage was mounted on a Nikon polarizing microscope.

Characterization. ^1H- and ^{13}C-NMR spectra were run on a Varian VXR-300 spectrometer (300MHz),

or on a Varian Gemini spectrometer (200 Mhz). 2-D NMR and HETCOR spectra were recorded on a Varian Unity Plus spectrometer (500 MHz). Chemical shifts are denoted in units (ppm) and referenced to residual protons in deuterated solvents for ^{1}H-NMR (CD_3OD: 3.31 or DMSO-d_6: 2.50) and to solvent resonances for ^{13}C-NMR (CD_3OD: 49.00 or DMSO-d_6: 39.50), coupling constants are given in Hz. Elemental analyses were performed at the Microanalytical Department of this laboratory by Mr. H. Draaijer, Mr. J. Ebels, and Mr. J. Hommes.

***N*-Alkyl-α,β-D-glucopyranosylamines.** D-Glucose (10 g, 56 mmol) and one mol equivalent of the appropriate alkylamine were stirred in methanol overnight. The product precipitated from the reaction mixture. The suspension was heated until a clear solution was obtained and subsequently cooled down slowly. The white crystals were filtered off and washed with cold methanol and acetone (to remove unreacted alkylamine). The yields were 61-79%. The products were crystallized from methanol (overall yields 42% (C_8), 50% (C_{10}), 68% (C_{12}), not optimized).

***N*-Dodecyl-α,β-D-glucopyranosylamine.** ^{1}H-NMR (COSY, CD_3OD), ppm): alkyl chain 0.89 (t, 3H, $^{3}J_{12\text{-}11}$ = 7.0), 1.29 (bs, 18H), 1.47-1.52 (m, 2H), 2.64 (m, H_{1A}), 2.90 (m, H_{1B}), sugar moiety 3.06 (t (dd), H_2, $^{3}J_{2\text{-}1} = {}^{3}J_{2\text{-}3}$ = 8.7), 3.23 (m, H_5, $^{3}J_{5\text{-}6A}$ = 2.3, $^{3}J_{5\text{-}6B}$ = 5.3), 3.28 (t (dd), H_4, $^{3}J_{4\text{-}3} = {}^{3}J_{4\text{-}5}$ = 8.7), 3.35 (t (dd), H_3, $^{3}J_{3\text{-}2} = {}^{3}J_{3\text{-}5}$ = 8.7), 3.66 (dd, H_{6B}, $^{2}J_{6B\text{-}6A}$ = 11.7, $^{3}J_{6B\text{-}5}$ = 5.3), 3.82 (d, H_1, β product, $^{3}J_{1\text{-}2}$ = 8.7), 3.83 (dd, H_{6A}, $^{2}J_{6A\text{-}6B}$ = 11.7, $^{3}J_{6A\text{-}5}$ = 2.3), 4.48 (d, H_1, α product, $^{3}J_{1\text{-}2}$ = 4.8), 4.71 (s, 4O<u>H</u>). ^{13}C-NMR (CD_3OD, ppm): alkyl chain 14.38 (C_{12}), 23.67 (C_{11}), 28.38 (C_3), 30.40, 30.64, 30.69, 30.73, 31.13 (C_2, C_4-C_9), 33.02 (C_{10}), 47.19 (C_1), sugar moiety 63.02 (C_6), 71.95, 74.98, 78.90, 78.98 (C_2-C_5), 91.89 (C_1, β product).

***N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]amines** were prepared according to Erickson's procedure.[29,13] The appropriate alkylamine (100 mmol) was dissolved in 2-propanol (200 mL) and added to a stirred solution of D-lactose (60 mmol) in water (100 mL). After a while the solution became turbid. After 48 hours, the suspension was heated at 60°C for 30 min, and a clear solution was obtained. The solvents were evaporated under reduced pressure. In order to remove all the water, the residue was taken up twice in ethanol and the solvents were re-evaporated, finally the compounds were dried under vacuum. The (slightly yellow) solids were dissolved in ethanol, filtered over celite and were then allowed to crystallize. The white crystals were washed with ethanol and ether (to remove residual amine). The yields averaged 68%, and were not optimized.

***N*-Octyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]amine.** ^{1}H-NMR (DMSO-d_6, ppm): alkyl chain 0.85 (t, 3H, $^{3}J_{8\text{-}7}$ = 6.7), 1.24 (bs, 10H), 1.40 (m, 2H), 2.19 (bs, 1H), 2.48 (m, H_{1A}, falls partly under the DMSO-d_6 signal), 2.77 (m, H_{1B}), sugar moiety 2.92 (m, H_2), 3.13-3.64 (m, H_3-H_6, $H_{2'}$-$H_{6'}$), 3.70 (d, H_1, β product, $^{3}J_{1\text{-}2}$ = 8.5), 4.19 (d, $H_{1'}$, $^{3}J_{1'\text{-}2'}$ = 7.0), 4.28 (d, H_1, α product, $^{3}J_{1\text{-}2}$ = 4.8), 4.30-5.11 (various peaks, 7O<u>H</u>). ^{13}C-NMR (DMSO-d_6, ppm): alkyl chain 14.31 (C_8), 22.45 (C_7), 27.17 (C_3), 29.08, 29.36, 30.28 (C_2, C_4, C_5), 31.64 (C_6), 45.95 (C_1), sugar moiety 60.71 (C_6), 61.21 ($C_{6'}$), 68.46 ($C_{4'}$), 70.89 ($C_{2'}$), 73.54 (C_2, $C_{3'}$), 75.81 ($C_{5'}$), 75.89 (C_5), 75.94 (C_3), 81.75 (C_4), 86.80 (C_1, α product), 90.96 (C_1, β product), 104.18 ($C_{1'}$).

***N*-Alkyl-1-amino-1-deoxy-D-glucitols.** D-Glucose (7 g, 39 mmol), the appropriate alkylamine (2 molar equivalents), and 0.75 g Pd/C (5 %) in ethanol (75 mL) were stirred in a Parr apparatus under hydrogen pressure (60 bar) at 40°C overnight. Subsequently, the carbon was filtered off and the ethanol was evaporated under reduced pressure. The white solid was crystallized twice from ethanol (overall yield ca. 76%). Reductive amination with sodium borohydride has been described in literature.[10]

***N*-Octyl-1-amino-1-deoxy-D-glucitol.** ^{1}H-NMR (COSY, CD_3OD, ppm): 0.90 (t, 3H, $^3J_{8-7}$ = 6.9), 1.33 (bs, 10H), 1.52 (m, 2H), 2.60 (m, 2H), sugar moiety 2.71-2.79 (m, 2H), 3.64 (m, H_5, H_{6B}), 3.71 (m, H_4), 3.78 (m, H_3, H_{6A}), 3.87 (m, H_2), 4.59 (s, 5O<u>H</u>). ^{13}C-NMR (HETCOR, CD_3OD, ppm): alkyl chain 14.12 (C_8), 23.42 (C_7), 28.19, 30.10, 30.36 (C_3, C_4, C_5), 32.73 (C_6), 50.51 (C_1), sugar moiety 52.34 (C_1), 64.87 (C_6), 72.61 (C_2, C_3), 72.72 (C_5), 72.96 (C_4).

***N*-Alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols**. Lactose (5 g, 14 mmol), the appropriate alkylamine (2 molar equivalents), and 0.75 g Pd/C (5 %) in ethanol (50 mL) were stirred in a Parr apparatus under hydrogen pressure (80 bar, the reaction does also proceed when the pressure is reduced to 20 bar) at 70°C overnight. The catalyst was filtered off and the ethanol was evaporated under reduced pressure. The white solid was stirred in ether to remove excess alkylamine and then extracted continuously to remove residual alkylamine (average yields ca. 88%).

***N*-Dodecyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols.** ^{1}H-NMR (CD_3OD, ppm): alkyl chain 0.89 (t, 3H, $^3J_{12-11}$= 7.0), 1.29 (bs, 18H), 1.53 (m, 2H), 2.54-2.79 (m, 2H), sugar moiety 2.54-2.79 (m, 2H), 3.47-3.89 (m, H_3-H_6, H_2-$H_{6'}$), 4.02 (m, H_2), 4.44 (d, $H_{1'}$, $^3J_{1'-2'}$ = 7.3), 4.83 (s, 8O<u>H</u>). ^{13}C-NMR (CD_3OD, ppm): alkyl chain 14.35 (C_{12}), 23.62 (C_{11}), 28.38 (C_3), 30.35, 30.47, 30.60, 30.65, 30.69 (C_2, C_4-C_9), 32.98 (C_{10}), 50.81 (C_1) sugar moiety 53.87 (C_1), 62.73 ($C_{6'}$), 63.83 ($C_{6'}$), 70.61, 71.60, 72.83, 72.99, 74.87, 77.15, 82.13 (C_{2-5}, $C_{2'-5'}$) 105.31 ($C_{1'}$).

Acylation, general prodedure. Acetic anhydride or propionic anhydride (1.5 molar equivalents) was added to the *N*-alkyl-α,β-D-glucopyranosylamines, *N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-α,β-D-glucopyranosyl]amines, *N*-alkyl-1-amino-1-deoxy-D-glucitols, and the *N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols, respectively, in ethanol and stirred overnight. The solution was neutralized with Dowex OH^-, filtered and the ethanol was removed by evaporation under reduced pressure. Yields of the crude products ranged from 85-95%. The compounds were purified by crystallization.

***N*-Acyl,*N*-alkyl-β-D-glucopyranosylamines** were dissolved in a small amount of acetone and hexane was added to the point of precipitation. The products separated out from acetone/hexane as slightly yellow oils. The yellow impurities (not detectable by ^{1}H-NMR) were also the first to crystallize from acetonitrile. The supernatant was decanted and allowed to crystallize. The products precipitated as white oils/gels which became solid after drying. The glucopyranosylamines were solid but were very hygroscopic and therefore stock solutions were prepared for this type of compounds. Purified yields

ranged from 41-53%.

***N*-Propionyl-*N*-octyl-β-D-glucopyranosylamine (NC_3nC_8 glucose).** ^{1}H-NMR (CD_3OD, ppm): alkyl chain 0.89 (bt, 3H), 1.30 (bs, 10H), 1.61 (m, 2H), both H_1 fall under the sugar moiety, acyl group 1.11 (2t, 3H, $^3J_{3\text{-}2}$ = 7.3), 2.50 (2q, 2H, $^3J_{2\text{-}3}$ = 7.3), sugar moiety 3.25-3.89 (m, H_2-H_6, 8H, including 2H_1 of the alkyl chain), 4.84 (d, H_1, $^3J_{1\text{-}2}$ = 8.1), 5.45 (d, H_1, $^3J_{1\text{-}2}$ = 8.8), 4.91 (s, 4O<u>H</u>). ^{13}C-NMR (CD_3OD, ppm): alkyl chain 14.42 (C_8), 23.67 (C_7), 28.18 (C_3), 28.37, 29.94, 30.41 (C_2, C_4, C_5), 32.98 (C_6), 42.94, 44.82 (C_1), acyl group 9.82 (C_3), 27.64 (C_2), 177.68 (C_1), sugar moiety 62.93 (C_6), 71.41, 71.98, 79.24, 80.37 (C_2-C_5), 84.40, 88.02 (C_1).

***N*-Acyl,*N*-alkyl-[4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]amines** were crystallized from ethanol. The compounds formed "geolids" (*vide supra*) from ethanol. The compounds were freeze-dried and they formed white fluffy solids which contains one mol of water per mol of product. Yields were in the range 51- 60%. The products contain one mol of water per mol of compound.

***N*-Propionyl,*N*-decyl-[4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]amine (NC_3nC_{10} lactose).** ^{1}H-NMR (COSY, CD_3OD), ppm): alkyl chain 0.90 (t, 3H, $^3J_{10\text{-}9}$ = 7.1), 1.29 (bs, 14H), 1.62 (m, 2H), 3.27, 3.42 (2m, H_{1A}, H_{1B}), acyl group 1.11 (2t, 3H, $^3J_{3\text{-}2}$ = 7.4), 2.48 (2q, 2H, $^3J_{2\text{-}3}$ = 7.4), sugar moiety 3.49-3.62 (m, H_2, H_3, H_5, H_2-$H_{5'}$), 3.71 (dd, $H_{6A'}$, $^2J_{6A'\text{-}6B'}$ = 11.4, $^3J_{6A'\text{-}5}$ = 4.3), 3.80 (dd, $H_{6B'}$, $^2J_{6B'\text{-}6A'}$ = 11.4, $^3J_{6B'\text{-}5'}$ = 7.4), 3.82-3.84 (m, $H_{4'}$, H_{6B}), 3.90 (dd, H_{6A}, $^2J_{6A\text{-}6B}$ = 12.1, $^3J_{6A\text{-}5HH}$ = 2.0), 4.38 (d, $H_{1'}$, $^3J_{1'\text{-}2'}$ = 7.8), 4.87 (s, 7O<u>H</u>), 4.92, 5.46 (2d, H_1 $^3J_{1\text{-}2}$ = 9.00 Hz). ^{13}C-NMR (HETCOR, CD_3OD, ppm): alkyl chain 14.42 (C_{10}), 23.67 (C_9), 27.78 (C_3), 28.19, 28.40, 29.98, 30.28, 30.39, 30.45, 30.65, 30.75 (C_2, C_4-C_7), 33.01 (C_8), 42.92, 44.91 (C_1), acyl chain 9.79, 9.88 (C_3), 27.69, 27.75 (C_2), 177.50, 178.13 (C_1) sugar moiety 62.03, 62.13 (C_6), 62.50 ($C_{6'}$), 70.25 ($C_{4'}$), 71.16, 71.67 (C_2), 72.49 ($C_{2'}$), 74.77 ($C_{3'}$), 77.06 ($C_{5'}$), 77.50, 77.64 (C_5), 78.75 (C_3), 80.38 (C_4), 84.28, 87.80 (C_1), 105.02 ($C_{1'}$).

***N*-Acyl,*N*-alkyl-1-amino1-deoxy-D-glucitols** were crystallized from ethanol-ether (NC_2nC_8 glucitol and NC_3nC_{12} glucitol, yields 78% and 86%, respectively), ethyl acetate (NC_2nC_{10} glucitol, yield 60%, NC_3nC_{10} glucitol, yield 84%), ethanol-ether and subsequently ethyl acetate (NC_2nC_{12} glucitol, yield 42%), or from acetonitrile (NC_3nC_8 glucitol, yield 73%).

***N*-Propionyl,*N*-decyl-1-amino-1-deoxy-D-glucitol (NC_3nC_{10} glucitol).** ^{1}H-NMR (COSY, CD_3OD, ppm): alkyl chain 0.90 (2t, 3H, $^3J_{10\text{-}9}$ = 6.9), 1.30 (bs, 14H), 1.55, 1.61 (2m, 2H), 3.26-3.60 (m, 2H), acyl group 1.11 (2t, 3H, $^3J_{3\text{-}2}$ = 7.3), 2.47 (m, 2H), sugar moiety 3.26-3.60 (m, H_1), 3.60-3.80 (m, H_3-H_6), 3.98 (m, H_2), 4.81 (s, 5O<u>H</u>). ^{13}C-NMR (HETCOR, CD_3OD, ppm): alkyl chain 14.44 (C_{10}), 23.67 (C_9), 27.83, 28.04 (C_3), 28.30, 29.71 (C_2), 30.37, 30.38, 30.42, 30.52, 30.60, 30.63, 30.65, 30.69 (C_4-C_7), 32.98, 33.00 (C_8), 47.41, 50.53 (C_1), acyl group 10.07 (C_3), 27.11, 27.39 (C_2), 177.12, 177.21 (C_1), sugar moiety 50.67, 51.36 (C_1), 64.67 (C_6), 71.07, 71.55, 72.64, 72.90, 73.02, 73.16, 73.51, 74.17 (C_2-C_5).

***N*-Acyl,*N*-alkyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols.** Acetic acid or propionic acid (1.5 mol equivalents) were added to the alkylated glucose or lactose derivatives and stirred overnight. The solution was neutralized with Dowex OH^-, filtered and the ethanol was evaporated under reduced pressure. Crude yields 85-95%. The compounds were crystallized once or twice from methanol-acetonitrile mixtures, purified yields ranged from 58-76%.

***N*-Propionyl,*N*-decyl-4-*O*-(β-D-galactopyranosyl)-1-amino-1-deoxy-D-glucitols (NC_3nC_{10} lactitol).** ^{1}H-NMR (COSY, CD_3OD, ppm): alkyl chain 0.89 (t, 3H, $^3J_{10\text{-}9}$ = 6.5), 1.29 (bs, 14H), 1.55, 1.60 (2m, 2H), 3.18-3.50 (m, 2H), acyl chain 1.09, 1.12 (2q, 3H, $^3J_{3\text{-}2}$ = 7.3), 2.35-2.60 (m, 2H), sugar moiety 3.18-3.50 (m, H_1), 3.50-3.68 (m, H_3, $H_{3'}$, $H_{2'}$), 3.68-3.79 (m, $H_{6'}$, H_6, $H_{4'}$), 3.79-3.97 (m, H_4, $H_{5'}$, H_5), 4.06, 4.08 (2m, H_2), 4.47 (2d, $H_{1'}$, $^3J_{1'\text{-}2'}$ = 7.8, $^3J_{1'\text{-}2'}$ = 7.3), 4.89 (s, 8O<u>H</u>). ^{13}C-NMR (HETCOR, CD_3OD) alkyl chain 14.41 (C_{10}), 23.67 (C_9), 27.84 (C_3), 28.05, 28.29, 29.72, 30.41, 30.53, 30.61, 30.64, 30.68, 30.72 (C_2, $C_{4\text{-}7}$), 33.02 (C_8), 47.37, 50.74 (C_1), acyl chain 10.01 (C_3), 27.13, 27.37 (C_2), 177.04, 177.25 (C_1), sugar moiety 50.79, 51.62 (C_1), 62.46 (C_6), 63.61 ($C_{6'}$), 70.17, 70.25 (C_5), 70.80, 70.87 (C_2), 72.00, 72.03 ($C_{4'}$), 72.86 ($C_{3'}$), 73.09 ($C_{5'}$), 74.79, 74.81 ($C_{2'}$), 77.08, 77.11 (C_3), 83.25, 83.78 (C_4), 105.50, 105.75 ($C_{1'}$).

N.B. The signals for the acetyl groups are positioned at: ^{1}H-NMR (CD_3OD): 2.11, 2.16 (2s, 3H), ^{13}C-NMR (CD_3OD): 21.34, 21.93 (C_2), 173. 93, 174.21 (C_1).

Table 2. Elemental analyses.

Compound	Formula	Calculated			Found		
		% C	% H	% N	% C	% H	% N
NC_2nC_8 glucose	$C_{16}H_{31}NO_6$	57.64	9.37	4.20	57.84	9.33	4.28
NC_3nC_8 glucose	$C_{17}H_{33}NO_6$	58.77	9.57	4.03	59.01	9.61	4.09
NC_2nC_{10} glucose	$C_{18}H_{35}NO_6$	59.81	9.76	3.87	60.00	9.88	3.92
NC_3nC_{10} glucose	$C_{19}H_{37}NO_6$	60.77	9.93	3.73	61.15	9.99	3.81
NC_2nC_{12} glucose	$C_{20}H_{39}NO_6$	61.67	10.09	3.60	61.86	10.12	3.66
NC_3nC_{12} glucose	$C_{21}H_{41}NO_6$	62.50	10.24	3.47	62.85	10.40	3.53
NC_2nC_8 lactose	$C_{22}H_{41}NO_{11}.H_2O$	51.43	8.44	2.73	51.51	8.40	2.73
NC_3nC_8 lactose	$C_{23}H_{43}NO_{11}.H_2O$	52.36	8.60	2.75	52.55	8.56	2.66
NC_2nC_{10} lactose	$C_{24}H_{45}NO_{11}.H_2O$	53.22	8.75	2.59	53.41	8.61	2.65
NC_3nC_{10} lactose	$C_{25}H_{47}NO_{11}.H_2O$	54.04	8.89	2.52	54.31	8.70	2.58
NC_2nC_{12} lactose	$C_{26}H_{49}NO_{11}.H_2O$	54.82	9.02	2.46	55.10	8.98	2.52
NC_3nC_{12} lactose	$C_{27}H_{51}NO_{11}.H_2O$	55.54	9.16	2.40	55.67	9.18	2.40
NC_2nC_8 glucitol	$C_{16}H_{33}NO_6$	57.29	9.92	4.18	57.32	9.85	4.22
NC_3nC_8 glucitol	$C_{17}H_{35}NO_6$	58.43	10.09	4.01	58.51	10.22	4.01
NC_2nC_{10} glucitol	$C_{18}H_{37}NO_6$	59.48	10.26	3.85	59.75	10.27	3.86
NC_3nC_{10} glucitol	$C_{19}H_{39}NO_6$	60.45	10.41	3.71	60.41	10.56	3.86
NC_2nC_{12} glucitol	$C_{20}H_{41}NO_6$	61.35	10.55	3.58	61.35	10.62	3.57
NC_3nC_{12} glucitol	$C_{21}H_{43}NO_6$	62.19	10.69	3.45	61.93	10.45	3.58
NC_2nC_8 lactitol	$C_{22}H_{43}NO_{11}$	53.11	8.71	2.81	53.14	8.66	2.84
NC_3nC_8 lactitol	$C_{23}H_{45}NO_{11}$	54.00	8.87	2.74	54.05	8.85	2.74
NC_2nC_{10} lactitol	$C_{24}H_{47}NO_{11}$	54.84	9.01	2.66	54.99	8.93	2.72
NC_3nC_{10} lactitol	$C_{25}H_{49}NO_{11}$	55.64	9.15	2.60	55.86	9.09	2.75
NC_2nC_{12} lactitol	$C_{26}H_{51}NO_{11}$	56.40	9.28	2.53	56.63	9.19	2.64
NC_3nC_{12} lactitol	$C_{27}H_{53}NO_{11}$	57.12	9.41	2.47	57.27	9.29	2.57

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Chapter 3

Aggregation Behavior of *N*-Acyl,*N*-alkyl-β-D-aldosylamines and *N*-Acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols

3.1 Introduction

Lyotropic mesophases of the carbohydrate-derived surfactants described in chapter 2 were examined both at 40°C, at which the critical micelle concentrations were determined, and at ambient temperature. The characteristics of the mesophases indicate the shape of micelles formed in dilute solution.

The critical micelle concentrations were determined by two different techniques: drop tensiometry and titration microcalorimetry. From plots of the surface tension *vs* surfactant concentration, the surface tensions at the CMC were determined and the headgroup areas of the surfactant molecules at the air-water interface were calculated from the slope of the curve below the CMC.

Titration microcalorimetry provided, in addition to the critical micelle concentrations, the standard enthalpy of micellization, $\Delta_{mic}H°$. The standard Gibbs energies of micellization were calculated from the CMC, and thus the standard entropies of micellization could also be determined. The increments in standard enthalpies, Gibbs energies, and entropies of micellization per CH_2 for each series at 40°C offer important insights into the relationship between surfactant structure and the thermodynamic parameters describing aggregation.[a]

3.2 Lyotropic liquid crystalline behavior

Surfactants adsorb strongly at air-water interfaces and at oil-water interfaces, reducing the surface tension and the interfacial tension, respectively. When added to water, surfactants start to aggregate at a certain concentration (the critical micelle concentration, see also Chapter 1). Above the CMC, added surfactant leads to an increase in the concentration of micelles. At substantially higher concentrations, there is a disorder/order transition with the formation of lyotropic liquid crystals (mesophases).[1]

Four well established mesophases are: lamellar, (inverted) hexagonal, cubic, and nematic (Figure 1). The lamellar phase (L_α) consists of surfactant bilayers separated by water layers. The hexagonal phase (H_I) consists of elongated micelles with circular cross sections. The headgroups reside at the micellar surface with a continuous water region separating adjacent

[a] These derived thermodynamic parameters describe the formation of micelles by a mole of monomer.

micelles (Figure 1). One class of cubic mesophase (I_1) can be found at compositions between the micellar solution and the hexagonal phase. This phase comprises closely packed cubical arrays of small globular micelles. A second type of cubic phase (V_1), found at compositions between hexagonal and lamellar phases, consists of a three-dimensional bicontinuous network with both surfactant and water forming continuous zones. Both types of cubic phases are optically isotropic.[2] Nematic phases, found between the micellar solution and either the hexagonal or lamellar phase, consist of cylindrical micelles or ordered small disc micelles.[1] We do not discuss a more detailed classification of the different mesophases.[1]

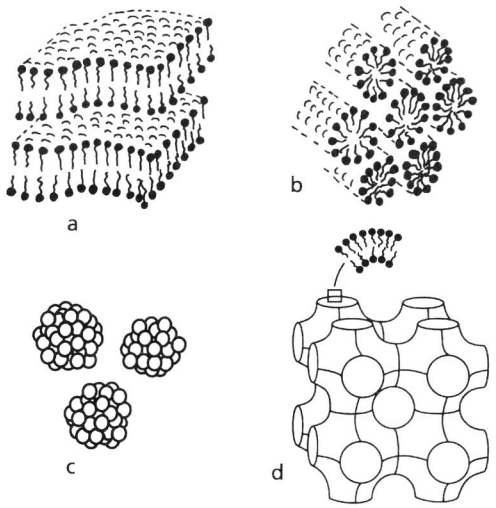

Figure 1. Some lyotropic mesophases: lamellar (L_α, a), hexagonal (b), and two cubic phases (I_1: c and V_1: d).

The shape of the aggregates in solution can be rationalized on the basis of the packing parameter (Chapter 1).[3,4] The packing parameter identifies the optimal cross-sectional surface area per molecule (a_0) for a particular shape of aggregate. For surfactants having alkyl chains with 8 - 12 carbon atoms, spheres are formed when $a_0 > 63$ Å^2, rods are formed if 42 Å^2 < a_0 < 63 Å^2, bilayers if 21 Å^2 < a_0 < 42 Å^2 and inverted structures are formed if $a_0 < 21$ Å^2.[5] Entropy favors the smallest possible micellar size and thus rods occur at a_0 values smaller than the a_0 values for a sphere, etc.[1]

The mesophase formed at the boundary of the micellar solution (the mesophase with the lowest surfactant concentration) provides an indication of the shape of the micelles in solution. An I_1 phase indicates spherical micelles, a hexagonal phase indicates rod-like micelles and a lamellar phase indicates either that the micelles in solution are disc-shaped or that vesicular aggregates are present in dilute solution. Further increases in surfactant

concentration lead to a continuing reduction of the surface area per molecule at the micelle surface. Therefore the expected mesophase transitions are:[1]

$$I_1 \rightarrow H_1 \rightarrow V_1 \rightarrow \text{lamellar } (L_\alpha)$$

Inverted phases will not be discussed, because these require relatively large hydrophobic tails and small hydrophilic headgroups.

Mesophases can be studied in various ways, including using the penetration technique. Pure surfactant is sandwiched between a microscope slide and a cover slip. The surfactant is melted and allowed to cool and, if possible, crystallize again. This process gives a well-defined surfactant boundary. The surfactant is then brought into contact with water. In these experiments, the whole concentration range from pure water to pure surfactant is covered.[6] Mesophases develop in concentric bands with characteristic optical textures which can be identified using a polarizing microscope.[1] The temperature dependence of the mesophase formation can be studied conveniently with the aid of a hot stage.[7]

3.2.1 Lyotropic mesophases formed by the carbohydrate-derived surfactants

To study the different lyotropic phases formed at ambient temperature and at 40°C, we performed penetration experiments at both temperatures; Table 1. The observations made at ambient temperature and at 40°C are similar in most cases. We did not investigate the nature of the optically isotropic phases further. For convenience, all optically isotropic phases are denoted as "cubic". This is an oversimplification, because not all optically isotropic phases are necessarily cubic.

The mesophase first encountered (*i.e.*, at the highest water concentration) is either a H_1 phase or a cubic phase. This result indicates the formation in solution of rods or spherical micelles, respectively. For most glucose- and glucitol-derived surfactants rod-shaped micelles are formed. The cubic phase formed from NC_3nC_{12} glucose is probably a V_1 phase, since the total number of alkyl carbons is too large to allow the formation of a hexagonal phase with the glucopyranoside headgroup. Propionylated glucitol-derived surfactants have higher Krafft temperatures than the acetylated ones. When mesophases did form in the contact experiments, they did not provide unambiguous clues as to the nature of the aggregates in dilute solution.

Table 1. Lyotropic mesophases of the glucose-, glucitol-, lactose- and lactitol-derived surfactants at ambient temperature and at 40 °C.

Compound	lyotropic mesophases at ambient temperature	lyotropic mesophases at 40 °C
NC_2nC_8 glucose	water-hex-bulk (isotropic)	water-hex-bulk (isotropic)
NC_2nC_{10} glucose	water-hex-bulk (viscous isotropic)	water-hex-bulk (viscous isotropic)
NC_2nC_{12} glucose	water-hex-cub-bulk (viscous isotropic)	water-hex-cub-bulk (viscous isotropic)
NC_3nC_8 glucose	water is absorbed without mesophases	water is absorbed without mesophases
NC_3nC_{10} glucose	water-hex-cub-bulk (viscous isotropic)	water-cub-bulk (viscous isotropic)
NC_3nC_{12} glucose	water-cub-cub-L_α-bulk (S_A)	water-cub-cub-L_α-bulk (S_A)
NC_2nC_8 glucitol	water-hex-cub-bulk (viscous isotropic)	water-hex-cub-bulk (viscous isotropic)
NC_2nC_{10} glucitol	water-hex-cub-L_α-bulk (S_A)	water-hex-cub-L_α-bulk (S_A)
NC_2nC_{12} glucitol	water-hex-cub-bulk (solid)	water-hex-cub-bulk (solid)
NC_3nC_8 glucitol	water is absorbed without mesophases	water is absorbed without mesophases
NC_3nC_{10} glucitol	$T_{krafft} = 28\,°C$[a]	water-hydrated bulk-bulk (solid)
NC_3nC_{12} glucitol	$T_{Krafft} = 48\,°C$	$T_{Krafft} = 48\,°C$[b]
NC_2nC_8 lactose	water-cub-hex-bulk (glass-like)	water-hex-bulk (glass-like)
NC_2nC_{10} lactose	water-cub-cub-hex-bulk (glass-like, S_A)[c]	water-cub-cub-hex-bulk (glass-like, S_A)[c]
NC_2nC_{12} lactose	water-cub-cub-hex-bulk (S_A)	water-cub-cub-hex-bulk (S_A)
NC_3nC_8 lactose	water-hex-bulk (viscous isotropic)	water-hex-cub-bulk (viscous isotropic)
NC_3nC_{10} lactose	water-hex-bulk (S_A)[c]	water-hex-cub-bulk (S_A)[c]
NC_3nC_{12} lactose	water-hex-bulk (S_A)	water-hex-cub-bulk (S_A)
NC_2nC_8 lactitol	water-cub-hex-bulk (solid)	water-cub-hex-bulk (solid)
NC_2nC_{10} lactitol	water-cub-cub-hex-bulk (S_A)	water-cub-cub-hex-bulk (S_A)
NC_2nC_{12} lactitol	water-cub-cub-hex-bulk (S_A)	water-cub-cub-hex-bulk (S_A)
NC_3nC_8 lactitol	water-hex-bulk (glass-like)	water-hex-bulk (glass-like)
NC_3nC_{10} lactitol	water-cub-cub-hex-bulk (solid)	water-hex-bulk (solid)
NC_3nC_{12} lactitol	water-hex-bulk (S_A)	water-hex-cub-bulk (S_A)

[a] The Krafft temperature (T_{Krafft}) is the temperature at which the solubility of the surfactant equals the CMC. The solubility of surfactants increases dramatically above T_{Krafft}.[8] [b]At 50 °C: water-cub-L_α-hydrated bulk-bulk (solid). [c]Although this compound does not show a clearing point in the DSC (Chapter 2), it can crystallize with an S_A-like texture.

Lactose- and lactitol-derived surfactants have larger headgroups than the monosaccharide-derived surfactants. Spherical micelles are formed by the acetylated lactose- and lactitol-derived surfactants,[9] whereas the propionylated surfactants most likely form rod-shaped micelles. This pattern demonstrates that a small change in the "lateral" substituent influences the morphology of micelles in solution. The NC_3nC_{10} lactitol appears to behave anomalously. From the mesophases observed, one would predict the formation of spherical micelles, whereas the corresponding C_8 and C_{12} derivatives form rod-shaped micelles.

3.3 Drop tensiometry

3.3.1 Critical micelle concentrations measured by drop tensiometry

Figure 2 is an example of the important plot involved in the determination of the CMC by drop tensiometry. Critical micelle concentrations were measured at 40 °C to preclude possible solubility problems. However, all carbohydrate-derived surfactants (except NC_3nC_{12} glucitol) dissolve in water at ambient temperature. Table 2 records the CMCs of the carbohydrate-derived surfactants measured by drop tensiometry at 40 °C. The critical micelle concentrations have the same order of magnitude as generally observed for nonionic surfactants and a number of trends are identified. The CMCs decrease by a factor of ten when the alkyl chain length is increased by two methylene groups. This tenfold decrease in CMC is also observed for polyethoxylated surfactants,[10] *N*-alkanoyl-*N*-methyl-glucamides (MEGAs),[11] and other nonionic surfactants[12-14]

Propionylated surfactants have slightly lower CMCs than their acetylated counterparts, which is accounted for by the larger hydrophobic components.[15] Addition of a methylene group in the short acyl chain, however, has a smaller effect (factor 1.5 - 2) on the CMC than the addition of a methylene group in the long alkyl chain (factor $\sqrt{10}$).

Generally speaking, the length of the alkyl chain determines the order of magnitude of the CMC. The headgroup size (monosaccharide *vs* disaccharide), shape (cyclic, acyclic, or a combination) as well as the configuration of the hydroxyl groups have only a small influence on the CMC. Table 2 shows that in our case, the nature of the headgroup influences the CMC within the order of magnitude determined by the chain length.[16,17]

Glucose-derived surfactants have lower CMCs than the lactose-derived surfactants, due to the smaller hydrophilic headgroup and the consequently relatively larger hydrophobic part. Surfactants with a reduced saccharide headgroup have lower CMCs than those with an intact cyclic structure. Probably, the (hydrated) alditol headgroup is somewhat smaller, but volumes of appropriate hydrated carbohydrate-derived headgroups are not known. (The values for the headgroup areas at the air-water interfaces are in most cases smaller for the alditols than for

the aldoses as will be shown in the next section).

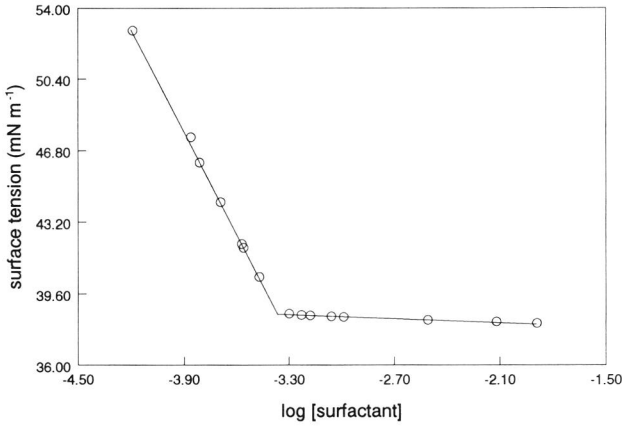

Figure 2. CMC determination of NC_2nC_{12} lactose by drop tensiometry.

Table 2. Critical micelle concentrations of the carbohydrate-derived surfactants measured by drop tensiometry at 40°C.[a]

compound	CMC (mM)	compound	CMC (mM)
NC_2nC_8 glucose[b]	25	NC_2nC_8 lactose[b]	40
NC_2nC_{10} glucose[b]	2.6	NC_2nC_{10} lactose[b]	3.4
NC_2nC_{12} glucose	0.31	NC_2nC_{12} lactose[b]	0.43
NC_3nC_8 glucose	18	NC_3nC_8 lactose	28
NC_3nC_{10} glucose	1.8	NC_3nC_{10} lactose	2.2
NC_3nC_{12} glucose	0.24	NC_3nC_{12} lactose	0.26
NC_2nC_8 glucitol	21	NC_2nC_8 lactitol	25
NC_2nC_{10} glucitol	1.9	NC_2nC_{10} lactitol	2.4
NC_2nC_{12} glucitol	0.20	NC_2nC_{12} lactitol	0.30
NC_3nC_8 glucitol	14	NC_3nC_8 lactitol	12
NC_3nC_{10} glucitol	1.1	NC_3nC_{10} lactitol	1.5
NC_3nC_{12} glucitol	0.13	NC_3nC_{12} lactitol	0.16

[a] The error in the measurements is about ± 2 in the last digit. [b] The CMCs of these surfactants have also been published by Rico-Lattes *et al.*,[18,19] the values are similar.

3.3.2 Surface tension at the CMC and headgroup area at the air-water interface

According to Table 3, the surface tension at the CMC decreases upon increasing chain lengths. Propionylated counterparts also display lower γ_{CMC} than the acetylated ones. Hence, the larger the hydrophobic part, the lower the surface tension at the CMC. This is not surprising. The interface becomes more alkane-like (*e.g.*, γ = 25.4 mN m^{-1} for dodecane).[14]

Surfactants with a glucitol headgroup seem to have slightly lower γ_{CMC} than the surfactants with a glucose headgroup. Both the monosaccharide-derived surfactants show much lower surface tensions at the CMC than the corresponding disaccharide-derived surfactants. Relatively high values for γ_{CMC} have also been observed for dodecyl β-D-maltose and for monododecyl esters of sucrose, raffinose, and stachyose.[5]

Lactose- and lactitol-derived surfactants show a similar reduction of the surface tension at the CMC (Table 3).

Table 3. Surface tension at the CMC of the carbohydrate-derived surfactants at 40 °C (mN m^{-1}).

	glucose	glucitol	lactose	lactitol
NC_2nC_8	35.6	35.0	43.4	42.9
NC_2nC_{10}	33.8	31.3	40.0	39.9
NC_2nC_{12}	30.6	30.3	38.5	39.4
NC_3nC_8	31.6	30.2	37.5	37.8
NC_3nC_{10}	29.3	29.3	34.1	37.1
NC_3nC_{12}	29.0	28.6	34.5	36.4

Table 4 records the area per molecule for each carbohydrate-derived surfactant at the air-water interface (A_0) at 40 °C. These areas are calculated from the maximum surface excess concentration Γ:[20,21]

$$\Gamma = -(RT)^{-1} \cdot (d\gamma/d(\ln[\text{surfactant}]) = (N_{AV}A_0)^{-1} = -(2.303RT)^{-1} \cdot (d\gamma/d(\log[\text{surfactant}]) \quad (1)$$

The smaller this value with respect to the cross section of the hydrocarbon chain, the better the surfactants can pack in the monolayer at the air-water interface and the more water can be eliminated from the surface.[22] For each series of carbohydrate-derived surfactants, the area is significantly lower for the C_{12} derivative than for the C_8 derivative. Further addition of methylene groups into the alkyl chain increases their mutual attraction in the monolayer. Consequently, the density of the monolayer is increased, thereby reducing A_0. This result is in contrast with the results obtained by Boullanger *et al.*[14] who found A_0 for alkyl 2-amino-2-

deoxy-β-D-glucopyranosides equal to ~50 Å^2 irrespective of the chain length (C_8-C_{12}), indicating that the packing at the interface is controlled solely by interactions between the headgroups (hydrogen bonding).

Table 4. Areas (Å^2) per surfactant molecule at the air-water interface of the carbohydrate-derived surfactants at 40°C.

	glucose	glucitol	lactose	lactitol
NC_2nC_8	56	55	68	64
NC_2nC_{10}	51	48	55	54
NC_2nC_{12}	38	35	57	55
NC_3nC_8	48	56	67	57
NC_3nC_{10}	48	52	57	59
NC_3nC_{12}	38	36	54	49

The areas at the air-water interface are similar for the surfactants having an acetyl or a propionyl substituent.

Based on our calculations, acylated disaccharide-derived surfactants containing eight carbon atoms in the alkyl chain possess large areas at the air water interface. The nonionic ethoxylated surfactants $C_{10}EO_8$ and $C_{12}EO_8$ also have large A_0 values (66 and 59 Å^2, respectively, at 40°C).[23] Probably, the relatively large hydrated hydrophilic part prevents a close packing at the air-water interface.

A clear correlation exists between the area per surfactant molecule at the air-water interface and the surface tension at the CMC - the closer the packing at the surface, the lower γ_{CMC}. Disaccharide-derived surfactants have a large A_0, and consequently also a high γ_{CMC}.[24] Söderberg *et al.*[5] found that A_0 increases with sequential addition of galactose structural units to the headgroup of carbohydrate-derived surfactants (sucrose < raffinose < stachyose).

In some cases, the area of the headgroups per molecule at the water-air interface (A_0) can be used as a rough estimation for a_0 in order to predict the micellar structure.[5] In our case, however, this procedure is not successful. Based on A_0 spherical micelles are predicted only for NC_2nC_8 lactose, NC_3nC_8 lactose, and NC_2nC_8 lactitol. This pattern disagrees with the predictions based on the mesophases formed by the surfactants.

3.4 Titration microcalorimetry

Standard enthalpies of micellization ($\Delta_{mic}H°$), Gibbs energies of micellization ($\Delta_{mic}G°$), and entropies of micellization ($\Delta_{mic}S°$), are important in understanding micelle formation in

aqueous solutions. In principle, the enthalpy of micellization for a given surfactant can be determined from the temperature dependence of the CMC. But this method has a major drawback, because $\Delta_{mic}H°$ is often significantly temperature dependent.[25,26] Enthalpies of micellization can be obtained accurately using modern, ultrasensitive titration microcalorimeters. With this technique the CMC is obtained and $\Delta_{mic}H°$ can often be read directly from a plot of the enthalpy of dilution *vs* the concentration.

3.4.1 Description of a microcalorimetric experiment

In a microcalorimetric experiment, a concentrated micellar solution (5-10 μL, concentration >> CMC) is injected into the sample cell which initially contains water. As the concentration of the surfactant in the sample cell is below the CMC of the surfactant, the micelles deaggregate upon injection. The accompanying heat is recorded by the microcalorimeter. The next aliquot of surfactant solution is injected when the system has reached thermal equilibrium. A typical titration plot is shown in Figure 3. The process takes place at constant pressure, an so the heat recorded in the titration experiment is equal to the change in enthalpy. Figure 4 shows the integrated plot, the enthalpy of dilution *vs* the injection

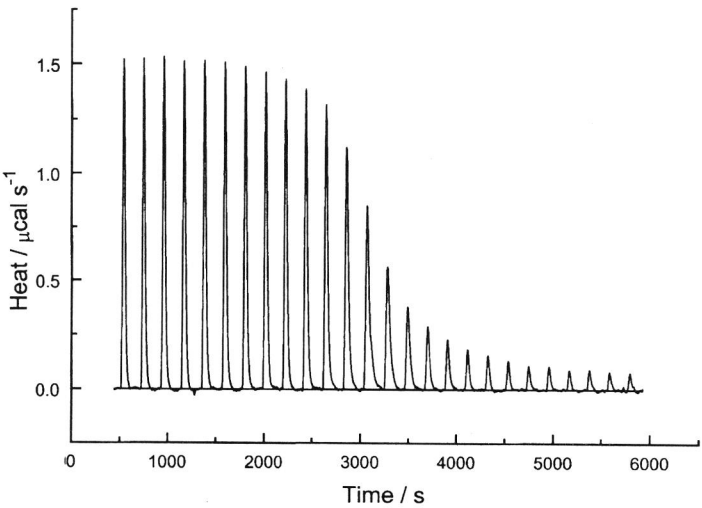

Figure 3. Calorimetric signals corresponding to dilution of a concentrated solution of NC_2nC_{12}lactitol at 40°C.

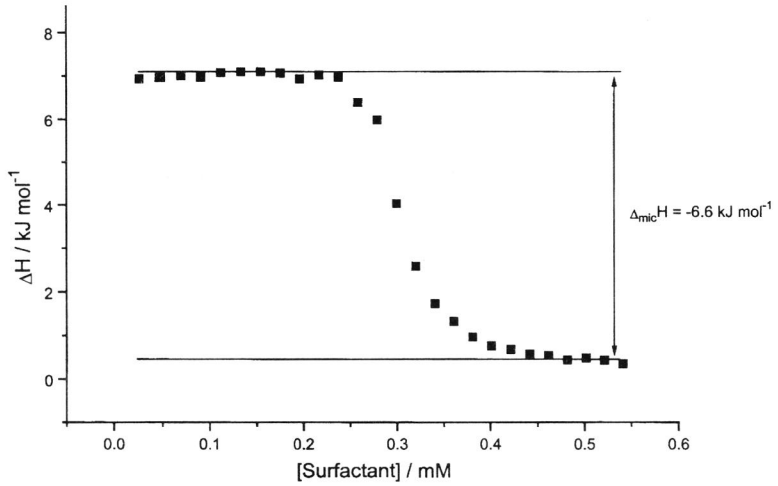

Figure 4. Enthalpy of dilution of NC_2nC_{12} lactitol at 40 °C.

number. The enthalpogram obtained is a step-shaped plot identifying two concentration regions where the recorded heats per mole of injected surfactant are almost constant.[27] In the low concentration region, the recorded heats are due to deaggregation and dilution of the monomers. As already explained, the surfactant concentration in the sample cell is below the

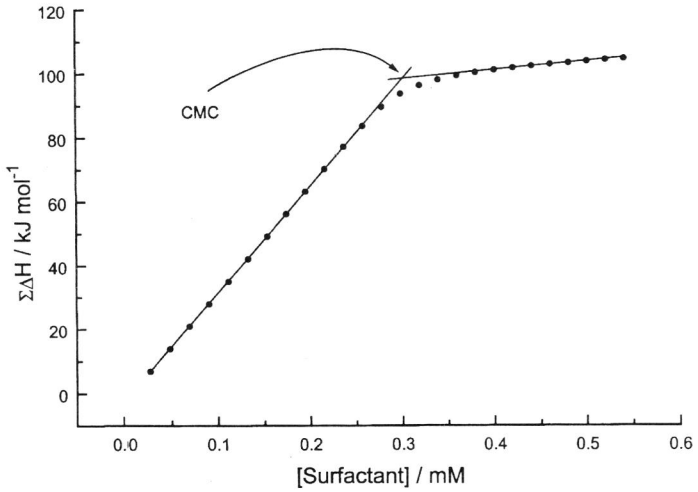

Figure 5. Cumulative enthalpy of dilution of NC_2nC_{12} lactitol vs concentration at 40 °C: determination of the CMC.

CMC and the micelles of the injected aliquots deaggregate. The large change in the recorded heat (in this particular case a decrease) over a small concentration range indicates that the CMC in the sample cell has been exceeded. Upon further additions of aliquots, the micelles in the injected micellar solution do not deaggregate and the recorded heat in the high concentration region can mainly be attributed to dilution of micelles. The enthalpy of micellization is the difference in recorded heat per mole of injected surfactant between the two horizontal parts of the step-shaped curve.

The CMC is obtained from a so-called van Os plot of the cumulative heats per mole of injected surfactant *vs* the concentration of surfactant in the sample cell (Fig. 5).[28-30]

3.4.2 Standard Gibbs energies and entropies of micellization

We used the phase equilibrium model to calculate the standard Gibbs energies and entropies of micellization (mole fraction scale).[31] According to the phase equilibrium model, the micelles in the system constitute a separate phase. The monomers are solutes in aqueous solution which are assumed to have ideal properties. Then for micelles in the micellar phase, at a fixed temperature and pressure, the chemical potential is denoted as:

$$(\text{chemical potential of micelles in the micellar phase})_{T,p} = \mu^* (X_N; \text{micellar}) \qquad (2)$$

Herein, X_N indicates the micellar phase with aggregation number N. The superscript * indicates a *pure* phase.

In the aqueous phase, there are monomers X(aq) which are assumed to have ideal properties. The chemical potential of the monomers expressed in the mole fraction scale[b] is given by equation (3):

$$\mu_x(aq) = \mu_x^\circ(aq) + RT \ln (x_x) \qquad (3)$$

Where x_x is the mole fraction of solute X and $\mu_x^\circ(aq)$ is the chemical potential of *solute* X in a *solution* when the mole fraction of aqueous X is *one*.

Surfactant monomers can go from one phase to the other: $X_N \rightleftharpoons N \cdot X(aq)$. At equilibrium, the potentials are balanced:

$$\mu^* (X_N; \text{micellar}) = N [\mu^\circ_x(aq) + RT \ln (x_x)] \qquad (4)$$

[b] The chemical potential of the surfactant in solution can also be expressed in a molar scale or in a molality scale.[31]

Divided by N:

$$\mu^* (X; \text{micellar}) \cdot N^{-1} = [\mu^\circ_x(aq) + RT \ln (x_x)] \quad (5)$$

By definition:

$$\Delta_{mic}G^\circ = [\mu^* (X_N; \text{micellar}) \cdot N^{-1}] - \mu^\circ_x(aq) \quad (6)$$

thus:

$$\Delta_{mic}G^\circ = RT \ln (x_x) \quad (7)$$

In words, $\Delta_{mic}G^\circ$ is the change in standard potential for one mole of monomer passing from the aqueous solution into the micellar phase formed by N monomers. Furthermore, the mole fraction x_x is:

$$x_x = n_x \cdot (n_x + n_1)^{-1} \quad (8)$$

Herein, n_1 is the amount of water and n_x the amount of surfactant in the aqueous surfactant solution. For dilute solutions, $n_x + n_1 \simeq n_1$, thus:

$$x_x = n_x \cdot n_1^{-1} = (n_x \cdot V^{-1}) \cdot (V \cdot n_1^{-1}) = CMC \cdot (V \cdot n_1^{-1}) \quad (9)$$

Where V is the volume of the system, which is approximately the volume of pure water in the ideal solution and consequently, $(V \cdot n_1^{-1})$ is approximately the molar volume of water, which is 55.08 mol L^{-1} at 40°C. The amount of monomers per volume is equal to the CMC of the surfactant. Thus the equation by which the standard Gibbs energies of micellization are calculated is given by (10):[32]

$$\Delta_{mic}G^\circ = RT \ln (CMC / 55.08) \quad (10)$$

The advantage of nonionic surfactants over ionic surfactants is that equation (10) can be used without the necessity to take into account the degree of counterion binding. For ionic surfactants, the extent of counterion binding has to be estimated[31] and as a result, equation (10) is more complicated and less accurate.

The standard entropy of micelle formation per mole of monomer is calculated from:

$$\Delta_{mic}S^\circ = (\Delta_{mic}H^\circ - \Delta_{mic}G^\circ) / T \quad (11)$$

In general, the entropy term provides the main driving force for micelle formation by nonionic surfactants.[28,33-36] As micelles are formed, the hydrophobic hydration layers around the alkyl chains are broken down (Chapter 1). This process is accompanied by a gain in entropy and represents the driving force for hydrophobic interactions within micelles. The nature of this hydrophobic effect has been discussed in detail.[37]

3.4.3 CMCs determined by titration microcalorimetry

Table 5 shows the experimental data obtained using titration microcalorimetry. The critical micelle concentrations are similar to the CMCs determined by drop tensiometry. The small discrepancies in the values obtained by the two different methods do not show a consistent trend, *i.e.*, one method does not always yield lower values than the other.

CMCs of surfactants with the same headgroup but with alkyl chains longer than C_{12} cannot be measured by drop tensiometry, due to the very low surfactant concentrations that need to be used. The migration of surfactant monomers to the expanding surface during drop formation disturbs the measurements. The sensitivity of the titration microcalorimeter is primarily determined by the magnitude of the enthalpy of micellization and by possible nonideality of the solutions.[27] $\Delta_{mic}H°$ increases with increasing chain length and nonideality is only observed when the CMCs measured are high. Thus CMCs of chain analogs with an alkyl chain containing more than 12 carbon atoms can be measured by microcalorimetry.

3.4.4 Enthalpy of micellization obtained by titration microcalorimetry

Standard enthalpies of micellization were obtained directly from the enthalpograms (Table 5, $\Delta_{mic}H°$ experimental). Surfactants with a decyl or dodecyl chain produced enthalpograms conforming to the text-book case in which the heats per mole of injected surfactant were constant over the two ranges, above and below the CMC, in the sample cell. But for octyl-chain analogs there was a slow increase in the injected heats in the premicellar region, indicating a concentration-dependent change in interactions. This slope is accounted for in terms of non-ideal thermodynamic properties of the solutions in both the syringe and the sample cell and reflects micelle-micelle, monomer-monomer, and monomer-micelle interactions.[27,38] This feature was especially pronounced for the C_8 surfactants because, as a consequence of high CMC, the concentration of surfactant in the syringe was high.[27,28]

Table 5. CMCs and thermodynamic parameters of micellization of glucose-, glucitol-, lactose-, and lactitol-derived surfactants at 40 °C.

Compound	CMC (mM)	$\Delta_{mic}H°$ (kJ mol^{-1}) experimental	$\Delta_{mic}H°$ (kJ mol^{-1}) calculated	$\Delta_{mic}G°$ (kJ mol^{-1})	$T\Delta_{mic}S°$ (kJ mol^{-1})
NC_2nC_8 glucose	21	endothermic	+1.4	-20.5	21.9
NC_2nC_{10} glucose	2.9	-3.0	-2.9	-25.6	22.7
NC_2nC_{12} glucose	0.26	-7.7	-7.5	-31.9	24.4
NC_3nC_8 glucose	20	~ +2.7	+3.4	-20.6	24.0
NC_3nC_{10} glucose	1.8	-1.3	-1.3	-26.9	25.6
NC_3nC_{12} glucose	0.19	-5.4	-5.7	-32.8	27.1
NC_2nC_8 glucitol	21	> +0.9	+1.7	-20.5	22.2
NC_2nC_{10} glucitol	2.0	-2.6	-2.5	-26.6	24.1
NC_2nC_{12} glucitol	0.18	-7.2	-7.0	-32.9	26.0
NC_3nC_8 glucitol	13	≥ +2.6	+3.0	-21.8	24.7
NC_3nC_{10} glucitol	1.2	-1.9	-1.8	-27.9	26.1
NC_3nC_{12} glucitol	0.11	-7.2	-7.2	-34.3	27.1
NC_2nC_8 lactose	35	+2.0	+4.3	-19.2	23.5
NC_2nC_{10} lactose	4.6	-1.4	-1.2	-24.4	23.2
NC_2nC_{12} lactose	0.45	-5.3	-5.3	-30.5	25.2
NC_3nC_8 lactose	24	+5.0	+7.5	-20.1	27.6
NC_3nC_{10} lactose	2.6	+0.1	0	-25.9	25.9
NC_3nC_{12} lactose	0.31	-4.1	-4.0	-31.5	27.5
NC_2nC_8 lactitol	24	>+1.1	+2.3	-20.2	22.5
NC_2nC_{10} lactitol	3.3	-1.9	-1.9	-25.3	23.5
NC_2nC_{12} lactitol	0.31	-6.6	-6.5	-31.5	25.0
NC_3nC_8 lactitol	18	> +2.3	+2.9	-20.8	23.7
NC_3nC_{10} lactitol	1.8	-1.5	-1.4	-26.9	25.5
NC_3nC_{12} lactitol	0.16	-6.1	-6.2	-33.1	26.9

Therefore, these enthalpograms were fitted using an iterative procedure incorporated into a Turbo-Basic program. The equations describing deaggregation of the micelles took account of the non-ideal properties of the solution in both sample cell and injected aliquots using

enthalpic pairwise interaction parameters involving micelles and monomers in the aqueous solutions. The aggregation number for the micelles was set at 50.[19,39] The enthalpies of micellization obtained via the program did not depend on the aggregation number. The remaining variable was the standard enthalpy of micelle formation. Satisfactory agreements were obtained between calculated and observed enthalpograms. The calculation and the method were supported by the results which produced enthalpies of micelle formation which conformed to the pattern observed for the C_{10} and C_{12} surfactants.

Figures 6 and 7 show the experimental and fitted enthalpograms of NC_2nC_{12} lactitol and NC_2nC_8 glucitol. Enthalpies obtained using the computer program, are listed in Table 5.
There are two contributions to $\Delta_{mic}H°$: (i) an endothermic contribution from headgroup interactions and (ii) an exothermic contribution from alkyl chain packing.[36,40-42] For alkylpolyethyleneglycol ethers the magnitude of the endothermic contribution of the headgroups depends on the extent to which water is liberated into the bulk solvent upon micellization. As the degree of ethoxylation increases, the hydration and $\Delta_{mic}H°$ increase correspondingly. Disaccharide derivatives have more hydroxyl groups and show an increase in $\Delta_{mic}H°$ (*i.e.* more endothermic) relative to their monosaccharide counterparts.

On going from C_8 to C_{12} the exothermic contribution of the alkyl chain increases, whereas the endothermic contribution of the headgroup remains constant and, therefore, the enthalpy of micellization becomes more favorable. Hence, $\Delta_{mic}H°$ changes from endothermic to exothermic. It is possible that for a given surfactant at a certain temperature, the endothermic contribution of the headgroup and the exothermic contribution of the chain cancel out and, consequently, $\Delta_{mic}H°$ equals zero. The temperature at which $\Delta_{mic}H° = 0$ may be called the transition temperature. According to Table 5 NC_3nC_{10} lactose has a transition temperature of 40°C. The transition temperature at which $\Delta_{mic}H°$ changes sign from positive to negative is lower for analogs with longer alkyl chains.[11] Therefore it is not surprising that at 40°C the analogs with a C_8 chain are below and the C_{12} analogs are above the transition temperature.[28,43]

The contribution of each methylene group to the enthalpy of micellization for each series, $\Delta_{mic}H°$ (CH_2), is approximately -2.4 kJ mol^{-1} (Table 6). This pattern is in good agreement with increments reported for other surfactants.[11,42,44-46] In our case, the $\Delta_{mic}H°$ (CH_2) are self-consistent and do not show large deviations from the average value.

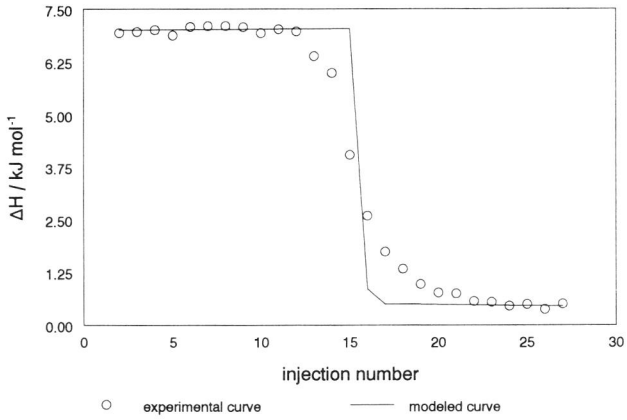

Figure 6. Experimental and fitted enthalpograms of NC_2nC_{12} lactitol.

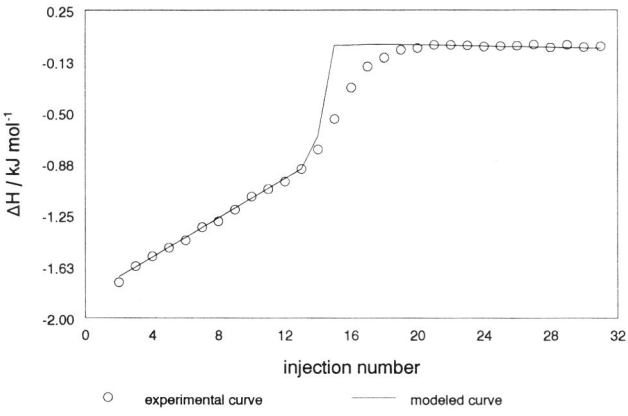

Figure 7. Experimental and fitted enthalpograms of NC_2nC_8 glucitol.

Table 6. Contributions of a CH_2 group to $\Delta_{mic}H°$, $\Delta_{mic}G°$, and $T\Delta_{mic}S°$ at 40 °C for a series of glucose-, glucitol-, lactose-, and lactitol-derived surfactants.

Compound	$\Delta_{mic}H°$ per CH_2 (kJ mol^{-1})	$\Delta_{mic}G°$ per CH_2 (kJ mol^{-1})	$T\Delta_{mic}S°$ per CH_2 (kJ mol^{-1})
NC_2nC_n glucose	-2.2	-2.9*	0.6*
NC_3nC_n glucose	-2.3	-3.1	0.8
NC_2nC_n glucitol	-2.2	-3.1	0.9
NC_3nC_n glucitol	-2.5	-3.1	0.6*
NC_2nC_n lactose	-2.4*	-2.8	0.4 ‡
NC_3nC_n lactose	-2.8*	-2.8	-[b]
NC_2nC_n lactitol	-2.2	-2.8	0.6
NC_3nC_n lactitol	-2.3	-3.1	0.8

[a] The regression constant exceeds 0.999, except for the results marked with * (0.98-0.99) and ‡ (0.81). [b] The value of $T\Delta_{mic}S°$ for NC_3nC_8 lactose deviates from the general trend. Therefore, $T\Delta_{mic}S°$ per CH_2 for this series was not calculated.

3.4.5 Gibbs energy and entropy of micellization obtained by titration microcalorimetry

All estimates of $\Delta_{mic}G°$ are negative, their absolute values increase with increasing chain length. The contribution of each CH_2 group to $\Delta_{mic}G°$ is -3.0 kJ mol^{-1}.[5,11,12,14,33,41,42,46-50] This is slightly lower than the standard Gibbs energy of transfer per CH_2 of *n*-alkanes from water to pure liquid, because the environment of a given CH_2 group in the interior of a micelle differs from that in the pure liquid.[33,35,50,51]

The entropy terms ($T\Delta_{mic}S°$) are positive and increase with increasing chain length. Estimates of $T\Delta_{mic}S°$ are large compared with those for ionic surfactants. The hydrophobic hydration of alkyl chains belonging to ionic surfactants is probably less than for nonionic surfactants, due to the strongly hydrated headgroups of the anionic surfactants. Consequently, the amount of entropy gained upon micellization is less for the anionic surfactants.[34,35,36] $T\Delta_{mic}S°$ per CH_2 is *c.* 0.7 kJ mol^{-1}. The main driving force for micellization at 40 °C is provided by the entropy term, supported in some cases by an exothermic enthalpy term.

3.4.6 The effect of variations in the carbohydrate-derived surfactants on the standard Gibbs energies of micellization

When the length of the alkyl chain is increased, the standard Gibbs energy of micellization becomes more favorable by 3.0 kJ mol^{-1} per CH_2. Surprisingly, this is mainly due to the decrease in *enthalpy* of micelle formation. Thus, although $\Delta_{mic}S°$ is the driving force for the micelle formation by surfactants with short chain lengths, the *enthalpy* change predominates for CH_2 increments as the length of the chain is increased. This pattern has also been observed for other surfactants and alcohols with long chains and has been accounted for by a degree of backfolding of the chains.[35]

Changing the acyl group from acetyl to propionyl leads to a more favorable standard Gibbs energy of micellization. This pattern is dominated by the *entropy* change and finds its origin in the increase in the hydrophobic character of the surfactant. Consequently, the hydrophobic hydration shell is larger and more entropy is gained when the monomers aggregate to form micelles. The CH_2 of the propionyl group is too small to give the effect of backfolding.

As mentioned earlier, a lactose-derived headgroup is less favorable for micelle formation compared to a glucose-derived headgroup. An increase in the number of hydroxyl groups increases the endothermic contribution to the enthalpy of micellization and renders the change in Gibbs energy less favorable.

An alditol headgroup is more favorable for micelle formation than an aldose headgroup. This pattern is mainly caused by the changes in the enthalpy term and indicates that the hydration layers of the reduced carbohydrate headgroups are smaller.

Consequently, NC_3nC_{12} glucitol exhibits the most favorable standard Gibbs energy of micellization and forms the most stable micelles.

3.5 Conclusions

Judging from their lyotropic liquid-crystalline behavior, the monosaccharide-derived surfactants and the propionylated disaccharide-derived surfactants form cylindrical micelles. The acetylated disaccharide-derived surfactants appear to form spherical micelles.

The disaccharide-derived surfactants show higher surface tensions at the CMC and larger areas per surfactant molecule at the air-water interface. Increasing alkyl chain lengths leads to lower γ_{CMC} values and smaller headgroup areas at the air-water interface.

The carbohydrate-derived surfactants show CMCs, standard enthalpies, standard Gibbs energies and standard entropies of micellization which are linear functions of alkyl chain length, indicating equivalence with respect to micelle formation of the methylene groups at least beyond C_7. The decrease in CMC is tenfold when the chain length is increased by two

methylene groups. The contribution of an additional CH_2 group to $\Delta_{mic}H°$, $\Delta_{mic}G°$, and $T\Delta_{mic}S°$ at 40 °C is -2.4 kJ mol^{-1}, -3.0 kJ mol^{-1}, and 0.7 kJ mol^{-1} respectively. The consistency of the increments per methylene group of $\Delta_{mic}H°$, $\Delta_{mic}G°$, and $T\Delta_{mic}S°$ sheds important light on the "hydrophobic " component in micelle formation of nonionic amphiphiles. The more favorable standard Gibbs energies (and the lower CMCs) for the longer chain analogs are caused predominantly by an exothermic shift in the enthalpy of micelle formation.

3.6 Experimental

Drop tensiometry. Critical micelle concentrations were determined with a TVT 1 Lauda drop tensiometer. Doubly distilled water was used. The determination of a CMC covered 15 measurements in the concentration range of roughly 0.1 · CMC to 10 · CMC. The measured surface tension is the mean value of 4 - 5 drop cycles.

Titration microcalorimetry. A Microcal Omega titration microcalorimeter (Microcal, Northampton, MA, USA) was used. Water was doubly distilled and all solutions were degassed before use. The solution in the sample cell was thermostatted at 40 °C, and stirred (350 rpm). An aqueous surfactant solution (5-10 μL, concentration >> CMC) was injected under computer control into the sample cell, which initially contained 1.3 mL of water. The heat absorbed or evolved was recorded and after thermal equilibrium was reached, the next aliquot of 5-10 μL was injected. This procedure was repeated until the concentration of surfactant in the sample cell was well above the CMC. The crude data (Figure 3) were analyzed using Omega software (Origin 2.9), yielding a plot of the enthalpy of dilution against surfactant concentration in the cell, the enthalpogram (Figure 4).[28,29,30]

Calculated enthalpies of micellization. The experimental enthalpograms were fitted using an iterative procedure incorporated into a Turbo-Basic program. Three variable interaction terms (a monomer-monomer interaction term, a monomer-micelle interaction term and a micelle-micelle interaction term) were introduced and accounted for the slopes of the step-shaped plot. The CMC indicated the turning point and, finally, an estimate for the enthalpy of micellization gave the right distance between the "horizontal" lines before and after the point at which the CMC had been reached. The fit was only reliable if initial estimates of the enthalpy of micellization were close to the final value.

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CMCs measured using drop tensiometry.

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Chapter 4

Practical Applications of *N*-Acyl,*N*-alkyl-β-D-aldosylamines and *N*-Acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols

4.1 Introduction

We synthesized the carbohydrate-derived surfactants described in Chapter 2 in order to investigate their potential use as (co-)surfactants in detergent systems. Their performance, foam capacity and foam stability, biodegradation, and biotoxicity have been determined.

The performance of the carbohydrate-derived surfactants in oily soil removal was determined by adding each to a typical laundry detergent (powder) formulation in mini-bottle tests. The results were compared to the performance of a benchmark formulation.

In order to determine their applicability, we further measured foamability and foam stability of the surfactants. Consumers often relate the presence of foam in wash water to the effectiveness of a detergent solution. The absence of extensive foam is associated, albeit incorrectly, with an absence of cleaning action. Therefore, detergents used for hand-wash should produce sudsy water. In contrast, high foamabilities may cause technical problems in washing machines.

Surfactants applied in detergents and other industrial and household cleaning products are large volume chemicals. After being used, they pass the waste water treatment plants (WWTP) and finally end up in the environment. It is therefore important that surfactants are biodegraded (completely) within the period they reside in a WWTP. Another important issue is the toxicity of these substances (if they are not fully degraded in the WWTP) and their degradation products. We determined biodegradability using closed-bottle tests and tested the influence of the surfactants on the growth of four different micro-organisms.

Each subject introduced in this chapter (performance, foamability and foam stability, biodegradation and biotoxicity) is preceded by introductory paragraphs in which some background information is given and the techniques are explained briefly.

4.2 Detergency

4.2.1 Trends in detergency

Surfactants have found applications in textiles and fibres (17%), cosmetics and pharmacy (7%), mining, flotation and oil production (7%), paints, plastics and resins (5%), food industry

(5%), pesticides (2%), and in the paper industry (2%). Their main application is in the washing and cleaning sectors (44%).[1,2]

Table 1 shows the ingredients of common laundry detergent systems. The actual concentrations of the ingredients depend on the type of detergent: heavy or low duty, powder or liquid, compact or conventional. Surfactants are the most important components in detergents.[3-9] Their main function consists of assisting in the soil removal process. Structures of some surfactants used in detergents are shown in Figure 1.

Table 1. Laundry detergent ingredients (phosphate-free).[a]

Component	Function	Weight %[b]
Surfactants:		
- anionics (alkyl benzenesulfonates alkylsulfates, alkyl ethersulfates)	cleaning and foam formation	10-30
- nonionics (fatty alcohol ethoxylates)		0-10
Builders/Cobuilders:		
- zeolite	reduction of water hardness: complexation of Ca^{2+}	20-40
- citrate	and Mg^{2+} and ion exchange	0-5
- polycarboxylate		0-5
- sodium carbonate	maintaining alkaline conditions	5-30
- sodium silicates	alkalinity, corrosion inhibition	5-20
Bleaches:		
- perborate, percarbonate	chemical oxidation of persistent stains	0-15
- activator	perborate bleaching at lower temperatures (TAED)	0-5
Enzymes (*e.g.* proteases)	removal of protein-based stains	0-3
Fluorescent whitening agents:		
- stilbene derivatives	adherance to fibers ("whiter look")	0.1-0.5
Antiredeposition agents:		
- sodium carboxymethylcellulose	keep dirt in suspension once it has been removed from a fabric	0-2
Filler		0-20
-sodium sulfate	filler, ionic strength	
Other	perfumes, dyes, anti-dye transfer polymers, soil release polymers, cationic surfactants (fabric softeners), bleaching stabilizers, foam inhibitors (silicon oils, surfactants), solvents (water, alcohols, glycols)	

[a] Phosphate-containing detergents still have a significant share in Europe and even predominate in Eastern Europe, Asia, Africa, Australia, and Latin America. [b] Actual amounts depend on the type of detergent.[3,4,5,6,7]

The cleaning properties of soaps (sodium or potassium neutralized fatty acids) were already known in antiquity.[9] Prior to World War I, laundry detergents were mainly composed of

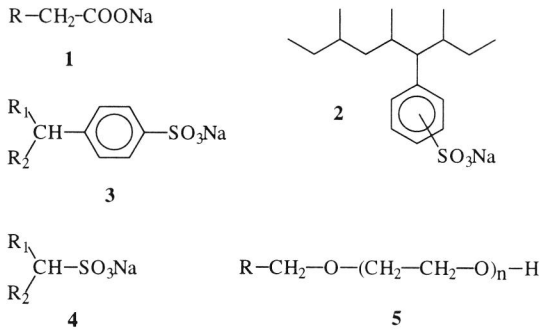

Figure 1. Soap (1), tetrapropylenebenzene sulfonates (2), linear alkylbenzene sulfonates (3), alkylsulfates (4), and fatty alcohol ethoxylates (5).

soaps. At the beginning of this century the limitations of soap (alkalinity and sensitivity to hard water) were recognized and the first successful synthetic surfactants (the fatty alcohol sulfates) were launched in 1928 to overcome these problems.[10] In the 1930s, long chain alkylbenzene sulfonates (ABS) were introduced as detergents. These first alkylbenzene sulfonates were highly branched and nonbiodegradable.[6,11] Tetrapropylenebenzene sulfonate (TPS) was the main component of synthetic laundry detergents until the 1960s. After a very hot summer, the nonbiodegradability of TPS resulted in large foam formations in sewage treatment plant and waterways.[1] Subsequently, TPS was replaced by the linear alkylbenzene sulfonates (LAS). To date, LAS is the main surface-active ingredient of commercial laundry detergents.[12]

Due to their implication in the eutrophication of waterways, phosphates were either banned in most Western countries in the 1980s (*e.g.* Switzerland) or their concentrations were fixed to a limit (*c.* 5.5% of the detergent formulation).[7,8,9] Their function was taken over by so-called zeolite-based builder systems. In large parts of the world, however, phospate-containing detergents (sodium tripolyphosphate, STP) either still have a significant market share (Great Britain, France, Spain) or even predominate (Eastern Europe, Central and Southern Asia, Africa, Australia and Latin America).[7]

In the early 1970s, liquid detergents were introduced.[6,13] Currently, liquid detergents have a majority market share of 50-60% in the U.S., whereas in Europe the use of liquid detergents is only about 13%.[13,14]

In 1987, the KAO Corporation in Japan launched the first compact high-density powder and evoked a revolution in this field.[6,13] Formulating concentrated liquid products creates all sorts of technical challenges, *e.g.* keeping the formulation stable. Developments in this field continue.[15,16] Today, compacts have largely taken over the market in the Western world.[6,13,15]

In the 1990s carbohydrate-derived surfactants have emerged as the fastest growing type of surfactants. Especially alkyl polyglucosides and alkyl glucamides are being used in detergents,

their major application field being dish-washing detergents[10,17-23] (see also Chapter 1). These surfactants show synergism with other surfactants and thus the total amount of active surfactants in formulations can be decreased. However, due to their high prices compared to LAS and alcohol ethoxylates, these surfactants still find limited application in laundry detergents.

The properties of carbohydrate-derived surfactants fit into current consumer requirements for detergents: environmentally friendly products and sensitive skin formulations, efficiency in cold water and reduced water levels, smaller volume detergent package for the ease of storage and above all else, value.[15]

4.2.2 Mechanism of detergency

Cleaning is a complex process due to the large variety of soils and substrates (*e.g.* cloth).[24] There are generally two types of soil.[24,25] Liquid (oily) soil which may contain sebum (skin fats), fatty acids, oils, fatty alcohols, *etc.*[24] Solid or particulate soil often contain hydrophobic and hydrophilic carbon, skin protein, iron oxide, and clay particles.[24] Adhesion of both types of soil to cloth occurs mainly by van der Waals forces. Nonpolar soils are therefore more difficult to remove than polar soils, especially when the substrate is hydrophobic (*e.g.*, polyester).[24]

Solid soil is removed by wetting of the substrate and the soil followed by adsorption of surfactants at the interfaces. Water induces the formation of electrical double layers at the substrate/liquid and particle/liquid interfaces. Adhesion is decreased by repulsion stemming from the charges on substrate and particle which almost always have the same sign. Anionic surfactants are especially effective in increasing the mutual repulsion between substrate and particle.[24] Adsorption of surfactants at interfaces reduces the interfacial tensions[26] and consequently the work of adhesion is diminished. Adsorption is probably the major mechanism of soil removal by nonionics.

The removal of oily soil is mainly accomplished by the "rollback" mechanism. The contact angle between the soil and fabric increases at the detergent interface and the liquid soil rolls up and becomes more globular.[25] Surfactant molecules align themselves at the surfaces of both fabric and soil, so that each is, in effect, covered with a layer in which hydrophilic groups are directed towards the detergent solution.[27] These layers will therefore attract water molecules, which push between the grease and the fabric and weaken their hold on each other. For both types of soil, agitation is needed to aid in the final release of the stain.[28]

Soil, removed from the substrate, should remain suspended in the liquid. Redeposition of the soil onto another part of the substrate should be prevented. Solid soil is kept in suspension mainly by electrical (ionic, particularly anionic, surfactants) and steric barriers (nonionic

surfactants) between the substrate and the soil.[24] Special components are also added to the detergent formulation to create electrical and steric barriers (e.g. sodium carboxymethylcellulose in laundry detergents).[24] Oily soil is suspended by micellar solubilization and by emulsification (see also section 6.4.1).[24] The adsorption and solubilizing power of surfactants seem to correlate well with detergency.[24]

4.2.3 Performance: mini-bottle tests

Carbohydrate-derived surfactants with a dodecyl chain were selected for the detergency tests because they show the lowest surface tension at the CMC in each series. Mini-bottle tests were kindly performed at Unilever Research Vlaardingen, The Netherlands. The effect of the addition of the surfactants (2.5%) to a standard powder formulation (a benchmark powder) was analyzed at 30°C. Table 2 shows the contents of the formulation. As nonionic carbohydrate-derived surfactants are not likely to replace the cheap and well performing NaLAS in the immediate future, we tested their applicability as cosurfactants (2.5%).

Table 2. Formulation, conditions and cloths used in the bottle tests.

Formulation	Conditions	Stain and cloth
24% NaLAS 2.5% carbohydrate-derived surfactant 21% STP 20% sodium sulfate 10% sodium carbonate 9% disilicate up to 100% water	temperature 30°C dosage[a] 1 g L^{-1} liquor : cloth = 20:1 hardness either 0 or 30 °FH Ca:Mg = 3:1 with or without 6 ppm metal ions (Cu:Fe:Zn = 1:1:1)	fat-pigment on polyester-cotton (AS-9) kaolin-sebum on cotton (WFK 10D) kaolin-sebum on polyester-cotton (WFK 20D) kaolin-sebum on polyester (WFK 30D) red wine on cotton (EMPA 114) tea on cotton (BC1)

[a] The total amount of detergent formulation in a dosage of 1 g/L is 0.840 g. The additional 0.160 g is reserved for possible additional ingredients such as enzymes, perfumes, or cosurfactants.

The mini-bottle test is a screening method that compares the influence of different ingredients under identical (optimized)[a] conditions. The method has the advantage that various ingredients and conditions can be tested in one run. Test cloths (4·4 cm) with a stain are put in a PE bottle containing the detergent system in a liquor/cloth ratio of 20:1. The bottles are put in a (front loader automatic) washing machine for 10 to 15 minutes (main wash) at 30°C.

[a] Prior to the washing process, the detergent is dissolved in the wash water, dissolution properties which might influence detergency are therefore excluded.

The performance of detergents under the conditions mentioned in Table 2 was determined from the reflectance of the cloth at 460 nm. A white cloth shows a reflectance of about 90 R units (460 nm). The performance of the formulation containing an additional 2.5% carbohydrate-derived surfactants was tested on three types of cloth (cotton, polyester-cotton, and polyester) with different stains under several conditions (in demineralized water (0°FH), in hard water (30°FH)[b], with or without 6 ppm transition metal ions ("metals") added).

The reflectance of each cloth washed with the formulation containing carbohydrate-derived surfactant was measured and these reflectances were summed. The same was done for the cloths washed with the plain formulation. The sum of the reflectances of the cloths washed with plain formulation was subtracted from the sum of the reflectances of the cloths washed with the carbohydrate-containing formulation. These led to ΔR values which are shown in Figures 2-9. When an additional amount of NaLAS (2.5%) is added to the plain formulation, the gain in performance was very low: 0.3-0.5 ΔR units in case demineralized water is used (0°FH) and 0.5 for water of 30°FH; the performance versus concentration curve of NaLAS levels off after about 24%.

The error in the measurements is ± 0.5 ΔR units. Consumer-perceivable is a change of 1.5 ΔR units.

4.2.4 Effects of the carbohydrate-derived surfactants on performance

Eight compounds were tested in demineralized water (0°FH), and in hard water (30°FH). The influence of metal ions was determined, except for NC_2nC_{12} glucose, NC_3nC_{12} glucose, and NC_3nC_{12} lactitol. Figures 2-9 show the results for these eight carbohydrate-derived surfactants compared with the standard formulation. All surfactants show a positive influence on the performance in demineralized water without addition of metals. The effect is particularly large in the case of NC_2nC_{12} glucitol (11.3 reflectance units better than the benchmark powder). When metals are added the performance decreases (except for NC_2nC_{12} glucitol) compared to the standard formulation.

In water of 30°FH, the acetylated carbohydrate-derived surfactants have a positive effect on the performance compared to the benchmark powder (in case of NC_2nC_{12} lactose and NC_2nC_{12} lactitol the effect is positive even when metals are added). The propionylated compounds show a decrease in performance compared to the benchmark powder at 30°FH.

Table 3 shows that although the performance of NC_2nC_{12} glucitol decreases at 30°FH compared to 0°FH, the effect of this surfactant on persistent stains like red wine (EMPA 114) and tea (BC 1) is still highly positive. Furthermore, the carbohydrate-derived surfactants are

[b] 1°FH = 0.1 mM Ca^{2+}.

particularly effective when the cloth is made of polyester (WFK 30D, 0°FH), which is more hydrophobic than the negatively charged cotton.

Overall, the monosaccharide surfactants show higher increases in performance at 0°FH, because these derivatives have a relatively larger hydrophobic part compared to the lactose and lactitol surfactants and thus show better surface-active properties (lower critical micelle concentrations and a lower surface tension at the CMC).

Table 3. Influence on the performance of the carbohydrate-derived surfactants on separate stains.[a]

0 °FH	AS[b]	WFK 10[b]	WFK 20[b]	WFK 30[b]	EMPA 114[b]	BC 1[b]
NC_2nC_{12} glucose	+	0	0	+++	0	0
NC_3nC_{12} glucose	0	+	+	++++	+	0
NC_2nC_{12} glucitol	++	+	++	+++++	+	+
NC_3nC_{12} glucitol	0	0	+	++++	0	0
NC_2nC_{12} lactose	0	+	0	+++	–	0
NC_3nC_{12} lactose	0	–	0	+	0	0
NC_2nC_{12} lactitol	0	+	0	+++	0	0
NC_3nC_{12} lactitol	+	+	0	+++	0	0
30°FH						
NC_2nC_{12} glucose	0	0	+	+	0	++
NC_3nC_{12} glucose	0	0	+	0	0	0
NC_2nC_{12} glucitol	0	0	---	0	+	+++
NC_3nC_{12} glucitol	0	0	0	---	+	0
NC_2nC_{12} lactose	+	+	+	++	+	–
NC_3nC_{12} lactose	+	0	0	0	0	–
NC_2nC_{12} lactitol	+	+	0	+	+	0
NC_3nC_{12} lactitol	0	0	0	–	0	–

[a] --- ≡ $-3.5 \leq \Delta R \leq -2.5$; -- ≡ $-2.5 \leq \Delta R \leq -1.5$; - ≡ $-1.5 \leq \Delta R \leq -0.5$; 0 ≡ $-0.5 \leq \Delta R \leq +0.5$; + ≡ $+0.5 \leq \Delta R \leq +1.5$; ++ ≡ $+1.5 \leq \Delta R \leq +2.5$; +++ ≡ $+2.5 \leq \Delta R \leq +3.5$ etc. [b] For an explanation of the abbreviations of the cloth see Table 2.

Generally, the acetylated carbohydrate-derived surfactants show better results than the propionylated surfactants, although the latter have lower CMCs and γ_{CMC} values. This difference is particularly pronounced at 30°FH. Probably, the propionylated compounds are more susceptible to calcium and magnesium ions (although they do not precipitate). It is unclear how the sugar-OH complex formation with these cations and metals is influenced by

the addition of one methylene group in the short acyl side chain.[29-32] We were not able to measure the binding capacity of these surfactants with a calcium selective electrode, due to adsorption of the surfactants to the (PVC) membrane of the electrode.

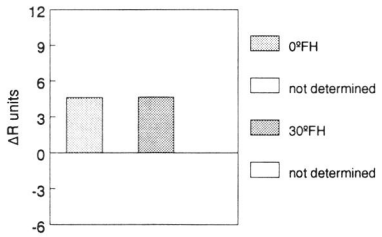

Figure 2. Effect of the addition of 2.5% NC_2nC_{12} glucose on the performance of a standard formulation in mini-bottle tests.

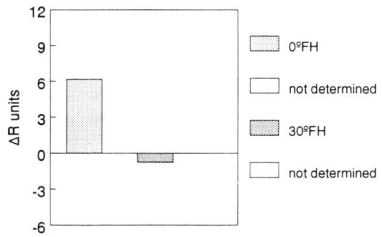

Figure 3. Effect of the addition of 2.5% NC_3nC_{12} glucose on the performance of a standard formulation in mini-bottle tests.

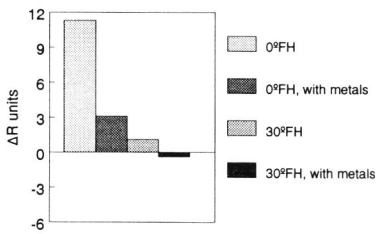

Figure 4. Effect of the addition of 2.5% NC_2nC_{12} glucitol on the performance of a standard formulation in mini-bottle tests.

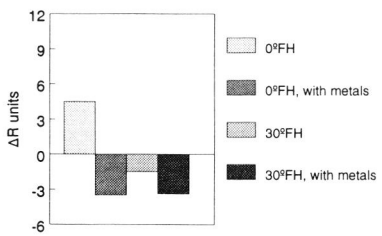

Figure 5. Effect of the addition of 2.5% NC_3nC_{12} glucitol on the performance of a standard formulation in mini-bottle tests.

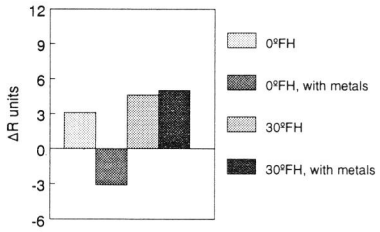

Figure 6. Effect of the addition of 2.5% NC_2nC_{12} lactose on the performance of a standard formulation in mini-bottle tests.

Figure 7. Effect of the addition of 2.5% NC_3nC_{12} lactose on the performance of a standard formulation in mini-bottle tests.

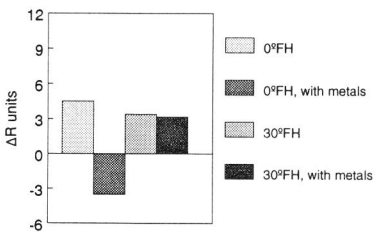

Figure 8. Effect of the addition of 2.5% NC_2nC_{12} lactitol on the performance of a standard formulation in mini-bottle tests.

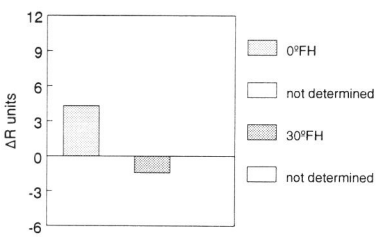

Figure 9. Effect of the addition of 2.5% NC_3nC_{12} lactitol on the performance of a standard formulation in mini-bottle tests.

4.2.5 Effects of the carbohydrate-derived surfactants on redeposition

The removed soil should stay in solution and redeposition of the soil on the cloth should be prevented. Clean polyester and cotton cloths were added to the mini-bottles to test the influence of the carbohydrate-derived surfactants on the redeposition of soil at 0°FH and 30°FH. The results were compared with the results for the benchmark powder (Figures 10 to 21). The higher the reflectance, the lower the redeposition on the cloth.

The surfactants do not have a large influence on the redeposition on both polyester and cotton at 0°FH compared to the benchmark powder. On polyester at 30°FH, NC_2nC_{12} glucitol,

increases redeposition. Again, NC_2nC_{12} glucitol, NC_2nC_{12} lactose, NC_2nC_{12} lactitol, and NC_3nC_{12} lactose show the same results on cotton at 30°FH.

There is no clear trend in the redeposition at 30°FH, but it is interesting to see that the surfactants that show the highest increase in performance, NC_2nC_{12} glucitol at 0°FH and NC_2nC_{12} lactose at 30°FH, also behave well in the redeposition tests (no influence on the redeposition at 0°FH and a decrease in redeposition at 30°FH) compared to the base powder.

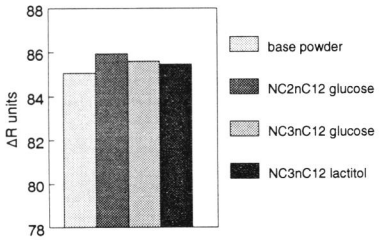

Figure 10. Effect on redeposition on polyester at 0°FH.

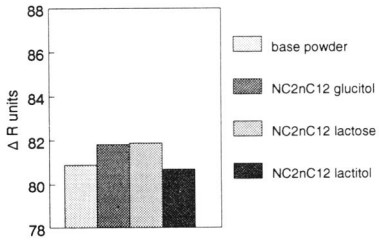

Figure 11. Effect on redeposition on polyester at 0°FH.

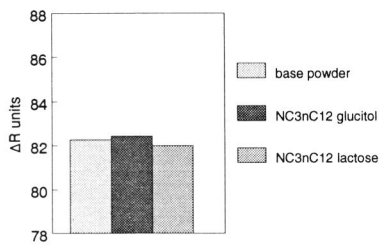

Figure 12. Effect on redeposition on polyester at 0°FH.

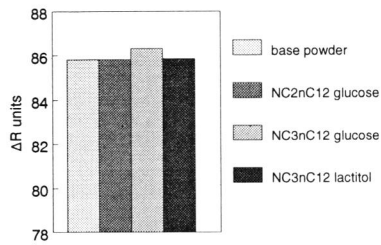

Figure 13. Effect on redeposition on polyester at 30°FH.

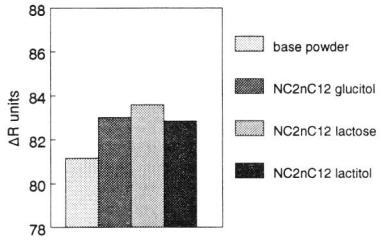

Figure 14. Effect on redeposition on polyester at 30°FH.

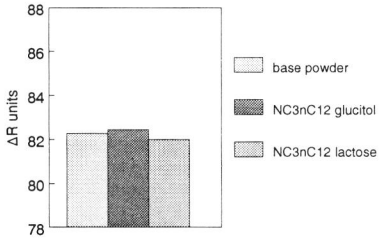

Figure 15. Effect on redeposition on polyester at 30°FH.

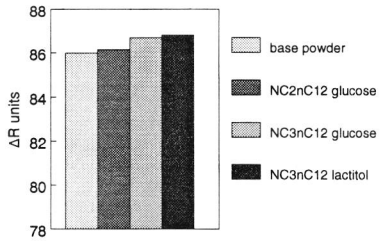

Figure 16. Effect on redeposition on cotton at 0°FH.

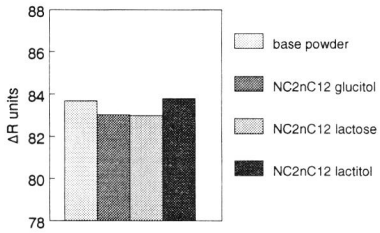

Figure 17. Effect on redeposition on cotton at 0°FH.

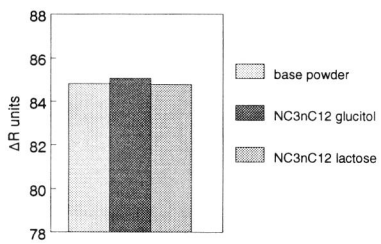

Figure 18. Effect on redeposition on cotton at 0°FH.

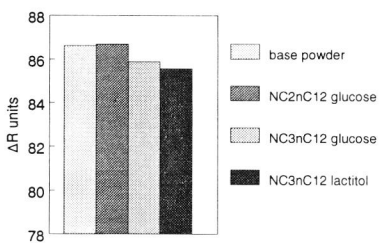

Figure 19. Effect on redeposition on cotton at 30°FH.

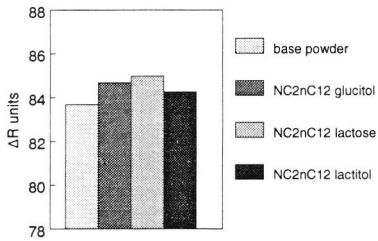

Figure 20. Effect on redeposition on cotton at 30°FH.

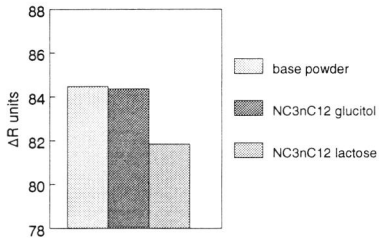

Figure 21. Effect on redeposition on cotton at 30°FH.

4.3 Foam formation and foam stability[33-39]

Excessive foaming of detergents in washing machines is undesirable. In contrast, abundant foam formation and high foam stabilities are required by consumers who use hand-wash protocols. This requirement is only for the consumer's eye; in reality good foaming properties do not imply good cleaning properties.

Foam is a dispersion of gas in liquid in which gas predominates.[33] Stable foam lamellae can be formed when substances are present that lower the surface tension and that impart viscoelastic behavior on the surface.[28] There are two types of foam. "Kugelschaum" is formed just above the liquid and the bubbles are spherical. Polyhedral foam is formed on top of the Kugelschaum due to drainage caused by gravity.[33]

The amount of foam formed under a given set of conditions is a measure of foamability (the capacity to form foam). The decay of the foam volume over time is a measure of foam stability.[40]

Anionic surfactants are generally good foamers. In contrast to the excellent foam production and stability of anionic surfactants, nonionics show less foam formation and stability.[41-44] APGs are moderate foamers, but they are excellent foam stabilizers and have synergistic effects in combination with anionic surfactants.[17]

The foamability and the stability of the foam formed were tested by means of the Ross-Miles technique for all eight carbohydrate-derived surfactants[40,45,46] with a dodecyl chain. Ross and Miles developed this widely-used technique in 1941.[44,47] A surfactant solution (200 mL) is poured quickly and from a 90 cm distance into a receiver filled with 50 ml of the same surfactant solution. As the solution pours into the receiver, foaming takes place.

The foamability and the foam stability of the pure surfactant solutions (0.5 g L^{-1}) were compared to NaLAS and Synperonic (an alcohol ethoxylate with an average composition of

$C_{12}EO_7$). The dependence of foaming properties on chain length was studied by measuring the foaming properties of the three acetylated glucitol derivatives (NC_2nC_8 glucitol, NC_2nC_{10} glucitol and NC_2nC_{12} glucitol).

The two surfactants which showed promising performance, NC_2nC_{12} glucitol (at 0°FH) and NC_2nC_{12} lactose (at 30°FH), were subjected to conditions more closely related to applications. The influence of salts and soil on foam formation and foam stability were tested and compared to NaLAS solutions. Then we added 2.5% of NC_2nC_{12} glucitol and NC_2nC_{12} lactose to a standard formulation (NaLAS, 3 g/L, 10 g/L soil, 16 °FH) to investigate whether our surfactants could stabilize the foam formation under these conditions.

4.3.1 Foaming properties of pure solutions of carbohydrate-derived surfactants

Figure 22 shows the foaming properties of the glucose and glucitol derivatives, compared to NaLAS and synperonic (nonionic) at room temperature (22°C). The initial foam height was measured after 20 seconds. Obviously, NaLAS shows very good foaming properties, with a high initial height (almost 150 mm). The structure of the foam is quite open and remains stable for at least half an hour. The bubbles are relatively large and shiny compared to foams of the other surfactants. The initial foam height of synperonic is much less (about 80 mm) than was observed for NaLAS and the foam becomes hollow and collapses after 20 minutes.

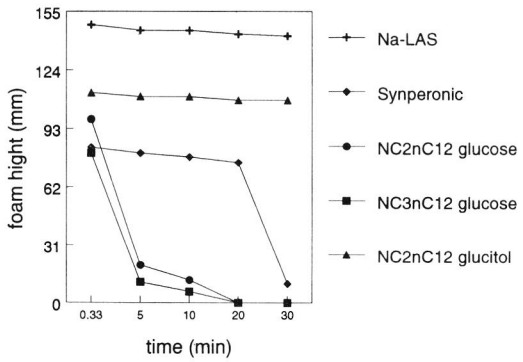

Figure 22. Foaming properties of glucose and glucitol derivatives, 0.5 g L^{-1}, 0°FH, 22°C.

Both glucose derivatives show moderate initial foam heights and the foams collapse rapidly.

NC_3nC_{12} glucitol does not dissolve in water at room temperature. NC_2nC_{12} glucitol forms a very stable foam with a fairly high initial foam height. After a while, the foam in the middle section becomes more transparant, but the foam does not either collapse or hollow.

In Figure 23, the foam formation and stabilities of the lactose and lactitol derivatives are compared to NaLAS and synperonic. NC_2nC_{12} lactitol collapses rapidly and NC_2nC_{12} lactose collapses somewhat slower. NC_3nC_{12} lactose and NC_3nC_{12} lactitol have higher initial heights and form more stable foams than their acetylated counterparts. However, they do hollow out and the foam heights presented for these two derivatives are a bit misleading. The hole in the foam formed by NC_3nC_{12} lactitol has a larger cross section than the hole in the NC_3nC_{12} lactose solution.

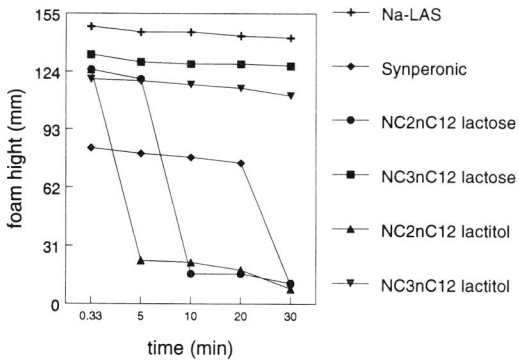

Figure 23. Foaming properties of lactose and lactitol derivatives, 0.5 g L^{-1}, 0°FH, 22°C.

The dependence of foaming properties on the alkyl chain length is shown in Figure 24.[48,49] NC_2nC_8 glucitol hardly foams and after 20 seconds almost all the foam formed has collapsed. Both NC_2nC_{10} and NC_2nC_{12} glucitol form stable foams. The foam of NC_2nC_{10} glucitol seems somewhat less stable than that formed by NC_2nC_{12} glucitol, the former becomes thinner and after a while, a few small holes appear. The initial height in case of the NC_2nC_{10} glucitol is higher. These results indicate that there might be an optimum in the relationship between foam height and chain length.[45] It should also be noted that the concentration of 0.5 g L^{-1} is lower than the critical micelle concentration of NC_2nC_8 glucitol, which is 7.4 g L^{-1}.[5]

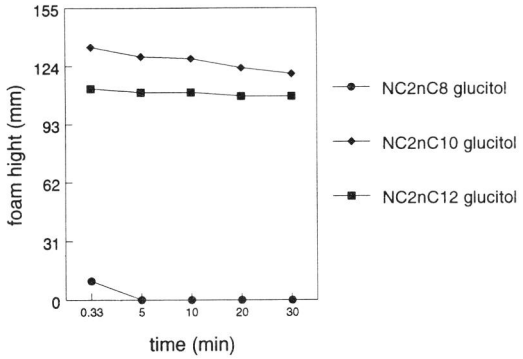

Figure 24. Dependence of foamability and foam stability on chain length, 0.5 g L^{-1}, 0°FH, 22°C.

4.3.2 Influence of salts and soil on the foaming properties of the carbohydrate-derived surfactants

The foaming properties of NC_2nC_{12} glucitol and NC_2nC_{12} lactose, which performed well in the mini-bottle tests in demineralized water and water of 30°FH, respectively, were

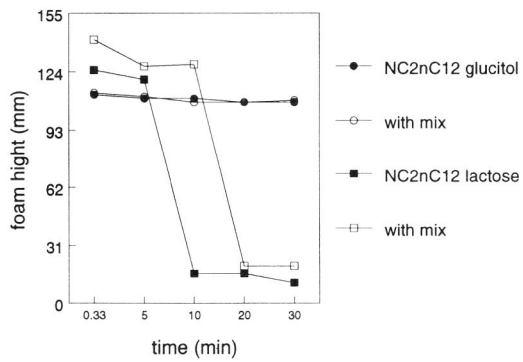

Figure 25. Influence of a basemix on the foamability and foam stability of NC_2nC_{12} glucitol (0°FH, 22°C) and NC_2nC_{12} lactose (30°FH, 22°C).

investigated further. The influence of salt and soil was determined at 0°FH (NC_2nC_{12} glucitol) and at 30°FH (NC_2nC_{12} lactose) and compared with NaLAS (Figures 25 and 26). The salts and the dosage were the same as in a detergent composition, about 2 g L^{-1} which consisted of 0.5 g L^{-1} surfactant (24%) and 1.25 g L^{-1} base mix (sodium carbonate (10%), sodium sulfate (20%), STP (21%) and disilicate (9%)).

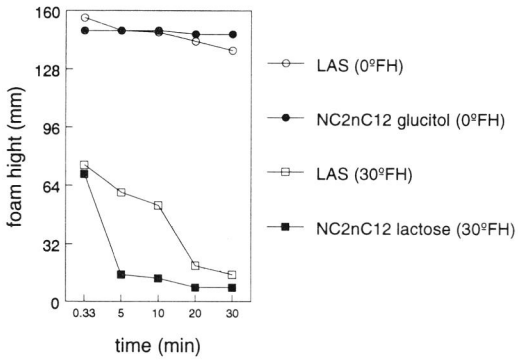

Figure 26. Influence of soil on the foamability and foam stability of NC_2nC_{12} glucitol (0°FH, 22°C) and NC2nC12 lactose (30°FH, 22°C).

The glucitol derivative (at 0°FH) behaved the same with and without mix. The lactose derivative also showed nearly the same behavior with base mix (at 30°FH) and without base mix (0°FH). The initial foam height was somewhat higher when base mix was added, and the foam seemed to be stable for a longer period (10 minutes). However, in this case the foam became hollow after 5 minutes.

When both base mix and soil (20 g L^{-1}) were added, the foam formation and foam stability of NC_2nC_{12} glucitol (at 0°FH) behaved identically to the detergent composition with NaLAS. The initial appearance of the foam has a close resemblance to the foam formed by pure NaLAS (the bubbles are larger and it is shiny). After a while, the structure of the foam formed by NC_2nC_{12} glucitol becomes transparant. In the NaLAS-containing formulation, the foam with soil has relatively smaller bubbles and the foam is less glossy than without the soil. The middle section of the foam becomes transparent (after 10 minutes).

At 30°FH, the NaLAS-formulation (with base mix and soil) shows a low initial foam height and the foam collapses gradually. The foam formed by NC_2nC_{12} lactose (with base mix and soil) collapses even faster.

4.3.3 A practical application of NC_2nC_{12} glucitol and NC_2nC_{12} lactose

Nonionic carbohydrate-derived surfactants may find application as cosurfactants in detergents, but in the forseeable future, they will not replace the cheap and well performing NaLAS. Therefore, we added 2.5% of these surfactants (the same amount as used in the mini-bottle tests) to a standard formulation of NaLAS to see whether these surfactants have a stabilizing effect on foam formation (Fig. 27). Addition of 2.5% of NC_2nC_{12} lactose does not stabilize the foam, but rather destabilizes it slightly. However, the surfactant that showed good performance in the mini-bottle tests (NC_2nC_{12} glucitol) also stabilizes the foam of the standard formulation. Figures 28 and 29 (taken after 20 minutes) clearly show this stabilization.

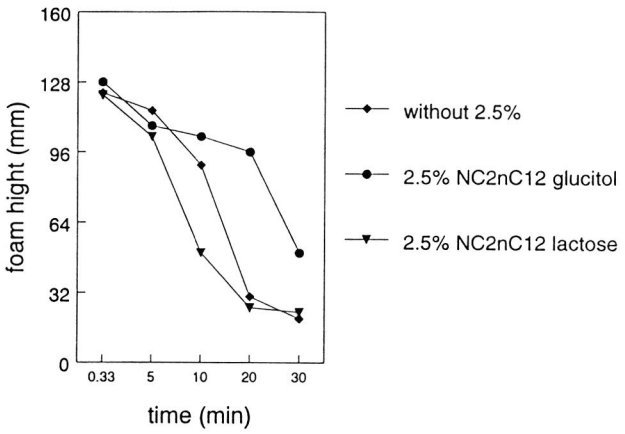

Figure 27. Addition of 2.5% NC_2nC_{12} glucitol or NC_2nC_{12} lactoses to a standard formulation of 3 g L^{-1}, 10 g L^{-1} soil (16°FH, 22°C).

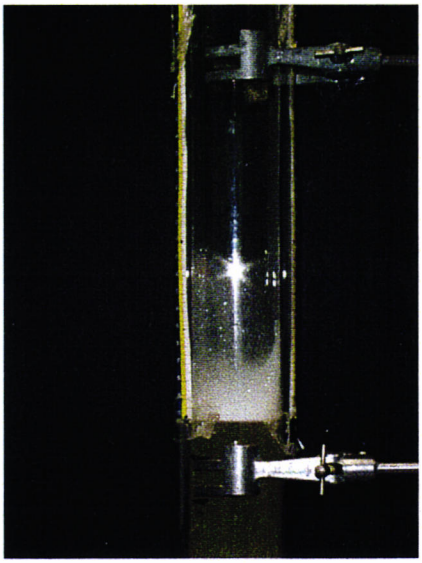

Figure 28. Collapsed foam of standard formulation with soil (16°FH).

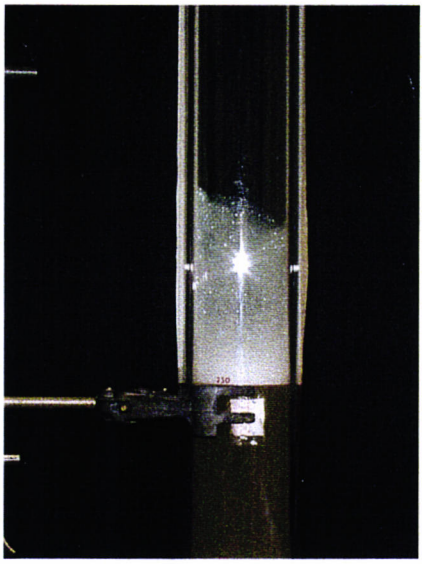

Figure 29. Stabilized foam of soil containing standard formulation with 2.5% of NC_2nC_{12} glucitol (16°FH).

4.4 Biodegradability[50,51]

The biodegradability of a substance indicates its ability to undergo microbial attack. Biodegradation can be described as the elimination of an organic compound from the ecosystem by metabolic activity of micro-organisms present in that system.[50] Biodegradation can either be primary or ultimate. Primary or functional biodegradation is the biodegradation to the minimum extent necessary to change the identity of the compound.[50] The ultimate biodegradation or mineralization is the conversion of the compound to CO_2, H_2O, and additional inorganic compounds if other elements than C, H, and O are present.[50] Degradation to such an extent that undesirable properties of the compound (such as toxicity, foaming) are removed is deemed environmentally acceptable. From an ecological point of view only complete biodegradation is sufficient. Moreover, the compound should not only biodegrade fully but also rapidly. A compound that biodegrades fully, but very slowly, may persist in the environment for a long time. Therefore, the rate of degradation is one of the most important factors.[50,52]

Factors that influence the rate of biodegradation are the rate at which the organic substrate can be oxidized biochemically, the initial number of bacteria, and the acclimation of the

micro-organisms. Biodegradability of hydrocarbons is impeded by branching and increasing chain length.[50]

In general, organic compounds are not completely degraded to CO_2, H_2O, and inorganic compounds. Part of the degraded surfactant will be used as a nutrient source and is built into the cells. This process should also be considered as biodegradation.

4.4.1 Biochemical oxygen demand

The technique we used to determine the ultimate biodegradability is based on the decrease in oxygen concentration of a surfactant solution containing micro-organisms from a WWTP. The decrease in oxygen concentration is due to oxidation of the surfactants by micro-organisms and is called the Biochemical Oxygen Demand (BOD).[50]

This technique was initially used to determine the contribution of compounds released into the aquatic environment to eutrophication by measuring the amount of oxygen withdrawn from surface water after *n* days upon oxidation (contribution to eutrophication) of the compounds (NEN 6634).[53] BOD measurements are now also used to determine the ultimate biodegradability of compounds. An incubation time is chosen of either five (BOD_5) or 28 days (BOD_{28}) and a compound is considered readily biodegradable if the amount of biodegradation is ≥ 60%.[50,51] In our case, the BOD was measured after 20 days.

BOD is measured in a closed-bottle test.[50,53] Each surfactant (2 mg L^{-1}) is added to a bottle with (a low number of) mico-organisms from a waste water treatment plant in a mineral nutrient solution that is saturated with oxygen. The surfactant is the only available carbon source. The bottles are closed in such a way that no air bubbles are introduced. After the incubation time in the dark at 20-21 °C, the oxygen concentration is measured electrochemically.

The amount of biodegradation can be calculated by comparing the BOD with the Theoretical Oxygen Demand (TOD), the amount of oxygen in grams required for a complete oxidation of 1 g of a given compound. The percentage biodegradation is (BOD/TOD) · 100%.

For a compound with molecular formula $C_cH_hO_oN_n$ the TOD can be calculated according to the following equation (if the nitrogen is released as ammonia):[50,54]

$$C_cH_hO_oN_n + [2c + (h-3n)/2 - o]\ O = c\ CO_2 + (h-3n)/2\ H_2O + n\ NH_3 \quad (1)$$

$$TOD = [(4c + h - 2o - 3n) \cdot 8] / M\ g/g \quad (2)$$

Oxidation of NH_4^+ is inhibited by the addition of *n*-allylthiourea.

4.4.2 Extent of biodegradation of the carbohydrate-derived surfactants

Table 4 shows the extent of biodegradation of the carbohydrate-derived surfactants after 20 days.[48,49] No clear trends can be observed between the different lengths of the alkyl chain. Therefore, the individual results for the different chain lengths per headgroup are not shown. The extent of biodegradation depends on the nature of the headgroup. The glucose-derived compounds are the least sensitive to microbial attack. The surfactants with a glucitol headgroup show the highest biodegradability. The glucitol-derived surfactants are followed by the surfactants with a lactose or lactitol headgroup. Most likely, micro-organisms hydrolyze the β-glycosidic linkage between the galactose and glucose/glucitol fragments of the lactose/lactitol headgroup.

Table 4. Biodegradation of glucose-, glucitol-, lactose-, and lactitol-derived surfactants, and three reference compounds.

Compound	Biodegradation after 20 days
Glucose-derived surfactant	30% (± 5%)
Glucitol-derived surfactants	45% (± 5%)
Lactose/lactitol-derived surfactants	35% (± 5%)
$C_{12}H_{25}N^{+}(CH_3)_3\ Br^{-}$	~ 70%
$C_{12}H_{25}(EO)_6$	~ 70%
NaLAS	0%

We used dodecyltrimethylammonium bromide,[55] hexaethylene glycol monododecylether and the sodium salt of dodecylbenzene sulfonate as reference compounds. Both dodecyltrimethylammonium bromide and hexaethylene glycol monododecylether can be termed readily biodegradable as they show a biodegradation of about 70% after 20 days. The results for NaLAS are striking. NaLAS is the main component in powder detergents and numerous studies on NaLAS have demonstrated that both primary and ultimate biodegradation occur rapidly under a variety of laboratory and field conditions.[12,56-58] The accuracy of the closed-bottle tests was established by correct values of the standards (a solution mixture of glucose and glutamic acid). Moreover, the biodegradation tests of NaLAS were performed in duplicate twice and the inability to biodegrade was reproducable. The result obtained might be due to a different composition of the linear alkylbenzenesulfonate than the one applied in detergents.

We expected the carbohydrate-derived surfactants to be more easily degraded by micro-organisms of a WWTP that are adapted to carbohydrate-derived compounds. We therefore

repeated the closed-bottle test for C_{12} lactose- and lactitol-derivatives with influent and effluent of the WWTP of AVEBE, a starch company. Indeed, the extent of biodegradation increases about 5%.

The biodegradation results of the carbohydrate-derived surfactants are in agreement with values for other nitrogen-containing, carbohydrate-derived surfactants.[59,60] However, the biodegradation is not sufficient to classify the compounds as readily biodegradable. As the APGs are readily biodegradable, the difference in biodegradability is probably due to the amide functionality. The results from the closed-bottle tests performed with micro-organisms from the AVEBE WWTP show that biodegradation might improve if more time for adaptation of the micro-organisms would be provided.[48,49,50,51] Also, the biodegradation will increase somewhat when a 28 days incubation period is selected.

This biodegradation test is an acceptancy test. Compounds that do not satisfy the 60% requirement are not rejected immediately and further biodegradation tests are warranted.[61]

4.5 Toxicity

Surfactants are surface-active agents and have the property of decreasing the surface tension of water. When detergents are drained into the aquatic environment, a critical situation arises for fish when the surface tension of water is reduced to 50 mN m^{-1}. At this value, irreversible damage occurs at the skin epithelium of fishes' gills.[11] The lower the biodegradability, the higher toxicity towards fish. Primary biodegradation of surfactants (in which *e.g,* their property to reduce the surface tension is removed) can already lower the aquatic toxicity by two orders of magnitude. The most important factor in determining the aquatic environmental tolerance of a compound is therefore its biodegradation, followed by its toxicity.[11] Compounds with a high acute toxicity, should be readily biodegradable in a short period. As already mentioned, the main ingredient in detergents until the 1960s was tetrapropylbenzyl sulfonate (TSP). Due to the branched alkyl chain, the compound was not biodegradable and was replaced by the linear alkylbenzensulfonates (LAS). LAS is more toxic than TPS, but the LAS compounds biodegrade readily (producing much less toxic products).[11]

Most tests to determine the aquatic toxicity of a compound are performed on fish, daphnia (water fleas), and additionally on bacteria and algae.[62] The acute fish toxicities of most surfactants are in the range 1-10 mg L^{-1} (this is an LC_{50} value; a concentration at which 50% of the fish do not survive).[11] Daphnia are generally about a factor of 5 - 7 less sensitive to surfactants than fish are. The effect of surfactants on bacteria is even smaller. Increasing the length of the alkyl chain of LAS increases the toxicity towards bacteria. Nonionic ethoxylated surfactants become less toxic upon increasing length of the polyethylene glycol residue.[11]

As a first indication of the toxicity, we measured the influence of the carbohydrate-derived surfactants on the growth rate of micro-organisms (acute biotoxicity).[63,64] The growth curves of micro-organisms in nutrient-rich media can be monitored by means of continuously measuring the optical density.[63]

A general growth curve starts with an adaptation period at which the growth rate is zero. After this lag phase the growth rate gradually increases and reaches exponential growth. Eventually, the cell growth ceases and ultimately, cells decay due to the exhaustion of the limiting substrate necessary for cell growth. The toxicity is assessed during the phase of exponential growth. It is based on the time elapsed before a specific growth (difference in optical density) has been reached. The IC_{50} value (Inhibitory Concentration) of a surfactant is the concentration at which the growth rate is lower than 50% of the controls.

4.5.1 Acute biotoxicity tests of the carbohydrate-derived surfactants

We used four different micro-organisms for the biotoxicity tests, the *Saccharomyces cerevisae* (a yeast), *Escherichia coli* (a gram - bacterium), *Pseudomonas putida* (a gram - bacterium), and *Bacillus subtilis* (a gram + bacterium).

The surfactant concentrations tested were 0, 1, 20, 100, 500, 1000, and 5000 mg L^{-1}, respectively. We used the same reference compounds as for the biodegradation experiments (NaLAS, dodecyltrimethylammonium bromide and hexaethylene glycol monododecylether). The IC_{50} values are shown in Tables 5 and 6.

The carbohydrate-derived surfactants show inhibitory concentrations ranging from 20 to 5000 mg/L towards *P. putida* and *B. subtilis*. The IC_{50} values decrease with increasing chain length. The surfactants become more toxic just below and in the concentration range where they tend to form micelles. At these concentrations, they probably start to disrupt the cell membranes. The biotoxicities of the surfactants with a C_{12} alkyl chain are comparable to the biotoxicities of the reference compounds, which also have alkyl chains containing twelve carbon atoms.

Table 5. Biotoxicities of glucose- and glucitol-derived surfactants, and three refererence surfactants.[a]

Compound	*S. cerevisae*	*E. coli*	*P. putida*	*B. subtilis*
		IC_{50} (mg L^{-1})		
NC_2nC_8 glucose	>5000	5000	5000	5000
NC_3nC_8 glucose	5000	5000	5000	5000
NC_2nC_{10} glucose	1000	1000	500	500
NC_3nC_{10} glucose	500	500	500	500
NC_2nC_{12} glucose	100	100[b]	100	100
NC_3nC_{12} glucose	100	100[b]	100	100
NC_2nC_8 glucitol	>5000	5000	5000	5000
NC_3nC_8 glucitol	5000	5000	5000	5000
NC_2nC_{10} glucitol	500	500	500	500
NC_3nC_{10} glucitol	500	500	500	500
NC_2nC_{12} glucitol	100	100	100	100
NC_3nC_{12} glucitol[c]	100	100	100	100
$C_{12}H_{25}N^+(CH_3)_3\ Br^-$	100	100	100	20
$C_{12}H_{25}(EO)_6$	100	5000	20	20
NaLAS	500	500	100	20

[a] The concentration at which the growth inhibition is exactly 50% lies between the value given in the tables and the next lower test concentration. [b] 5000-100: Growth curve starts very slowly, followed by a rapid growth. [c] 5000-500: The compound precipitates.

The effect on the growth is similar for all four micro-organisms in the case of the monosaccharide-derived surfactants. However, the lactose- and lactitol-derived surfactants with a C_{10} and a C_{12} alkyl chain are much less toxic towards *S. cerevisae* and *E. coli* than towards *P. putida* and *B. subtilis*. NC_2nC_{12} lactose, NC_2nC_{12} lactitol, NC_3nC_{12} lactose, and NC_3nC_{12} lactitol were tested at concentrations as high as 10 and 15 g L^{-1} and even at these high concentrations (much higher than would ever be encountered in waste water) the growth curves of *S. cerevisae* and *E. coli* were unaffected. The toxicity of the disaccharide-derived surfactants towards these two microroganisms (*S. cerevisae* and *E. coli*) is also much lower than that for the monosaccharide-derived surfactants. As already mentioned, the toxicity of polyethylene glycols towards bacteria also decreases with increasing headgroup size.

Table 6. Biotoxicities of lactose- and lactitol-derived surfactants.[a]

Compound	*S. cerevisae*	*E.coli*	*P. putida*	*B. subtilus*
		IC_{50} (mg L^{-1})		
NC_2nC_8 lactose	>5000	>5000	5000	>5000
NC_3nC_8 lactose	>5000	>5000	5000	>5000
NC_2nC_{10} lactose	>5000	>5000	500	5000
NC_3nC_{10} lactose	>5000	>5000	500	1000
NC_2nC_{12} lactose	>5000	>5000	100	500
NC_3nC_{12} lactose	>5000	>5000	20	100
NC_2nC_8 lactitol	>5000	>5000	5000	>5000
NC_3nC_8 lactitol	>5000	>5000	1000	5000
NC_2nC_{10} lactitol	>5000	>5000	500	500
NC_3nC_{10} lactitol	>5000	>5000	500	500
NC_2nC_{12} lactitol	>5000	>5000	100	500
NC_3nC_{12} lactitol	>5000	>5000	20	100

[a] The concentration at which the growth inhibition is exactly 50% lies between the value given in the tables and the next lower test concentration.

NaLAS shows considerable growth inhibition towards *P. putida* and *B. subtilis* far below its CMC (about 0.9 g L^{-1}). Dodecyltrimethylammonium bromide[55] has IC_{50} values far below its CMC value (which is about 1.9 g L^{-1}) for all four micro-organisms. As is the case for the lactose- and lactitol-derived surfactants, NaLAS and $C_{12}H_{25}(EO)_6$ show larger IC_{50} values for *S. cerevisae* and *E. coli* than for *P. putida* and *B. subtilis*.

Matsumura et *al.* also determined the toxicity of a number of surfactants with a monosaccharide headgroup.[48,49] In accordance with our results, they also found an increase in toxicity when the alkyl chain length is increased. Some compounds were less toxic towards *E. coli* than towards other bacteria, including the reference compounds (several ethoxylated dodecanols and tetradecanols).

4.6 Conclusions

Three carbohydrate-derived surfactants show promising results in preliminary tests for their use as cosurfactants. NC_2nC_{12} glucitol would be a good cosurfactant in detergency products in

Brazil, for example, where tap water contains limited amounts of calcium and magnesium ions (2°FH). NC_2nC_{12} lactose and NC_2nC_{12} lactitol have potential as cosurfactants in hard water. In India, for example, the hardness of the water is very high (30°FH, or even higher). NC_2nC_{12} glucose shows good performance under both conditions (in demineralized water and in water of 30°FH), however, further tests are needed to see how the performance of this surfactant is influenced by the addition of metals.

NC_2nC_{12} glucitol and NC_2nC_{10} glucitol show high initial foaming heights and good foam stabilities. NC_2nC_{12} glucitol also stabilizes the foam formed by the standard detergent formulation in the presence of soil at 16°FH. These properties also make them interesting components for dish washing detergents.

In preliminary biodegradability tests, extents of biodegradation of 30-45% (depending on the nature of the headgroup) were found. These percentages are insufficient to award the surfactants the specification of readily biodegradable. Further research into their biodegradability and their biodegradation pathways is clearly warranted.

The surfactants show low to very low biotoxicity compared to the reference compounds used (NaLAS, dodecyltrimethylammonium bromide and hexaethylene glycol monododecylether)

In conclusion, these carbohydrate-derived surfactants have a pleasing potential as cosurfactants in detergency systems. Shortly before this thesis was written, Borculo patented applications of these surfactants in detergent systems.[65]

4.7 Experimental

Materials. The carbohydrate-derived surfactants used in the experiments were synthesized as described in Chapter 2. Sodium dodecylbenzene sulfonate, sodium salt and dodecyltrimethylammonium bromide were purchased from Aldrich. Hexaethylene glycol monododecyl ether was purchased from Fluka. Synperonic A7 (alcohol ethoxylate C12/EO7 on average, supplied from ICI) and the NaLAS used in the foam experiments were kindly provided by Unilever Research, Vlaardingen.

4.7.1 Performance (mini-bottle tests)

The performance of the carbohydrate-derived surfactants was determined at Unilever Research Vlaardingen (The Netherlands). Test cloths (4·4 cm) with a stain (Table 3) were put in a PE bottle containing the detergent system (Table 3) in a liquor/cloth ratio 20:1. The bottles were put in a washing machine for 10 minutes (main wash) at 30°C. The cloths were quickly rinsed twice and dried and the reflection was measured at 460 nm with a Minolta reflection spectrophotometer.

NC_2nC_{12} glucitol, NC_3nC_{12} glucitol, NC_2nC_{12} lactose, NC_3nC_{12} lactose, and NC_2nC_{12} lactitol were tested in demineralized water (0°FH), and in hard water (30°FH), both with and without 6 ppm

transition metal ions ("metals") added. NC_2nC_{12} glucose, NC_3nC_{12} glucose and NC_3nC_{12} lactitol were also tested in demineralized water (0°FH) and in hard water (30°FH). 1°FH = 0.1 mM Ca^{2+}.

4.7.2 Foam formation and foam stability

The formation of foam and the stability of the foam was measured by means of the Ross-Miles method.[4] Each time, 200 mL of a surfactant solution was poured into 50 mL of the same solution. The foam height was read after 20 seconds (initial foam height), 5, 10, 20, and 30 minutes. All measurements were performed in duplicate, the reproducability was good.

Preparation of the solutions, pure solutions

Solutions of 0.5 g L surfactant in demineralized water (0°FH, 22°C) were prepared and measured.

Solutions containing base mix

NC_2nC_{12} glucitol (0.5 g L^{-1}), base mix (1.25 g L^{-1}, containing 35% of STP, 16.7% of sodium carbonate, 33.3% of sodium sulfate and 15% of disilicate). Final composition of the solution: dosage ca. 2 g L^{-1}, 24% of NC_2nC_{12} glucitol, 21% of STP, 10% of sodium carbonate, 20% of sodium sulfate and 9% of disilicate, demineralized water (0°FH, 22°C).

NC_2nC_{12} lactose (0.5 g L^{-1}), base mix (1.25 g L^{-1}, containing 35% of STP, 16.7% of sodium carbonate, 33.3% of sodium sulfate and 15% of disilicate). Final composition of the solution: dosage ca. 2 g L^{-1}, 24% of NC_2nC_{12} lactose, 21% of STP, 10% of sodium carbonate, 20% of sodium sulfate and 9% of disilicate, water (30°FH Ca:Mg = 3:1, 22°C).

Solutions containing base mix and soil

NC_2nC_{12} glucitol (0.5 g L^{-1}) or NaLAS, base mix (1.25 g L^{-1}, containing 35% of STP, 16.7% of sodium carbonate, 33.3% of sodium sulfate and 15% of disilicate), soil 20 g L^{-1}. Final composition of the solution: dosage ca. 2 g L^{-1}, 24% of surfactant (NC_2nC_{12} glucitol or NaLAS), 21% of STP, 10% of sodium carbonate, 20% of sodium sulfate and 9% of disilicate, 20 g/L soil, demi water (0°FH, 22°C).

0.5 g/L NC_2nC_{12} lactose or NaLAS, 1.25/L g base mix (containing 35% STP, 16.7% sodium carbonate, 33.3% sodium sulfate and 15% disilicate) and soil 20 g L^{-1}. Final composition of the solution: dosage ca. 2 g L^{-1}, 24% of surfactant (NC_2nC_{12} lactose or NaLAS), 21% of STP, 10% of sodium carbonate, 20% of sodium sulfate and 9% of disilicate, soil 20 g L^{-1}, water (30°FH, Ca:Mg = 3:1, 22°C).

Solutions containing base mix, soil, and 2.5% of cosurfactant

NaLAS (0.720 g L^{-1}), cosurfactant (0.075 g L^{-1}, NC_2nC_{12} glucitol or NC_2nC_{12} lactose), base mix (1.80 g L^{-1}, containing 35% of STP, 16.7% of sodium carbonate, 33.3% of sodium sulfate and 15% of disilicate) and soil (10 g L^{-1}). Final composition of the solution: dosage 3 g L^{-1}, 24% of surfactant NaLAS, 2.5% of cosurfactant (NC_2nC_{12} glucitol or NC_2nC_{12} lactose), 21% of STP, 10% of sodium carbonate, 20% of sodium sulfate and 9% of disilicate, soil (10 g L^{-1}), water (16°FH, 22°C).

Soil composition (AS-8)

Filter cell (SiO_2, 10 g L^{-1}), black indian ink (1 g L^{-1}), black iron oxide (0.5 g L^{-1}), yellow iron oxide (0.75 g L^{-1}), groundnut oil (20 g L^{-1}), emulsifier emulgator (12 g L^{-1}), carboxymethyl guar (12.5 g L^{-1}).

4.7.3 Biodegradation

The biodegradation experiments were performed according to the Dutch Standard: Water-Determination of biochemical oxygen demand after *n* days (BOD_n). Dilution and seeding method. NEN 6634; UDC 543.371:628.312.3, June 1991.

Stock solution

Demineralized water (20°C) was saturated with air. For each liter, 1 ml of the following aqueous solutions were added: phosphate buffer (KH_2PO_4 (8.5 g L^{-1}), K_2HPO_4 (21.75 g L^{-1}), $Na_2HPO_4.7H_2O$ (33.4 g L^{-1}), and 1.7 g L^{-1} NH_4Cl; pH 7.2), magnesium sulphate solution ($MgSO_4.7H_2O$ (22.5 g L^{-1})), calcium chloride solution (anhydrous $CaCl_2$ (27.5 g L^{-1})), iron(III)cloride solution ($FeCl_3.6H_2O$ (0.25 g L^{-1})), and *n*-allylthioureum solution ($C_4H_8N_2S$ (2.5 g L^{-1})). Influent and effluent were collected from the wastewater treatment plant of the city of Groningen, situated in Garmerwolde. The influent was filtered and had a chemicaloxygen demand between 300 and 600 mg L^{-1}. Influent and effluent, both 2 mL per liter, were added to the air-saturated mineral solution.

Preparation

Bottles (content exactly known; ca. 300 mL) were filled half way with stock solution. A solution of test compound was prepared (concentration exactly known ca. 60 mg in 100 mL) and 1 mL was added to the stock solution. The final concentration was about 2 mg L^{-1}. The bottles were filled to the rim with stock solution and the oxygen concentration was measured electrochemically with an oxygen electrode (in mg L^{-1}, t = 0). The bottles were sealed with stoppers and care was taken that no air bubbles were closed in. All tests were performed in duplicate. Two controls (no addition of substrate) and two standard solutions (anhydrous glucose and anhydrous glutamic acid, final concentration of each 3 mg L^{-1}) were also included in the test. The bottles were placed in the dark at 20°C (± 1°C). After a time period of 20 days, the oxygen concetration was measured again (t = 20). The controls gave a decrease in oxygen concentration of ca. 1.30 mg/L. The BOD_5 of the standards should give values of 200 ± 20 mg L^{-1}. We measured values of 250 ± 25 mg L^{-1} for BOD_{20} of the standards. From the results of the control measurements and the standards, we can conclude that the test method is reliable.

Calculation of the biodegradability

The BOD was calculated from the difference in oxygen concentration at t = 0 and at t = 20 of the compound minus the average difference in oxygen concentration at t = 0 and t = 20 for the controls. The percentage biodegradation is (BOD/TOD) · 100%. (TOD for $C_cH_hO_oN_n$: [(4c + h - 2o - 3n) · 8] / M).

4.7.4 Biotoxicity

Saccharomyces cerevisae was grown overnight (30°) in a PDB (potato dextrose broth) medium. *Escherichia coli*, *Pseudomonas putida*, and *Bacillus subtilis* were grown overnight (30°) in a TSB (trypton soya broth) medium on a rotary shaker. Microtitre plates were filled with 250 µL diluted culture (initial optical density about 0.05). 100 µL surfactant solutions (final concentrations 0, 1, 20, 100, 500, 1000, and 5000 g L^{-1}) were added to the microtitre plates. The growth of the micro-organisms was monitored at 30°C every 10 minutes for at least 15 hours by measuring the optical density using a Labsystems Bioscreen C apparatus. The curves were analyzed either with BioRTN or BioLink-Win software. The time needed to reach a difference in optical density from 0.15 to 0.50 was

compared to the cases where no surfactant was present in the medium (the controls). All measurements were performed twice in triplicate.

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Chapter 5 [a]

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[1-6] and good (oil) solubilization properties.[7-9]

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 α,ω-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.

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5.2 History of gemini surfactants

The name gemini surfactant was introduced by Menger in 1991,[11] as outlined in Chapter 1. The first gemini surfactants, however, had already been prepared twenty years before by Bunton *et al.*[12]. 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.*[12] 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.[12] The first evaluation of the properties of (anionic) gemini surfactants was described by Okahara *et al.*[13] 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.[13-16]

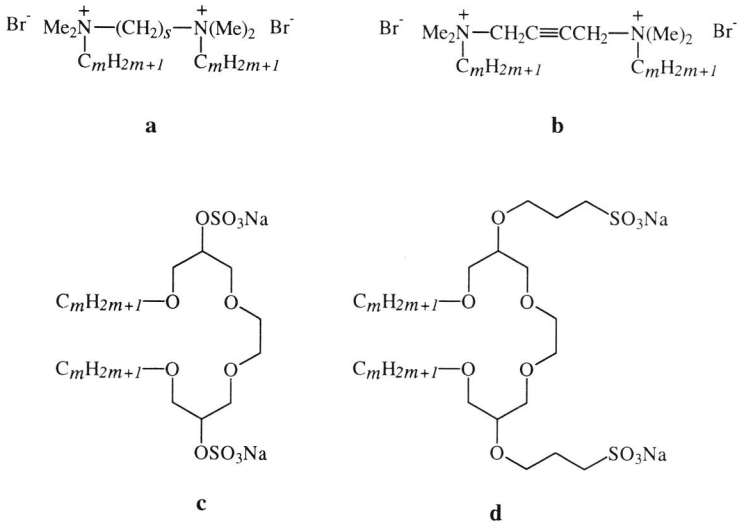

Figure 1. a: Alkanediyl-α,ω-bis(dimethylalkylammonium bromide) surfactants (abbreviated as *m-s-m*, $2Br^-$), b: alkanediyl-α,ω-bis(dimethyl-2-butyn-ammonium bromide) surfactants, c: disodium 1,8-bis(alkoxymethyl)-3,6-dioxaoctane-1,8-disulfates and d: disodium 5,12-bis(alkoxymethyl)-4,7,10,13-tetraoxahexadecane-1,16-disulfonates.

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.

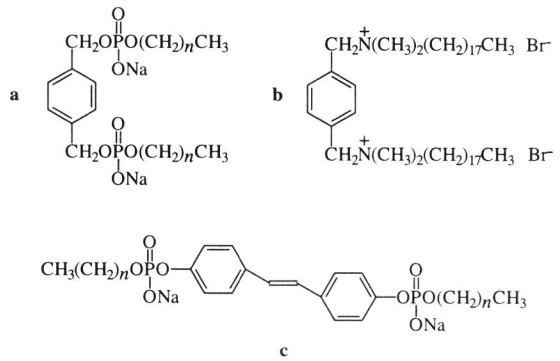

Figure 2. Gemini surfactants with a rigid spacer prepared by Menger *et al.*.[11,17]

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 ($\Delta_{mic}G^\circ$ = -3.2 ± 0.3 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 slighly 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.[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.[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.[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 *cis* conformation.[26] It has been proposed that in this *cis* conformation, the chains would already experience contact, resulting in a lower, slightly less favorable $\Delta_{mic}G°$ per CH_2 group and higher CMCs.[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.[18,26,28]

Bis(quaternary ammonium halide) geminis with a flexible hydrophilic spacer (Rosen *et al.*[29]: s = -$CH_2CHOHCHOHCH_2$-) 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.[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.[17] This unexpected behavior has been ascribed to the formation of submicellar aggregates. The same behavior has been observed with the flexible hydrophilic spacers.[31]

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

Maiti *et al.*[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.[34] The 12-*s*-12, $2Br^-$ series of the 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 α,ω-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 *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 ≥ 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 *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]

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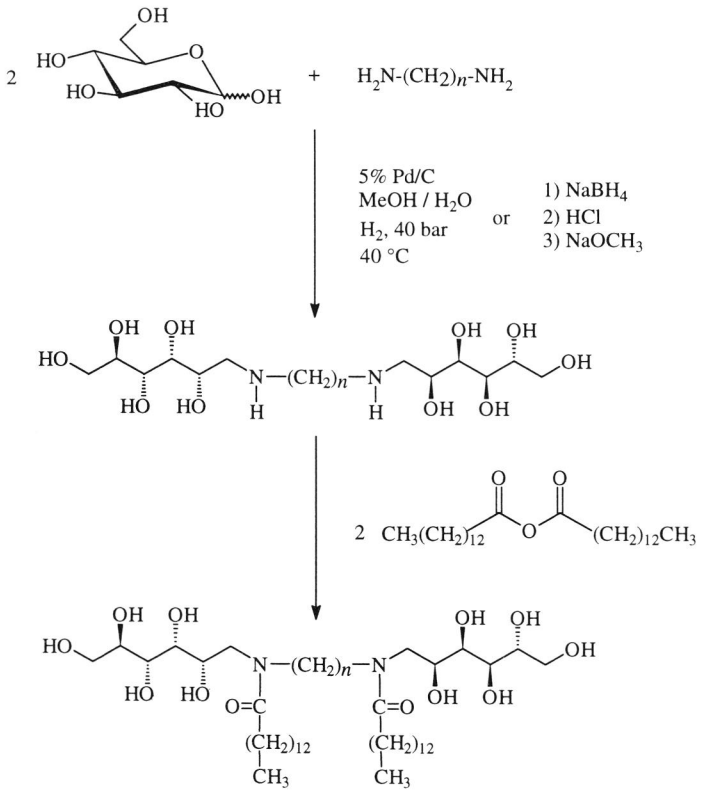
[b] The surfactant 12-24-12 is at the borderline between a bolaamphiphile and a gemini surfactant. As no clear distinction has been made in literature between these two types of surfactants, we consider the surfactants to be bolaamphiphiles when $2m < s$ and gemini surfactants when $2m > s$, on the presumption that when $2m < s$ 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 α,ω-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 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-1-amino-1-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),[44] 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.[45-48]

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

compound	mp (°C)	ΔH_{melt} (kJ.mol^{-1})	T_{Krafft} (°C)[a]	ΔH_{Krafft} (kJ.mol^{-1})
bola-6	151.4-153.4	112.8	53	28.0
bola-8	151.9-154.2	116.0	74	55.0
bola-10	150.0-152.0	116.5	90	81.4
14-6-14	76.8-82.2[b]	57.4	32	45.5
14-8-14	94.4-96.9[c]	83.7	43	63.7
14-10-14	83.1-87.6	63.9	38	50.7

[a] Broad transition. [b]Clearing point 135.2 °C (smectic A phase).[25,49,50] [c]Monotropic smectic A, clearing point upon cooling 44.5 °C.[49,50]

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.[21,51] 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_α phase) in the temperature range from 40°C to about 60°C (Figure 3), which suggests that vesicles will be formed in dilute solution.[22,44,51] 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,

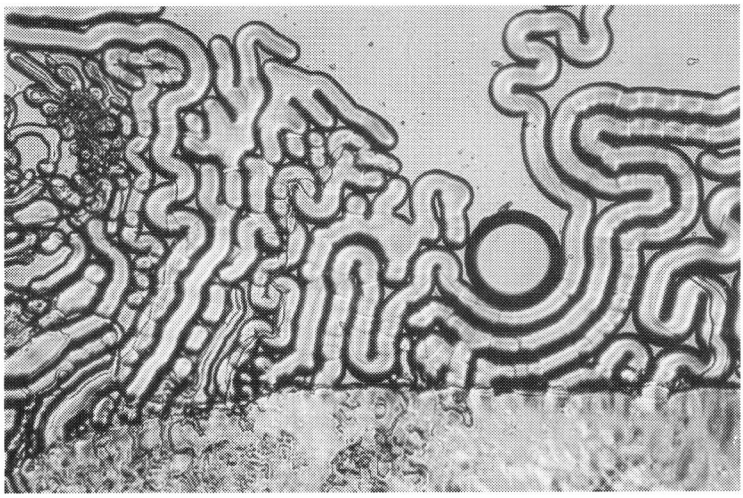


Figure 3. Formation of lyotropic mesophases in a contact preparation of water and 14-10-14, 45°C: from top to bottom, water-myelin figures-L_α-compound.

since the exact relationship between cubic phases and the corresponding aggregates in aqueous solution is unclear in most cases.

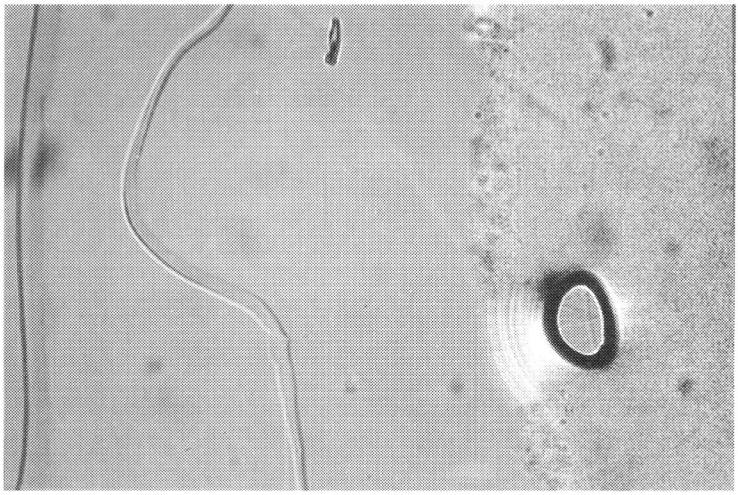


Figure 4. Formation of lyotropic mesophases in a contact preparation of water and 14-8-14, 53 °C: from left to right, water-cub-cub-crystalline material.

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,[52] since negative staining may give rise to staining and drying artefacts.[53,54]

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.

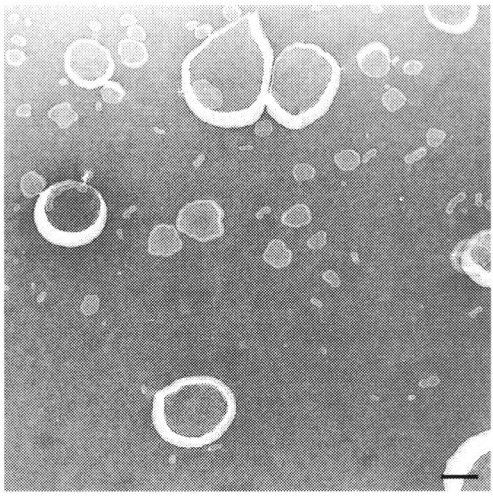


Figure 5. Negatively stained (2% PTA) electron micrograph of 14-10-14 shows vesicles. The bar represents 100 nm.

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.*[54] 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, $3Br^-$ form branched thread-like micelles.[41] 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.[54-65] 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.

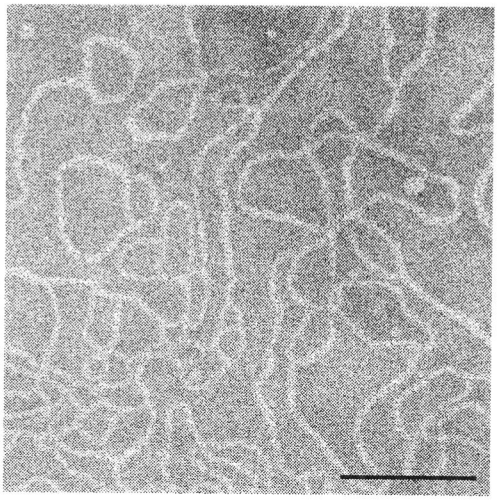


Figure 6. Negatively stained (2% PTA) electron micrograph of 14-6-14: presence of thread-like micelles. The bar represents 100 nm.

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 ($\frac{1}{3} < P < \frac{1}{2}$).[37] If $s < 4$, the equally charged headgroups are closer than the optimal distance. The thread-like micelles are

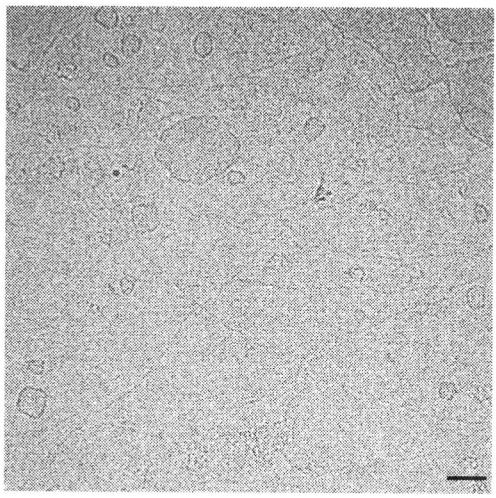


Figure 7. Cryo-transmission electron micrograph showing sheets, vesicles, and thread-like micelles formed by 14-6-14. The bar represents 100 nm.

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 ⅓ 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_0) is reduced, which leads to a larger value for the packing parameter ($p = v \cdot (a_0 \cdot l_c)^{-1}$; 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.[36,66,67] 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 gemini surfactants based on carbohydrates.

Compound	EM (negative staining)	cryo-TEM	viscoelastic behavior
14-6-14	thread-like micelles	threads, sheets, vesicles	at room temperature
14-8-14	thread-like micelles	not determined	at 4 °C
14-10-14	vesicles	vesicles	no viscoelasticity observed

5.6 Introduction to rheology[68]

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.[69] 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 ω and maximum strain γ 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, $G^*(\omega)$:[c]

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

Herein: $G' = G^*\cos\delta$; the elastic or storage modulus
$G'' = G^*\sin\delta$; the viscous or loss modulus
δ is the phase shift angle
ω 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° out-of-phase is called viscous ($\delta = 90°$, $\sin\delta = 1$). A system is viscoelastic if $0 < \delta < 90°$.

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

[c] $i = (-1)^{1/2}$

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-1-amino-1-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

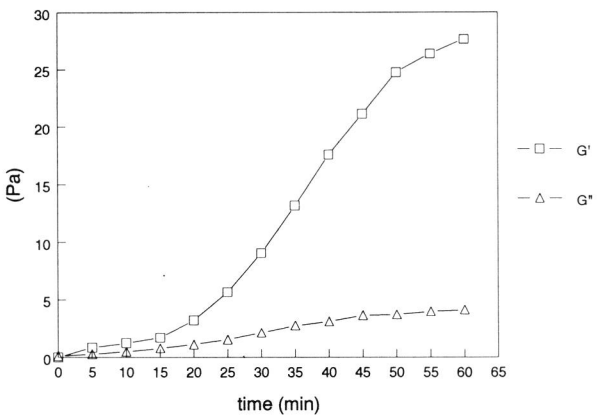


Figure 8. Dynamic properties of a 5 mM solution of 14-6-14 as a function of time (γ = 0.5%, ω = 1 rad s^{-1}, 7.5°C).

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.*[75], the Encyclopedia Britannica describes a gel as

"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%.[76]

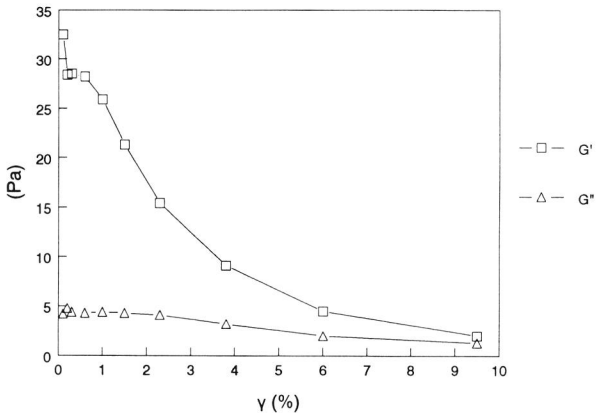


Figure 9. Dynamic properties of a 5 mM solution of 14-6-14 as a function of strain γ (ω = 1 rad s^{-1}, 7.5°C).

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.

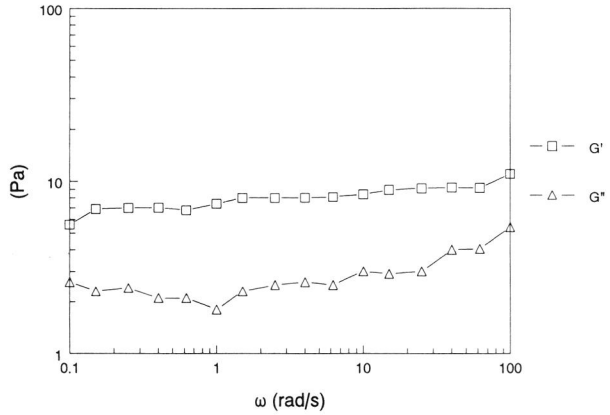


Figure 10. Dynamic properties of a 5 mM solution of 14-6-14 as a function of angular frequency, ω (γ = 0.5%, 7.5 °C).

5.7 Conclusions

The nonionic carbohydrate-derived gemini 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 gemini surfactant 14-6-14 forms a weak gel.

5.8 Experimental

Characterization. ^{1}H- and ^{13}C-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.

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 appropiate 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 $NaBH_4$ (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 bolaamphile 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 bolaamphiles 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). ^{1}H-NMR (DMSO-d_6, ppm): 1.14 (m. 4H), 1.26 (m, 4H), 2.36 (m, 8H), 3.39 (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).

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_3OD, 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_3OD, 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 ($C_{2'}$-$C_{3'}$; $C_{2''}$-$C_{13''}$), 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 ($C_{1''}$). 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.

Compound	Formula	Calculated			Found		
		% C	% H	% N	% C	% H	% N
bola-6	$C_{18}H_{40}N_2O_{10}$	48.64	9.07	6.30	48.68	8.99	6.31
bola-8	$C_{20}H_{44}N_2O_{10}$	50.83	9.38	5.93	50.88	9.35	5.84
bola-10	$C_{22}H_{48}N_2O_{10}$	52.78	9.66	5.60	52.55	9.39	5.48
14-6-14	$C_{46}H_{92}N_2O_{12}$	63.89	10.72	3.24	63.56	10.55	3.32
14-8-14	$C_{48}H_{96}N_2O_{12}$	64.54	10.83	3.14	64.57	10.79	3.21
14-10-14[a]	$C_{50}H_{100}N_2O_{12}$	65.18	10.94	3.04	65.60	10.75	3.07

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

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Chapter 6

Bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes and Bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes

6.1 Introduction

In the previous chapter, a limited series of gemini surfactants, based on carbohydrates, was described. Their aggregation behavior was found to depend on the spacer length within the series. To gain more insight into the role of the spacer and the alkyl chain lengths with respect to their aggregation behavior, we prepared two larger series of gemini surfactants.

The first series involves gemini surfactants with a fixed acyl chain length (containing 10 carbon atoms) and a spacer length varying from 2 to 12 methylene groups, the bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes (abbreviated as 10-*s*-10). The second series involves gemini surfactants with an acyl chain containing 5 to 16 carbon atoms and a fixed spacer length of 10 methylene groups, the bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes (abbreviated as *m*-10-*m*). The aggregation of these gemini surfactants based on carbohydrates was studied using polarizing and electron microscopy.

Searching for appropriate applications for these geminis, our attention was drawn by an article by Dam *et al.*[1], who observed that the cationic alkanediyl-α,ω-bis(dimethylalkylammonium bromide) gemini surfactants have an enhanced tendency for oil solubilization. Therefore, we determined the capacity of the two series of carbohydrate-derived gemini surfactants to solubilize hexane and toluene in water. The sections on the results of the oil solubilization experiments are preceded by a short introduction in which some aspects with repect to oil solubilization are discussed.

6.2 Physical properties of bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes and bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes

The melting points and the accompanying melting enthalpies of the 10-*s*-10 and *m*-10-*m* series are shown in Table 1. All compounds were solids, except for 10-12-10. In the series 10-*s*-10, the melting points decrease with increasing spacer length up to $s = 6$. As anticipated, a longer spacer length probably prevents close packing in a crystal lattice. For $s > 6$, the melting points of the gemini surfactants with an even number of methylene groups in the spacer are nearly constant and about the same as those for the 14-*s*-14 series ($s = 6, 8, 10$; section 5.3). There seems to be an odd-even effect[2] as the melting points of 10-7-10 and 10-9-10 are lower than the melting points of the gemini surfactants with an even spacer

length. The enthalpies of melting of the former geminis are also lower (30.3 and 26.0 kJ mol^{-1}, respectively), the enthalpies of melting are between 37 and 51 kJ mol^{-1} for even spacer lengths. Besides from the odd-even effect, the melting enthalpies do not show a clear trend with spacer length.

Compound $NC_{10}nC_4$ glucitol (*N*-decanoyl,*N*-butyl-1-amino-1-deoxy-D-glucitol) was prepared in order to compare its properties with those of its dimeric counterpart, gemini surfactant 10-8-10. The melting point and enthalpy of melting of $NC_{10}nC_4$ glucitol lies in the same range as for the gemini surfactants with an even spacer length from $s = 6$ to $s = 10$.

Table 1. Melting points and melting enthalpies of bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes and bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes.

Compound	mp (°C)	ΔH (kJ mol^{-1})	Compound	mp (°C)	ΔH (kJ mol^{-1})
10-2-10	101.9-107.3[a]	50.7	5-10-5	93.1-101.5	43.9
10-4-10	88.1-93.7[b]	37.6	6-10-6	36.4-49.0	34.7
10-6-10	76.1-84.2	37.1	7-10-7	44.6-54.3	29.8
10-7-10	53.8-61.8	30.3	8-10-8	77.9-81.4	54.1
10-8-10	79.8-87.9	54.5	9-10-9	66.2-75.0	26.9
10-9-10	42.2-48.3	26.0	12-10-12	80.1-86.0	49.3
10-10-10	73.1-82.2	45.7	14-10-14	83.1-87.6	63.9
10-12-10	not solid	-	16-10-16	88.9-93.1	51.6
$NC_{10}nC_4$ glucitol	83.1-85.1	39.2			

[a] Clearing point 172.6°C (6.16 kJ mol^{-1}), S_A.[3] [b]Clearing point in second run 91.9°C (2.07 kJ mol^{-1}), S_A.

Gemini 5-10-5 (which is a "borderline gemini", since $2m = s$) has a relatively high melting point compared to the other members of the *m*-10-*m* series. The short side chains may be able to fold back (the two chains together are as long as the spacer), thus allowing a closer packing. For even $m \geq 8$, the melting points and the enthalpies of melting are in the same range (78-93°C and 49-51 kJ mol^{-1}) as those for the 10-*s*-10 series with *s* even and larger than 4. Again, the gemini surfactants with uneven chain lengths have lower melting points and melting enthalpies.

Thus, the melting points for gemini series 10-*s*-10 with *s* being even and ranging from 6 to 10 and series *m*-10-*m* with *m* being even and ranging from 8 to 16 are in the range 75-90°C. We suggest the molecules are packed with the carbohydrate moieties forming hydrogen bonded double layers and interdigitizing chains (Figure 1). To confirm this model for the packing, a few representative gemini surfactants were submitted for X-ray analysis. Visually

and under the microscope, the solids formed by the gemini surfactants appear crystalline. X-ray analysis, however, was not successful, and indicates amorphous materials.

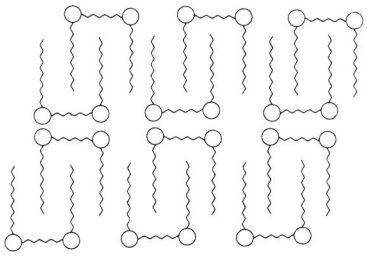

Figure 1. Possible crystal lattice for the *m-s-m* gemini surfactants.

The only compounds which show Krafft temperatures in the DCS are those with spacer length 10 and chain lengths 12, 14, and 16. The fact that other compounds do not show peaks in the DSC scan does not indicate whether they are readily or poorly soluble in water (Table 2).

Table 2. Krafft temperature and associated enthalpies of bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes with s = 12, 14, 16.

Compound	T_{Krafft} (°C)	ΔH_{Krafft} (kJ mol^{-1})
12-10-12	29	32.5
14-10-14	38[a]	50.7
16-10-16	43	60.3[b]
$NC_{10}nC_4$ glucitol	29	28.2

[a] Broad transition. [b] Transition upon cooling 10°C (-46.0 kJ mol^{-1}). The second heating run shows a dip (4.1-8.3°C (-9.2 kJ mol^{-1})) a peak (22.0-23.8°C (53.2 kJ mol^{-1})) and a peak with a shoulder (29.8-31.7°C (21.6 kJ mol^{-1})). This behavior is reproducable.

As expected, the Krafft temperatures and the associated enthalpies increase with increasing chain length. Compound 16-10-16 shows peculiar but reproducable solution behavior. In the first heating scan, one endothermic peak is observed, the Krafft temperature, with an associated enthalpy of about 62 kJ mol^{-1}. When the sample is cooled down, a crystallization peak is observed with an enthalpy of -47 kJ mol^{-1}, which is lower than the solubilization enthalpy. Upon heating for the second time, a dip is observed, probably due to further crystallization of the compound (4.1-8.3°C (-9.2 kJ mol^{-1})). The compound then also dissolves in two different stages: at 22.0-23.8°C (53.2 kJ mol^{-1}) and at 29.8-31.7°C (21.6 kJ mol^{-1}).

6.3 Aggregation behavior

6.3.1 Aggregation behavior of bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes and bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes studied using the penetration technique

Table 3. Lyotropic liquid crystalline behavior from ambient temperature (22°C) to 90°C shown by bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes and bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes.

Compound	Polarizing Microscopy
10-2-10	H_I(< 55°C)-L_α-bulk
10-4-10	H_I(< 73°C)-cub-bulk
10-6-10	cub-cub-H_I(< 65°C)-L_α(45-63°C)-bulk
10-7-10	cub-H_I(< 39°C)-L_α(33-39°C)-cub(33-56°C) bulk
10-8-10	cub-bulk
10-9-10	cub-bulk
10-10-10	myelins(< 46°C)-L_α(< 53°C)-cub(38-85°C)
10-12-10	cub(< 47°C)-L_α(< 50°C)-bulk
5-10-5	no lyotropic mesophases
6-10-6	cub-L_α(< 43°C)-cub-(32-76°C)-bulk
7-10-7	myelins(< 46°C)-cub(46-56°C)-L_α(< 56°C)-cub(< 56°C)-bulk
8-10-8	myelins(< 57°C)-cub(> 57°C)-L_α(< 60°C)-bulk
9-10-9	myelins(< 54°C)-L_α(< 54°C)-cub(< 35-79°C)-bulk
12-10-12	cub-L_α(> 45°C)-cub(>45°C)-bulk
14-10-14	myelins(37-57°C)-cub(> 57°C)-L_α(37-73°C)-cub(>49°C)-bulk
16-10-16	myelins(< 90°C)-L_α-cub(> 70°C)-bulk
$NC_{10}nC_4$ glucitol	myelins(< 70°C)-cub(> 70°C)-L_α-cub(> 53°C)-bulk

Table 3 shows the lyotropic mesophases obtained by applying the penetration technique (see section 3.2) for the 10-*s*-10 and *m*-10-*m* geminis. The lyotropic behavior was studied by heating a sample with water from ambient temperature (c. 22°C) to about 90°C.

The formation of a hexagonal phase at the water-compound boundaries is observed for gemini series 10-*s*-10 for s = 2 and 4. This is an indication for the formation of rod-like micelles in aqueous solution. For s = 6 and 7, cubic and hexagonal phases are observed. These compounds may also form some type of micellar aggregates. Although we are not sure of the

exact nature of the isotropic phases (all optically isotropic phases are classified as "cub", cubic phases), the cubic phases for s = 8 and 9 are probably of the V_I-type. The relationship between the V_I-phase and aggregates in dilute solution is not quite clear, oblate spheroids as well as vesicles may be formed. The myelin structures observed for 10-10-10 provide an indication for vesicle formation. Gemini 10-12-10 is also likely to form vesicles.

Compound 5-10-5 does not show lyotropic mesophases. The nature of the aggregation behavior (if any) is unclear. The vast majority of the *m*-10-*m* series and $NC_{10}nC_4$ glucitol show myelin structures. In electron microscopy experiments, the observation of vesicles is expected.

6.3.2 Aggregation behavior of bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes and bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes studied using electron microscopy

Aggregate formation was enhanced by sonicating 5 mM aqueous samples of geminis 10-*s*-10 and *m*-10-*m*. Only compounds 10-2-10 and 10-4-10 gave a clear solution. Therefore, sodium dodecylbenzene sulfonate (NaLAS, 5 mol%) was added to increase the solubility of the compounds (as was done for the gemini surfactants described in Chapter 5). The samples used for electron microscopy were negatively stained with PTA (sodium phosphotungstate pH 7.2). As most hexagonal and lamellar lyotropic mesophases were stable from room temperature up to about 50°C, nearly all solutions were prepared at 35°C. Solutions of 12-10-12, 14-10-14, and 16-10-16 were prepared at 55°C because lamellar lyotropic mesophases had been observed in a higher temperature range (about 45-60°C, Table 3).

Gemini surfactant 10-2-10 shows short thread-like micelles. Some dots are also observed, which might be the top view of the short threads. Geminis 10-4-10, 10-6-10 and 10-7-10 show thread-like micelles and some loops (as was observed for 14-6-14 and 14-8-14 described in Chapter 5), see Figure 2. The thread-like micelles are about 60 Å thick, which is about twice the length of the extended monomers. It seems as if the lengths of the thread-like micelles increase with increasing spacer length, but this might also be a concentration effect (the grids are covered to a greater extent with threads for the longer spacer lengths). The solutions of the series 10-*s*-10 are not viscoelastic at ambient temperature or at 4°C. In most images, the thread-like micelles of this series are much shorter than those formed by 14-6-14 and 14-8-14 (Chapter 5). Entanglement is therefore less likely to occur.

Compounds 10-8-10 and 10-9-10 show very peculiar aggregation behavior. Compound10-8-10 forms thread-like micelles immediately after preparation (Figure 3). Some loops and also a few small clusters (25-50 nm) are observed. When the solution is cooled to 4°C or when more NaLAS (7.5%) is added, the threads start to cluster (Figure 4). Gemini 10-9-10 shows large clusters (60-500 nm) just after the solution has been prepared (Figure 5).

No individual thread-like micelles are observed. The clusters resemble two dimensional balls of wool. The clusters may be two dimensional in reality: there is no accumulation of staining material around the clusters (they are equally colored on the inside and on the boundaries) as there is around vesicles (which are three dimensional). We have not encountered examples of any such structures in the literature.

Gemini surfactant 10-10-10 is the first in the 10-*s*-10 series that forms lamellar aggregates. Thread-like micelles are not observed. The aggregation behavior of 10-10-10 is not consistent. When the solution was prepared the first time, only unilamellar vesicles were observed (30-150 nm). The second time unilamellar vesicles were observed in addition to multilamellar vesicles and tubular vesicles (Figure 6). The bilayers of the multilamellar vesicles are about 45 Å thick, which is slighly less than twice the extended monomer length.

Tubular vesicles seem to grow from multilamellar vesicles. Tubular vesicles have been observed before.[4-7] Di-*n*-dodecyldimethylammonium bromide, for example, forms large tubules, spherical vesicles, vesicles connected to tubules and tubules protruding from vesicles when a solution was gently shaken.[5] The morphological transformations were recorded on video tape. In the case of a tubule attached to a vesicle, the tubule elongated as the vesicle shrank. A vesicle with a protruding tubule was converted into a round vesicle. These conversions occurred within a few seconds. The 10-10-10 solutions transform into a strong gel upon standing in the refrigerator for about two weeks. This behavior is reproducable. The existence of long tubular structures could account for the gelling of the solution at 4 °C.

The 10-12-10 gemini was not sufficiently soluble to permit electron microscopy experiments, even with the addition of extra NaLAS.

The first member of the *m*-10-*m* series, 5-10-5, shows undefined material under the electron microscope. We do not know what kind of aggregates are formed, if any. The following two gemini surfactants, 6-10-6 and 7-10-7, show bilayered material, but the material is not clearly defined. From 8-10- 8 on, the bilayered material is more structured and for 9-10-9, 12-10-12, 14-10-14, and 16-10-16 vesicles are clearly observed (Figure 7). As for 10-10-10, a few tubular vesicles are observed for 9-10-9. A few "ribbons" are also observed with 16-10-16. The slow transformation of vesicles into a helical morphology has been observed for an α-amino-acid based, double-chain surfactant.[7] When the solution was warmed in this case, the helices were transformed into large, flexible vesicles. Helical fibers were also observed for aldonamides (see Chapter 1).

As opposed to its dimeric counterpart that forms (clusters) of thread-like micelles, $NC_{10}nC_4$ glucitol (including 5 mol% NaLAS) shows bilayered material. Table 4 summarizes the types of aggregates formed by the two series of gemini surfactants.

The predictions of the types of aggregates formed by the gemini surfactants which we obtained via studying their lyotropic mesophases are quite satisfactory: micelles for the gemini surfactants having spacer lengths shorter than 10 methylene groups, bilayer formation for

surfactants with a spacer length of 10 (or more), no (defined) aggregate formation for 5-10-5 (which is at the borderline of what may be called a surfactant) and the formation of bilayers for $NC_{10}nC_4$ glucitol.

It has already been mentioned that gemini surfactants 10-2-10 and 10-4-10 give clear solutions also in absence of NaLAS. These samples show also short, thread-like micelles. It would be interesting to know where the NaLAS is situated in the aggregates. A study of mixed micelles of ethanediyl-1,2-bis(dodecyldimethylammonium bromide) and dodecyltrimethylammonium bromide revealed a rather uniform distribution of DTAB throughout the micelles and not a preferential location at the higher curved thread end-caps as might have been suspected.[8]

As the trends in morphology inferred for negatively stained samples were very consistent, no additional cryo-transmission electron microscopy experiments were performed.

Table 4. Aggregates of bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes and bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes observed by electron microscopy.

Compound	appearance	EM
10-2-10	clear	short thread-like micelles
10-4-10	clear	thread-like micelles, a few loops
10-6-10	clear	thread-like micelles, a few loops
10-7-10	blueish	thread-like micelles, a few loops
10-8-10	milky	thread-like micelles, loops and small clusters which grow in time
10-9-10	milky	clusters of thread-like micelles (60-500 nm; like 2D balls of wool)
10-10-10	milky	vesicles and tubular vesicles, no threads observed
10-12-10		not soluble enough
5-10-5	clear	undefined material
6-10-6	milky	bilayered material, not very defined
7-10-7	blueish	bilayered material, not very defined
8-10-8	clear	bilayered material
9-10-9	blueish	vesicles (50-200 nm) and tubular vesicles
12-10-12	blueish (55 °C)	vesicles and sheets (35-250 nm)
14-10-14	blueish (55 °C)	vesicles
16-10-16	blueish (55 °C)	vesicles (a few ribbons)
$NC_{10}nC_4$ glucitol	clear	bilayered material (sheets)

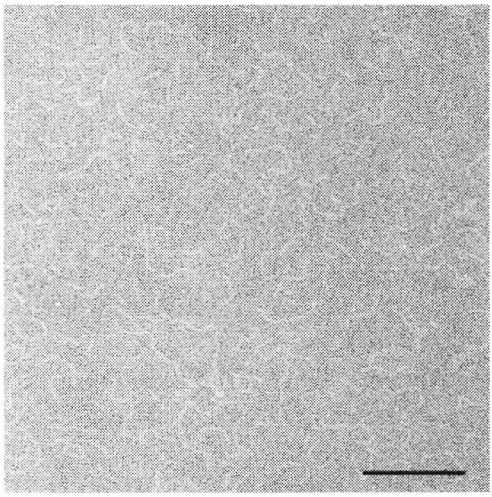

Figure 2. Negatively stained (2% PTA) electron micrograph of thread-like micelles formed by 10-4-10. The bar represents 100 nm.

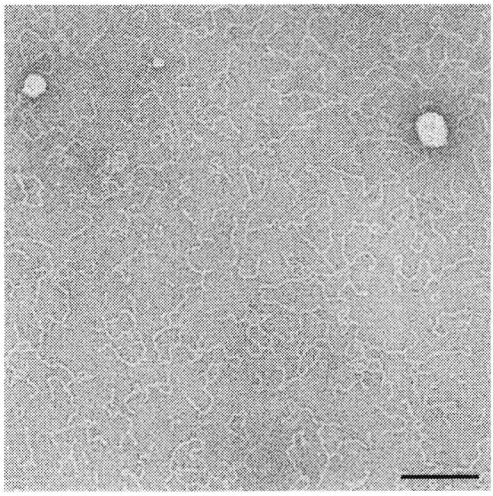

Figure 3. Negatively stained (2% PTA) electron micrograph of thread-like micelles formed by 10-8-10, immediately after preparation of the solution. The bar represents 100 nm.

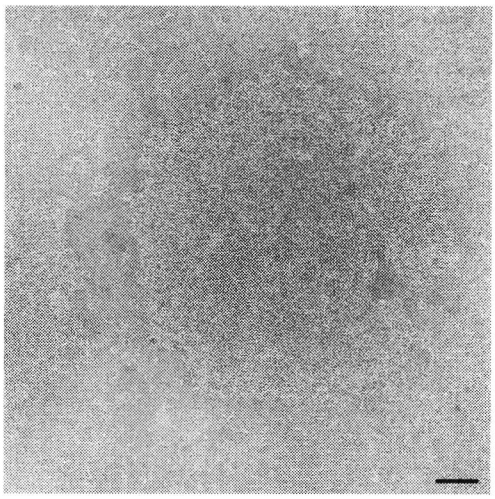

Figure 4. Negatively stained (2% PTA) electron micrograph of 10-8-10. The thread-like micelles cluster when the solution has been kept at 4 °C for 30 min. The bar represents 100 nm.

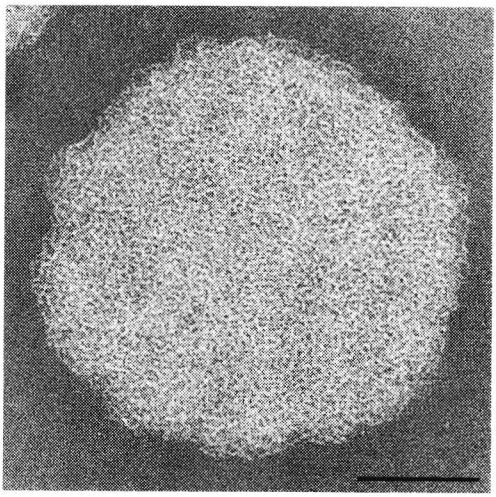

Figure 5. Negatively stained (2% PTA) electron micrograph of large clusters formed by 10-9-10. In this particular case, 7.5% NaLAS was added,however,the same clusters were observed when 5% NaLAS was added. The bar represents 100 nm.

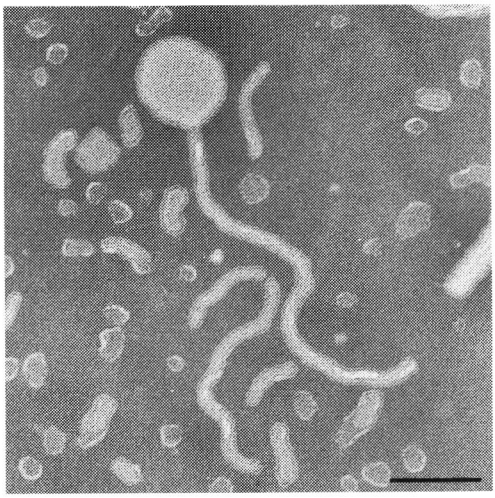

Figure 6. Negatively stained electron micrograph of 10-10-10. Vesicles and tubular vesicles are observed. The bar represents 100 nm.

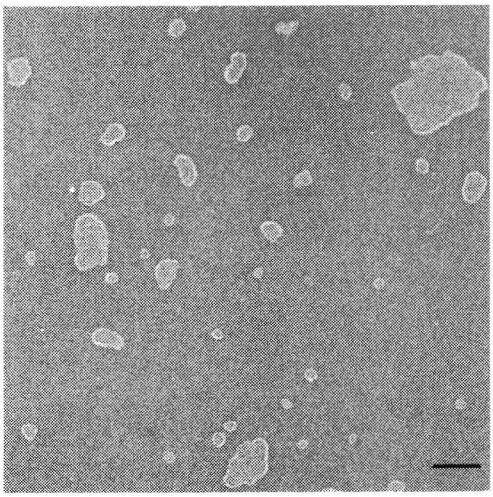

Figure 7. Negatively stained (2% PTA) electron micrograph of vesicles formed by 12-10-12. The bar represents 100 nm.

6.4 Oil solubilization experiments

The enhanced solubility of insoluble or sparingly water soluble hydrophobic compounds (oily compounds) in aqueous micellar solutions is called solubilization.[9,10] Solubilization not only occurs in micellar solutions, but also in larger aggregates such as microemulsions, vesicles and cylindrical micelles.[9] Solubilization plays an important role in, *e.g.*, the food industry (margarine, ice cream, coffee whiteners, soups, sauces), in the pharmaceutical industry, in cosmetics, in paints, and in the petrochemical industry (tertiary oil recovery).

6.4.1 Introduction to solubilization

Karaborni *et al.*[11-13] performed molecular dynamics simulations of the transfer of oil molecules from an oil droplet to an aqueous solution of surfactants and micelles. Analysis of the solubilization sites showed that at the onset of solubilization, oil molecules are located between the surfactant chains. At later stages of the simulation, oil molecules were found either between the chains or in oil pools in the micellar centers.[11]

The MD-simulations are in agreement with experimental results for the location of alcohols and benzene in micelles. At low concentrations they are located at the micellar surface; at higher solute concentrations they penetrate into the micellar core.[10] The view that alkanes will be solubilized in the hydrocarbon micellar core is an oversimplification. The solubility of alkanes in micellar solutions is less than their solubility in hydrocarbon solvents. Taking into account the size of micelles, at least a fraction of the solute will be close to the surface.[10]

Additives may change the shape of the aggregates. When spherical micelles are transformed into elongated structures, it appears that the solubilization of alkanes increases, whereas the solubilization of polar solutes such as alcohols decreases.[10]

It may be questioned to what extent of solubilization the system is still a micellar solution. If solubilization significantly affects the shape and/or size of the aggregates, an emulsion may form. There is, however, no clearly defined borderline.[9,14]

Based on the size of the emulsions, micro- and macroemulsions can be distinguished. The size of microemulsions ranges from 10-200 nm. Microemulsions are thus transparent or semitransparent to visible light. Microemulsions are thermodynamically (*i.e.*, indefinitely) stable.[14,15] Macroemulsions have sizes ranging from 0.2 to 50 μm; the emulsions are milky white. Macroemulsions are metastable.

Another distinction can be made regarding the nature of the dispersed phase. In an oil-in-water emulsion (abbreviated as o/w), oil (which stands for any type of water-immiscible liquid) is dispersed in water. This type of emulsion is mainly formed by emulsifying agents that are more soluble in water than in oil. The water-in-oil emulsion (abbreviated as w/o) is a

dispersion of water in an oily liquid. Water-in-oil emulsions are mainly formed by emulsifiers that are more soluble in oil than in water.[15] In principle, w/o and o/w emulsions can interconvert when the conditions are changed.[15]

An application of solubilization by emulsifiers/surfactants that may need further explanation is the use of surfactants in tertiary (enhanced) oil recovery.[16-20] In the first stage of oil recovery, oil flows from the reservoir to the producing wells without additional energy input. This primary production is followed by secondary recovery methods for which water is injected into the reservoir to maintain reservoir pressure and to assist in oil displacement. At the end of this second stage, only 30-40% of the oil has been recovered. Due to the low viscosity of oil and the high interfacial tension between water and oil, residual oil is trapped in the pores of the reservoir rock. If the diameter of the oil droplet is larger than the pore throat, the residual oil does not flow towards the producing wells. A tertiary method, also called enhanced oil recovery (EOR), has been developed to recover more oil. The pressure cannot be raised further, but alternatively, the interfacial tension might be reduced by surfactants. Enhanced oil recovery by surfactants has been termed surfactant, micellar, microemulsion, soluble oil, ultra low tension, and chemical flooding.[16]

Surfactants that could be useful in enhanced oil recovery should be able to form microemulsions with oil and water and because oil recovery is a slow process, the surfactants used must be stable for a period of months and mostly even years at elevated temperatures (70-130°C) in the presence of brine.[16,18] Furthermore, they should not adsorb at the rock surface, since in that case they would be lost for solubilization.

EOR by surfactants has so far not been applied owing mainly to economics of the process as well as technical difficulties. About 100 to 200 kg of chemicals would be needed to recover 1 m^3 of oil. This would mean that oil would cost twice as much as today. If oil prices remain low and if no effort will be made to look for very effective, low cost surfactants or other methods (polymer flooding), 70% of the oil will be lost for the future.[17]

6.4.2 Experimental method

Dam *et al.*,[1] measured the solubilization of hexane and toluene by solutions of the cationic alkanediyl-α,ω-bis(dimethylalkylammonium bromide) gemini surfactants. They analyzed the aqueous layer in terms of the total amount of organic carbon. Jacobsen *et al.*[21] determined the solubilization of hexane and a series of polycyclic aromatic compounds in dodecyltrimethylammonium bromide and tetra-*n*-decyltrimethylammonium bromide micelles by direct injection of the aqueous solution into a gas chromatograph (hexane) or by ultraviolet-visible spectrophotometry. Analysis of the aqueous layer by direct injection into a gas chromatograph was also applied by Chaiko *et al.*[22], who examined the solubility of a

number of hydrocarbons (a.o. hexane and toluene) in three different surfactant solutions (1-cetylpyridinium chloride, dodecylammonium chloride, and sodium *n*-dodecylsulfate). Chaiko defined a molar solubilization ratio (MSR) as follows:

MSR = (total amount of solubilizate in the aqueous phase - moles of singly dispersed solubilizate in the aqueous phase) / (total moles of surfactants in the aqueous phase - moles of singly dispersed surfactant in the aqueous phase)[a]

We developed a method for determining the solubilities of hexane and toluene in aqueous solutions of carbohydrate-derived gemini surfactants based on these three studies (see experimental part). The reproducibility was acceptable (Tables 5 and 6).

Critical aggregation concentrations of the gemini surfactants have not been measured due to their low solubility in the absence of NaLAS.[b] We therefore express the solubility of hexane and toluene in aqueous carbohydrate-derived gemini solutions as a "molar solubilization quotient", MSQ:

MSQ = ((moles of solubilized oil in aqueous surfactant solution) - (moles of oil in aqueous solution without surfactant))/ (moles of surfactant)

If the critical aggregation concentrations are low (<< 5 mM) then MSQ = MSR. In the cases of the carbohydrate-derived surfactants, the critical aggregation concentration are most likely fairly low, so MSQ ≈ MSR.

6.4.3 Solubilization of hexane and toluene by series 10-*s*-10

Table 5 and Figure 8 report the solubilization of hexane and toluene by gemini surfactant series 10-*s*-10. The amounts of hexane and toluene solubilized increase with increasing spacer length up to $s = 9$. The increase is particularly pronounced for toluene. In the case of gemini surfactant 10-10-10 the extent of solubilization collapses.[23] This is also the first gemini surfactant that does not form thread-like micelles but vesicles in ascending values for *s*. Up to $s = 9$, the hexane-containing gemini solutions are clear. This means that the aggregate type is either micellar or that stable microemulsions have been formed. The number of hexane molecules solubilized by one gemini surfactant monomer increases from 1.3 for 10-2-10 to

[a] The moles of singly dispersed surfactant in the aqueous phase is equal to the critical micelle concentration of the surfactant.

[b] We only determined the surface tensions of the 5 mM gemini solutions containing 5 mol% NaLAS. The values were in the range 28 - 31 mN m^{-1}.

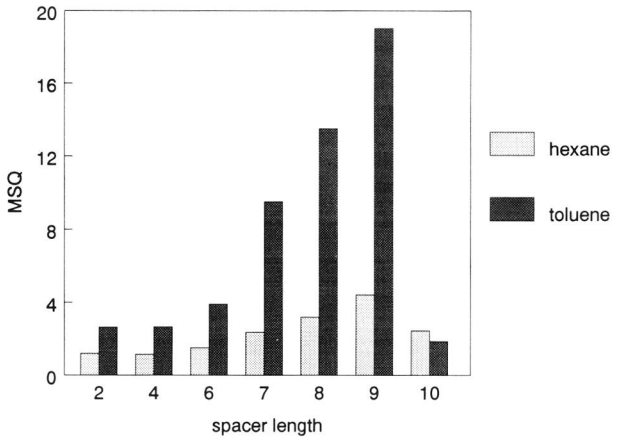

Figure 8. Solubilization of hexane and toluene in aqueous solutions of carbohydrate-derived gemini surfactant series 10-*s*-10.

4.5 for 10-9-10. It seems likely that the hexane molecules are solubilized in the gap between the two chains of the surfactant molecule. As this gap increases with increasing spacer length, so does the amount of hexane solubilized. Gemini surfactant 10-9-10 shows the highest solubilization both for hexane and toluene. This is the surfactant that forms the 2D clusters observed with EM (section 6.3.2).

Table 5. Solubilization of hexane and toluene in 5 mM solutions of geminis 10-*s*-10.

surfactant	MSQ hexane	appearance[a]	MSQ toluene	appearance[b]
10-2-10	1.21 ± 0.05	clear	2.66 ± 0.16	clear
10-4-10	1.15 ± 0.09	clear	2.68 ± 0.16	clear
10-6-10	1.53 ± 0.08	clear	3.92 ± 0.40	milky
10-7-10	2.37 ± 0.07	clear	9.52 ± 1.64	milky
10-8-10	3.21 ± 0.40	clear	13.51 ± 1.91	blueish
10-9-10	4.42 ± 0.44	clear	19.04 ± 3.54	milky
10-10-10	2.46 ± 0.10	milky	1.89 ± 0.17	milky

[a] The hexane layer was milky in all cases. [b] The toluene layer was milky in all cases.

Toluene does not pack as easily in the gap as the linear hexane and so macroemulsions are formed when s = 6-9. The solutions have a milky appearance. The number of toluene molecules solubilized per gemini monomer mounts to 20 for 10-9-10. The toluene-containing solutions of 10-2-10 and 10-4-10 are clear, which might indicate the formation of microemulsions.

All organic upper layers are milky. This means that water-in-oil emulsions are formed in the organic solvent and, consequently, a small amount of gemini surfactant resides in this layer. Hence the amount of solubilized oil in the aqueous surfactant solution is even higher than presented here, due to the reduced concentration of gemini surfactant in the aqueous layer.

6.4.4 Solubilization of hexane and toluene by geminis *m*-10-*m*

In case of the *m*-10-*m* series (Table 6 and Figure 9), solubilization of hexane and toluene is low up to the point where vesicles are clearly visible using electron microscopy. Hexane is solubilized slightly better than toluene, which is the reverse of the 10-*s*-10 series, but the differences are smaller. The solubilization appears to reach a maximum at a chain length of 14. The origin of this maximum is not understood.

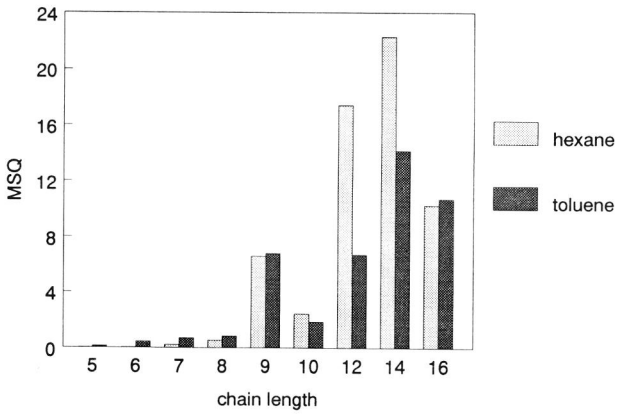

Figure 9. Solubilization of hexane and toluene in aqueous solutions of carbohydrate-derived gemini surfactant series *m*-10-*m*.

We explained the dip observed in the 10-*s*-10 series for s = 10 by the fact that 10-10-10 forms vesicles. 10-10-10 is also part of the *m*-10-*m* series, which all form bilayered material or vesicles. Compound 10-10-10 also accounts for a lower extent of solubilization in this vesicle-forming series. This would contradict our explanation for the dip in the 10-*s*-10 series. However, if the solubilization ratios for 10-10-10 would fit in the trend of the vesicle-forming series *m*-10-*m*, it would have a value for toluene of about 12, which would still produce a dip in the 10-*s*-10 series.

The organic upper layers were milky, as was the case for the 10-*s*-10 series.

Table 6. Solubilization of hexane and toluene in 5 mM solutions of gemini series *m*-10-*m*.

surfactant	MSQ hexane	appearance[a]	MSQ toluene	appearance
5-10-5	0.03 ± 0.01	clear	0.15 ± 0.08	almost clear[b]
6-10-6	0.04 ± 0.02	clear	0.45 ± 0.07	almost clear[b]
7-10-7	0.21 ± 0.04	blueish	0.73 ± 0.20	milky[b]
8-10-8	0.54 ± 0.04	blueish	0.86 ± 0.08	milky[b]
9-10-9	6.59 ± 1.06	blueish	6.81 ± 1.30	milky[b]
10-10-10	2.46 ± 0.10	milky	1.89 ± 0.17	milky[b]
12-10-12	17.43 ± 0.41	blueish	6.70 ± 0.42	milky[c]
14-10-14	22.29 ± 1.34	blueish/milky	14.16 ± 1.95	milky[c]
16-10-16	10.26 ± 0.78	blueish	10.72 ± 0.81	milky[c]

[a] The hexane layer was milky in all cases, except for 16-10-16. In this particular case it was clear. [a] The toluene layer was milky. [b] The toluene layer was clear.

6.4.5 Solubilization of hexane and toluene by reference compounds

Table 7 and Figure 10 report the solubilization of hexane and toluene in 5 mM aqueous solutions of three conventional surfactants, an anionic (NaLAS), a cationic (cetyltrimethylammonium bromide, CTAB), and a nonionic (hexaethylene glycol monododecyl ether, $C_{12}E_6$), in two nonionic carbohydrate surfactants which have been described in Chapter 2, 3, and 4 (NC_2nC_{12} glucitol and NC_2nC_{12} lactitol), and in the monomeric counterpart of gemini surfactant 10-8-10, namely $NC_{10}NC_4$ glucitol. The MSR values are also reported (all surfactants have CMCs lower than 5 mM).

$NC_{10}nC_4$ glucitol shows the highest hexane solubilization. The value is even higher than that for the dimeric counterpart, 10-8-10. NC_2nC_{12} glucitol shows the highest toluene

solubilization. Solubilization ratios for conventional surfactants are much lower than the values obtained for most gemini surfactants. Even if the results are divided by two in the case of dimeric surfactants (which hold, in fact, two monomeric surfactants) the solubilization ratios are still much higher. Thus the majority of the gemini surfactants are superior oil solubilizers. Carbohydrate-derived gemini surfactants are also superior to the cationic alkanediyl-α,ω-bis(dimethylalkylammonium bromide) gemini surfactants. The solubilization of hexane and toluene by solutions of these surfactants obtained by Dam *et al.*[1] amount to 3.84 for hexane (12-2-12) and 2.77 for toluene (14-2-14).

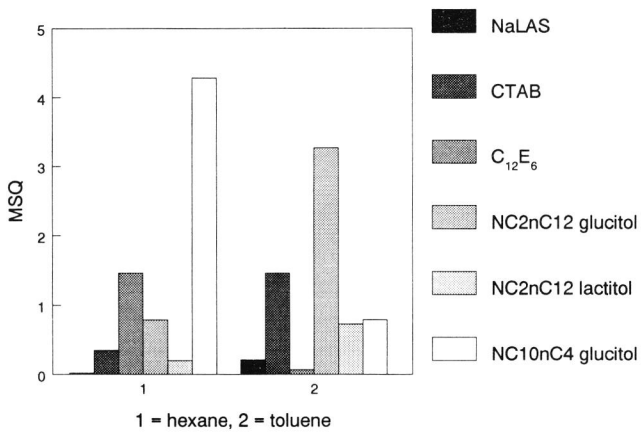

Figure 10. Solubilization of hexane and toluene in aqueous solutions of reference surfactants.

Table 7. Solubilization of hexane in 5 mM solutions of conventional surfactants.

surfactant	MSQ hexane	MSR	appearance[a]	MSQ toluene	MSR	appearance[b]
NaLAS	0.02 ±0.02	0.03	clear	0.21 ± 0.09	0.36	clear
CTAB	0.35 ± 0.03	0.43	clear	1.46 ± 0.12	1.79	clear
$C_{12}E_6$	1.46 ± 0.17	1.48	clear	0.07 ± 0.09	0.07	clear
NC_2nC_{12} glucitol	0.79 ± 0.04	0.81	clear	3.27 ± 0.26	3.39	clear
NC_2nC_{12} lactitol	0.20 ± 0.03	0.21	clear	0.73 ± 0.19	0.78	clear
$NC_{10}nC_4$ glucitol	4.28 ± 0.31	-	almost clear	0.79 ± 0.16	-	milky

[a] The hexane layer was milky. [b] The toluene layer was milky.

6.4.6 Stability of the micellar solutions and emulsions

After one day, all hexane and toluene solutions were still stable (no precipitation), except for 10-8-10, 10-9-10, and 6-10-6. Stable for at least five months were: hexane solutions of 10-2-10, 10-4-10, 10-6-10, 10-7-10, 5-10-5, and 9-10-9 and toluene solutions of 10-2-10, 10-4-10, 5-10-5, 8-10-8, 9-10-9, 12-10-12, 14-10-14, and 16-10-16. A few solutions showed some phase separation after five months: 12-10-12, 14-10-14 and 16-10-16 (hexane) and 10-6-10 and 10-7-10 (toluene).

Solutions of the non-gemini surfactants were stable for at least five months. Only $NC_{10}nC_4$ glucitol showed some phase separation in case of toluene.

The oil solubilization experiments and the stability of the micellar solutions and emulsions show that nonionic carbohydrate-derived surfactants are very interesting compounds for solubilization purposes. The solubilization values are high at low concentrations. The results show that gemini surfactants might, in principle, be interesting compounds for utilization in enhanced oil recovery. The high salinity conditions need not necessarily provide a problem for these nonionic geminis.

6.5 Conclusions

The nonionic gemini surfactants described in this chapter can be easily prepared from glucose, the appropriate diamines and alkanoic anhydrides. Two series, 10-*s*-10 and *m*-10-*m*, show consistent aggregation behavior. For $s < 10$, thread-like micelles are formed. For $s = 10$, vesicles and tubes are observed. Gemini surfactants with $5 < m < 9$ form bilayered material. When $m > 8$ vesicles are observed.

Solubilization experiments in which hexane and toluene are solubilized in aqueous carbohydrate-derived gemini solutions indicate that these geminis could find application as emulsifiers or oil solubilizers. The results agree with the trends in aggregation behavior observed by electron microscopy.

6.6 Experimental

Materials. Starting materials and solvents were purchased from large chemical suppliers. Anhydrides were distilled if necessary (possible traces of acetic anhydride leads to undesired competitive acylation between the appropriate anhydride and acetic anhydride). Anhydrides, which were not commercially available, and decanoic anhydride were prepared from the corresponding acids and acetic anhydride and purified by destillation according to literature procedures.[24] *N*-butyl-1-amino-1-deoxy-D-glucitol was kindly provided by Dr. R. Beck, Cerestar, Vilvoorde, Belgium.

Methods. See section 2.6. Gas chromatography was performed on a Carlo Erba VEGA 6000) gas chromatograph which contained a Poraplot Q fused silica 10 m x 0.53 mm ID column (Chrompack 7553). Helium was used as the carrier gas. Temperature program: T = 70°C, (1 min), T = 70°C→210°C (15°C min^{-1}), T = 210 °C (5 min). Detector: flame ionization detector (FID). Injection volume: 1.5 µL

Characterization. See section 2.8 and 5.8.

Vesicle preparation. See section 5.8.

Electron microscopy. See section 5.8. The 5 mM gemini solutions containing 5 mol% NaLAS were diluted five fold to obtain optimal electron micrographs. The solutions were prepared at 35°C, except for gemini surfactants 12-10-12, 14-10-14, and 16-10-16, which were prepared at 55°C.

Oil solubilization experiments. A sonicated gemini solution (5 ml, 5mM, containing 5 mol% NaLAS) and 0.5 ml of hexane or toluene were mixed for 18 hours in 10 ml round-bottomed tubes with screw-caps in a tumbling device at room temperature. The tubes were centrifuged carefully in a swing out centrifuge (700 x g; Sigma 4K10) to induce phase separation and to avoid long waiting times. The organic layer was removed as completely as possible with a FINN pipette. A syringe with a small needle tip was immersed into the aqueous phase whilst pushing out a small amount of air to avoid sampling of the residual organic layer. A 100 µL sample was taken from below. The needle was dipped into water and dried with a tissue to remove any possible organic solvent from the needle surface. An exactly known amount of the sample was brought into two round-bottomed tubes (about 25 mg each) with screw-caps. An internal standard solution (benzene in dichloromethane, 5 mL) was added immediately to the tubes. The solutions were shaken vigourously. About 150 mg of sodium sulfate was added to obtain a homogeneous sample, suitable for GC-analysis. Analysis of a sample before and after addition of Na_2SO_4 showed that Na_2SO_4 did not influence the outcome of the results.
The amount of hexane and toluene could be related to the internal standard (benzene). The peak areas of hexane and toluene were divided by that peak area of benzene. Concentration calculations were performed with theoretical response factors for FID response based on effective carbon numbers (ECN [3]). The correctness of these factors was tested by injection of a standard mixture of hexane and toluene in an internal standard solution. The concentrations in this standard solution calculated with the theoretical response factors were on average 99.9% (s = 1.4; n = 12) in the case of hexane and 100.6% for toluene (s = 1.0; n = 12). These results clearly indicate that the theoretical response factors can be used for the concentration calculations.
The experiments were repeated (including the preparation of fresh surfactant solutions). The values presented in sections 6.4.3 to 6.4.5 are therefore the results of two individual experiments, each covering two GC-injections.
Due to the high sensitivity of the GC-apparatus, direct injection of the aqueous sample was not possible.

The solubilities of hexane and toluene in water were low: $2 \cdot 10^{-4}$ and 3 mM, respectively. This is in reasonable agreement with literature values: $7 \cdot 10^{-4}$ M and 7 mM.[22]

Bis(1-amino-1-deoxy-D-glucityl)alkanes. The appropriate α,ω-diaminoalkane (0.014 mol), two mole equivalents of glucose (5 g, 0.028 mol), and Pd/C 5% (0.80 g) in a water-methanol mixture were stirred in a Parr apparatus under hydrogen pressure (40 bar, 40°C, 24 h). The carbon was filtered off and the products were crystallized from the reaction mixture. The products were obtained in yields up to 75% (not optimalized). For representative NMR spectra, see section 5.8.

Bis(N-alkanoyl-1-amino-1-deoxy-D-glucityl)alkanes. The appropriate anhydride (3 mol equivalents) was added to the bis(1-amino-1-deoxy-D-glucityl)alkane in methanol and stirred overnight. The solution was subsequently heated at 60°C for one hour. The solution was cooled, neutralized with Dowex OH^-, filtered and the methanol was removed by evaporation under reduced pressure. Residual acid was distilled off by Kugelrohr destillation (50°C, 1 h; 75°C, 30 min; 100°C, 30 min; 150°C, 30 min). In some cases, the product became slightly yellow; the product was then stirred in methanol with activated carbon and subsequently filtered. The solvent was evaporated under reduced pressure. In the cases of 12-10-12 and 16-10-16, residual anhydride was removed by continuous extraction with hexane. The compounds of series 10-*s*-10 precipitated from ethanol, except for 10-2-10, which precipitated from methanol. The supernatant was decanted. Overall yields ranged from 75 to 80%. The compounds of series *m*-10-*m* precipitated from methanol-ether mixtures, overall yields ranged from 60 to 80%. For representative NMR data see section 5.8. (The NMR spectra could be run at room temperature).
The elemental analyses are shown in Table 8.

***N*-Decanoyl,*N*-butyl-1-amino-1-deoxy-D-glucitol ($NC_{10}nC_4$ glucitol).** *N*-butyl-1-amino-1-deoxy-D-glucitol was acylated with decanoic anhydride as decribed above for the gemini surfactants. Residual decanoic acid was removed by Kugelrohr destillation (100°C, 30 min; 150°C, 30 min). The crude yield was 95%. The compound crystallized nicely from acetonitrile.
^{1}H-NMR (500 MHz, CD_3OD,ppm): alkyl and acyl chain 0.89-1.00 (m, 6H), 1.31 (bs, 14H), 1.53-1.63 (2m, 4H), 3.23-3.40 (m, 2H), sugar moiety 3.23-3.40 (m, 2H), 3.42-3.78 (m, 5H), 3.95 (m, 1H), 4.78 (s, 5OH). ^{13}C-NMR (200 MHz, CD_3OD, ppm): alkyl chain and acyl chain 13.54, 14.58, 19.11 ($C_{4,\ alkyl}$, $C_{10,\ acyl}$), 20.99, 21.17, 23.70, 26.60, 26.74, 30.46, 30.56, 31.98, 33.03, 33.92, 34.25 ($C_{2,\ 3,\ alkyl}$, $C_{2\text{-}9,\ acyl}$), 47.13, 50.54 ($C_{1,\ alkyl}$), 176.50 ($C_{1,\ acyl}$), sugar moiety 51.50 (C_1), 64.72 (C_6), 71.08, 71.58, 72.78, 72.93, 73.06, 73.28, 73.53, 74.22 ($C_{2\text{-}5}$). Elemental analysis is taken up in Table 8.

Table 8. Elemental analyses of bis(*N*-decanoyl-1-amino-1-deoxy-D-glucityl)alkanes (abbreviated as 10-*s*-10), bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)decanes (abbreviated as *m*-10-*m*), and $NC_{10}nC_4$ glucitol.

Compound	Formula	Calculated			Found		
		% C	% H	% N	% C	% H	% N
10-2-10	$C_{34}H_{68}N_2O_{12}\cdot\frac{1}{2}H_2O$	57.85	9.85	3.97	57.90	9.92	4.02
10-4-10	$C_{36}H_{72}N_2O_{12}\cdot\frac{1}{2}H_2O$	58.91	10.02	3.82	58.95	9.96	3.85
10-6-10	$C_{38}H_{76}N_2O_{12}\cdot\frac{1}{2}H_2O$	59.90	10.19	3.68	60.21	10.20	3.67
10-7-10	$C_{39}H_{78}N_2O_{12}\cdot\frac{1}{2}H_2O$	60.36	10.26	3.61	60.25	10.17	3.61
10-8-10	$C_{40}H_{80}N_2O_{12}$	61.51	10.32	3.59	61.18	10.30	3.60
10-9-10	$C_{41}H_{82}N_2O_{12}$	61.94	10.39	3.52	62.11	10.38	3.53
10-10-10	$C_{42}H_{84}N_2O_{12}\cdot\frac{1}{2}H_2O$	61.66	10.47	3.42	61.95	10.50	3.50
10-12-10	$C_{44}H_{88}N_2O_{12}\cdot H_2O$	61.80	10.61	3.28	62.07	10.51	3.18
5-10-5	$C_{32}H_{64}N_2O_{12}\cdot\frac{1}{2}H_2O$	56.71	9.66	4.14	56.97	9.36	4.19
6-10-6	$C_{34}H_{68}N_2O_{12}\cdot\frac{1}{2}H_2O$	57.86	9.85	3.97	57.88	10.07	4.01
7-10-7	$C_{36}H_{72}N_2O_{12}\cdot\frac{1}{2}H_2O$	58.92	10.03	3.82	58.81	10.04	3.85
8-10-8	$C_{38}H_{76}N_2O_{12}$	60.61	10.17	3.72	60.31	10.05	3.70
9-10-9	$C_{40}H_{80}N_2O_{12}$	61.51	10.32	3.59	61.21	10.41	3.65
12-10-12	$C_{46}H_{92}N_2O_{12}$	63.86	10.72	3.24	63.61	10.80	3.34
14-10-14	$C_{50}H_{100}N_2O_{12}$	65.18	10.94	3.04	65.60	10.75	3.07
16-10-16	$C_{54}H_{108}N_2O_{12}$	66.36	11.14	2.87	66.49	11.29	2.92
$NC_{10}nC_4$ glucitol	$C_{20}H_{41}NO_6$	61.35	10.55	3.58	61.44	10.70	3.56

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Chapter 7

Estimates of the Bulk Prices of the Carbohydrate-Derived Surfactants and Perspectives

7.1 Introduction

In Chapter 4, we showed that *N*-acyl,*N*-dodecyl-β-D-aldosylamines and *N*-acyl,*N*-dodecyl-1-amino-1-deoxy-D-alditols have potential as cosurfactants in, for example, laundry detergents. The gemini surfactants based on carbohydrates proved to be good oil solubilizers (Chapter 6). For the actual application of these surfactants on an industrial scale, the price-performance ratio is of great importance.

In this final chapter, bulk[a] prices of the surfactants are estimated. The bulk prices of most chemicals needed for the production of the carbohydrate-derived surfactants can be found in the list of Chemical Prices (Chemical Market Reporter, November 1997). Prices of starting materials that were not available had to be estimated. There are several ways to estimate these prices. For example, acetic anhydride can be found in the price list (2.20 Hfl kg^{-1})[b], but the price of propionic anhydride is not available. Acetic acid and propionic acid, however, are both provided by the Chemical Marketing Reporter. The ratio of the prices of acetic acid and propionic acid is 1.14. The price estimated for propionic anhydride is 2.20 · 1.14 = 2.51 Hfl kg^{-1}. Another approach, which leads to a rough estimate, is to divide the price of a chemical for use on a laboratory scale (found in *e.g.* the Fluka catalogue) by a factor of 10. For readily available compounds such as glucose monohydrate and lactose monohydrate, this factor is about 20 and 25, respectively. Most chemicals used as starting materials for the *N*-acyl,*N*-dodecyl-β-D-aldosylamines and *N*-acyl,*N*-dodecyl-1-amino-1-deoxy-D-alditols and the gemini surfactant 14-10-14 were available from the Chemical Prices list.

The cost of industrial processes is estimated at 0.50 Hfl kg^{-1} per reaction step for plain operations and 0.75 Hfl kg^{-1} if more complex or energy-consuming steps are involved (additional distillations etc.).[1]

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[a] "Bulk" is defined here as multi-ton commercial production as (co)surfactant in detergent fomulations.

[b] The prices are converted to Dutch guilders (Hfl) per kilogram. One guilder is about $ 0.50.

7.2 Calculation of the bulk prices of *N*-acyl,*N*-alkyl-β-D-aldosylamines and *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols

Table 1 shows the calculation of the bulk prices of NC_2nC_{12} glucose and NC_3nC_{12} glucose. The process involves stirring glucose and dodecylamine in methanol. The product precipitates from the reaction mixture. The methanol can be reused. The acylation can be achieved with the appropriate anhydrides. The reaction mixture is neutralized with Dowex OH^- and the methanol is evaporated. The prices calculated are 6.10 Hfl kg^{-1} and 6.00 Hfl kg^{-1}, respectively. Although propionic anhydride is more expensive than acetic anhydride, the price per kg of NC_3nC_{12} glucose is lower than the price of NC_2nC_{12} glucose, due the higher molecular weight of the former. The price per mole of compound is higher for NC_3nC_{12} glucose. In industry the prices are, however, always given per kilogram of product.

The reaction solvent for NC_2nC_{12} lactose and NC_3nC_{12} lactose is 2-propanol-water. The removal of this reaction solvent requires more energy (due to the high boiling point of water) and therefore, the costs of the process are higher (estimation 0.75 Hfl kg^{-1}). Lactose is more expensive than glucose, but as the molecular weight of lactose is higher, NC_2nC_{12} lactose and NC_3nC_{12} lactose are cheaper (5.80 Hfl kg^{-1} and 5.90 Hfl kg^{-1}, respectively, Table 2) because fewer moles of the relatively expensive alkylamine are required.

The first step in the preparation of NC_2nC_{12} glucitol, NC_3nC_{12} glucitol, NC_2nC_{12} lactitol, and NC_3nC_{12} lactitol is a reductive amination with Raney Ni. In the syntheses of our compounds (Chapter 2) we used Pd/C (5%). Raney Ni is also an efficient catalyst and much cheaper.

The carbohydrate, the dodecylamine (an excess) and Raney Ni are stirred at elevated H_2 pressure and temperatures (40°C and 70°C, respectively). After filtration (to remove the Raney Ni, which can be reused) the glucitol-derivatives precipitate from the reaction mixture upon cooling. The mother liquor (containing the excess of dodecylamine) can be reused. In case of the lactitol derivatives, the solvent has to be evaporated. Because of the relatively high molecular weight of lactose, the lactitol derivatives are slightly cheaper than the glucitol derivatives. Moreover, the lactitol derivatives can also be prepared in a one-pot synthesis. This might even further reduce the price of these compounds.

Table 1. Calculation of the bulk prices of NC_2nC_{12} glucose and NC_3nC_{12} glucose.

Synthesis of nC_{12} glucose							
Chemicals, processes	amount	price (Hfl kg^{-1})	price (Hfl)	total costs (Hfl)	yield	price (Hfl kg^{-1})	price (Hfl mol^{-1})
glucose·H_2O	1 kg (5.1 mol)	1.12	1.12	5.95	75%	4.50	1.56
dodecylamine	0.93 kg (5.1 mol)	4.00	3.73				
MeOH	20 L	0.45 (5% loss)	0.35				
process			0.50				
regeneration MeOH			0.25				
isolated 0.75 · 5.1 = 3.83 mol ≈ 1.33 kg ⇒ price per kg: total costs / 1.33 = 4.50 Hfl kg^{-1}							
Acetylation of nC_{12} glucose							
nC_{12} glucose	1.33 kg (3.83 mol)		5.95	8.70	95%	**6.10**	2.35
$(CH_3CO_2)O$	0.47 kg (4.59 mol)	2.20	1.03				
MeOH	20 L	0.45 (5% loss)	0.35				
Dowex OH^-	1.5 kg[a]	no loss	0.60[b]				
process			0.50				
regeneration MeOH			0.25				
isolated 0.95 · 3.83 = 3.64 mol ≈ 1.42 kg ⇒ price per kg: total costs / 1.42 = 6.10 Hfl kg^{-1}							
Propionylation of nC_{12} glucose							
nC_{12} glucose	1.33 kg (3.83 mol)		5.95	9.15	95%	**6.20**	2.50
$(CH_3CH_2CO_2)O$	0.60 kg (4.59 mol)	2.50	1.50				
MeOH	20 L	0.45 (5% loss)	0.35				
Dowex OH^-	1.5 kg[a]	no loss	0.60[b]				
process			0.50				
regeneration MeOH			0.25				
isolated 0.95 · 3.83 = 3.64 mol ≈ 1.47 kg ⇒ price per kg: total costs / 1.47 = 6.20 Hfl kg^{-1}							

[a] Amount of acetic acid to be neutralized: (4.59 · 2) - 3.83 = 5.4 mol. Dowex OH^- can neutralize 4.4 meq g^{-1}, thus at least 1.2 kg of Dowex is needed. [b] For the regeneration of Dowex at least 1.5 · 4.4 = 6.6 mol of NaOH is needed. We calculated the price of 10 mol of NaOH (1.50 Hfl kg^{-1}).

Table 2. Calculation of the bulk prices of NC_2nC_{12} lactose and NC_3nC_{12} lactose.

Synthesis of nC_{12} lactose							
Chemicals, processes	amount	price (Hfl kg^{-1})	price (Hfl)	total costs (Hfl)	yield	price (Hfl kg^{-1})	price (Hfl mol^{-1})
lactose·H_2O	1 kg (2.78 mol)	1.20	1.20	4.69	75%	4.40	2.25
dodecylamine	0.51 kg (2.78 mol)	4.00	2.05				
2-propanol	10 L	1.50 (5% loss)	0.59				
process[a]			0.75				
regeneration excess amine			0.10				
isolated 0.75 · 2.78 = 2.08 mol ≈ 1.06 kg ⇒ price per kg: total costs / 1.06 = 4.40 Hfl kg^{-1}							
Acetylation of nC_{12} lactose							
nC_{12} lactose	1.06 kg (2.08 mol)		4.69	6.55	95%	**5.85**	3.30
$(CH_3CO_2)O$	0.25 kg (2.50 mol)	2.20	0.56				
MeOH	15 L	0.45 (5% loss)	0.25				
Dowex OH^-	0.75 kg[b]	no loss	0.30[c]				
process			0.50				
regeneration MeOH			0.25				
isolated 0.95 · 2.08 = 1.98 mol ≈ 1.12 kg ⇒ price per kg: total costs / 1.12 = 5.85 Hfl kg^{-1}							
Propionylation of nC_{12} lactose							
nC_{12} lactose	1.06 kg (2.08 mol)		4.69	6.82	95%	**5.90**	3.45
$(CH_3CH_2CO_2)O$	0.33 kg (2.50 mol)	2.50	0.83				
MeOH	15 L	0.45 (5% loss)	0.25				
Dowex OH^-	0.75 kg[b]	no loss	0.30[c]				
process			0.50				
regeneration MeOH			0.25				
isolated 0.95 · 2.08 = 1.98 mol ≈ 1.16 kg ⇒ price per kg: total costs / 1.16 = 5.90 Hfl kg^{-1}							

[a] Including regeneration of the reaction medium (2-propanol-water). [b]Amount of acetic acid to be neutralized: (2.50 · 2) - 2.08 = 2.92 mol. Dowex OH^- can neutralize 4.4 meq g^{-1}, thus at least 0.66 kg of Dowex is needed. [b] For the regeneration of Dowex at least 0.75 · 4.4 = 3.3 mol of NaOH is needed. We calculated the price of 5 mol of NaOH (1.50 Hfl kg^{-1}).

Table 3. Calculation of the bulk prices of NC_2nC_{12} glucitol and NC_3nC_{12} glucitol.

Synthesis of nC_{12} glucitol							
Chemicals, processes	amount	price (Hfl kg^{-1})	price (Hfl)	total costs (Hfl)	yield	price (Hfl kg^{-1})	price (Hfl mol^{-1})
glucose·H_2O	1 kg (5.1 mol)	1.12	1.12	6.05	95%	3.55	1.25
dodecylamine	0.93 kg (5.1 mol)	4.00	3.73				
MeOH	10 L	0.45 (5% renew)[b]	0.20				
Raney Ni	50 g	50 (10% loss)	0.25				
process[a]			0.75				
isolated 0.95 · 5.1= 4.85 mol ≈ 1.69 kg ⇒ price per kg: total costs / 1.69 = 3.55 Hfl kg^{-1}							
Acetylation of nC_{12} glucitol							
nC_{12} glucitol	1.69 kg (4.85 mol)		6.05	9.25	95%	**5.15**	2.00
$(CH_3CO_2)O$	0.59 kg (5.82 mol)	2.20	1.30				
MeOH	20 L	0.45 (5% loss)	0.35				
Dowex OH^-	2.0 kg[c]	no loss	0.80[d]				
process			0.50				
regeneration MeOH			0.25				
isolated 0.95 · 4.85 = 4.60 mol ≈ 1.80 kg ⇒ price per kg: total costs / 1.80 = 5.15 Hfl kg^{-1}							
Propionylation of nC_{12} glucitol							
nC_{12} glucitol	1.69 kg (4.85 mol)		5.95	9.78	95%	**5.25**	2.15
$(CH_3CH_2CO_2)O$	0.77 kg (5.82 mol)	2.50	1.93				
MeOH	20 L	0.45 (5% loss)	0.35				
Dowex OH^-	2.0 kg[c]	no loss	0.80[d]				
process			0.50				
regeneration MeOH			0.25				
isolated 0.95 · 4.85 = 4.60 mol ≈ 1.86 kg ⇒ price per kg: total costs / 1.86 = 5.25 Hfl kg^{-1}							

[a] The Raney Ni can be filtered off and the compound precipitates from the reaction solvent when cooled. The mother liquor can be reused. [b] The methanol will have to be renewed after a certain number of cycles. [c] Amount of acetic acid to be neutralized: (5.82 · 2) - 4.85 = 6.79 mol. Dowex OH^- can neutralize 4.4 meq g^{-1}, thus at least 1.5 kg of Dowex is needed. [d] For the regeneration of Dowex at least 2 · 4.4 = 8.8 mol of NaOH is needed. We calculated the price of 13 mol of NaOH (1.50 Hfl kg^{-1}).

Table 4. Calculation of the bulk prices of NC_2nC_{12} lactitol and NC_3nC_{12} lactitol.

Synthesis of nC_{12} lactitol							
Chemicals, processes	amount	price (Hfl kg^{-1})	price (Hfl)	total costs (Hfl)	yield	price (Hfl kg^{-1})	price (Hfl mol^{-1})
lactose·H_2O	1 kg (2.78 mol)	1.20	1.20	4.70	95%	3.50	1.80
dodecylamine	0.51 kg (2.78 mol)	4.00	2.05				
MeOH	10 L	0.45 (5% loss)	0.20				
Raney Ni	50 g	50 (10% loss)	0.25				
process[a]			1.00				
isolated 0.95 · 2.78 = 2.64 mol ≈ 1.35 kg ⇒ price per kg: total costs / 1.35 = 3.50 Hfl kg^{-1}							
Acetylation of nC_{12} lactitol							
nC_{12} lactitol	1.35 kg (2.64 mol)		4.70	6.81	95%	**4.90**	2.70
$(CH_3CO_2)O$	0.32 kg (3.17 mol)	2.20	0.71				
MeOH	15 L	0.45 (5% loss)	0.25				
Dowex OH^-	1.0 kg[b]	no loss	0.40[c]				
process			0.50				
regeneration MeOH			0.25				
isolated 0.95 · 2.64 = 2.51 mol ≈ 1.39 kg ⇒ price per kg: total costs / 1.39 = 4.90 Hfl kg^{-1}							
Propionylation of nC_{12} lactitol							
nC_{12} lactitol	1.35 kg (2.64 mol)		4.70	7.13	95%	**5.00**	2.85
$(CH_3CH_2CO_2)O$	0.41 kg (3.17 mol)	2.50	1.03				
MeOH	15 L	0.45 (5% loss)	0.25				
Dowex OH^-	1.0 kg[b]	no loss	0.40[c]				
process			0.50				
regeneration MeOH			0.25				
isolated 0.95 · 2.64 = 2.51 mol ≈ 1.42 kg ⇒ price per kg: total costs / 1.42 = 5.00 Hfl kg^{-1}							

[a] The Raney Ni can be filtered. The methanol has to be removed by distillation. The excess of dodecylamine can be recovered by extraction of the crude product with hexane. [b]Amount of acetic acid to be neutralized: (3.17 · 2) - 2.64 = 3.7 mol. Dowex OH^- can neutralize 4.4 meq g^{-1}, thus at least 0.85 kg of Dowex is needed. [c] For the regeneration of Dowex at least 1 · 4.4 = 4.4 mol of NaOH is needed. We calculated the price of 6.5 mol of NaOH (1.50 Hfl kg^{-1}).

7.3 Calculated bulk prices of the carbohydrate-derived surfactants compared with bulk prices of commercially available surfactants

The calculated bulk prices of the carbohydrate-derived surfactant are in the range of 4.90 - 6.10 Hfl kg^{-1}. The best performing surfactants (NC_2nC_{12} glucitol and NC_2nC_{12} lactose, Chapter 4) will cost 5.15 Hfl kg^{-1} and 5.80 Hfl kg^{-1}, respectively. If cruder starting materials would be used, the prices might even be reduced (*e.g.* cocoamine instead of dodecylamine). Table 5 shows the bulk prices of some commercially available surfactants. The prices of the surfactants we synthesized are in the same range as those of the carbohydrate-derived surfactants which are already produced on an industrial scale (alkylpolyglucosides, APGs, and glucamides, see also Chapter 1). However, they are 2 - 4 times more expensive than the major petroleum-based anionic and nonionic surfactants.[c] In the detergency tests described in Chapter 4, only 2.5% of NC_2nC_{12} glucitol and NC_2nC_{12} lactose already gave appreciable increases in performance. Taking account of the calculated bulk prices, these carbohydrate-derived surfactants are promising cosurfactants. Costs for applications in, for example, cosmetics would likely be significantly higher owing to higher standards of purity.

Table 5. Bulk prices of some commercially available surfactants.

commercial surfactants	guideline to prices (Hfl kg^{-1})
NaLAS	1.3 - 1.6
Nonionics (e.g. $C_{12}E_7$)	1.9
alkylether sulfates	2.4 - 2.7
APG	4.5
Glucamides	4.5- 5.5
Sodium dodecyl sulfate	2.7

[c] A profit margin should be added to the calculated bulk prices of the carbohydrate-derived surfactants presented in this thesis.

7.4 Calculated bulk price of gemini surfactant 14-10-14

Table 6 shows the calculation of the bulk price of gemini surfactant 14-10-14. The price of α,ω-diaminodecane was estimated from the price of decanedioic acid (8.8 Hfl kg^{-1}).[d] Tetradecanoic anhydride can be prepared from myristic acid and acetic anhydride.[e]

The price is about twice the price of the monomeric carbohydrate-derived surfactants (11.35 Hfl kg^{-1}). Although the estimated bulk price is high, these gemini surfactants can probably still compete with conventional surfactants, *e.g.*, in enhanced oil recovery, due to their high oil solubilization efficiency (Chapter 6).

Table 6. Calculation of the bulk prices of gemini surfactant 14-10-14.

Synthesis bola 10							
Chemicals, processes	amount	price (Hfl kg^{-1})	price (Hfl)	total costs (Hfl)	yield	price (Hfl kg^{-1})	price (Hfl mol^{-1})
glucose·H_2O	1 kg (5.1 mol)	1.12	1.12	6.71	90%	5.90	2.90
diaminodecane	0.44 kg (2.55 mol)	10	4.39				
MeOH	10 L	0.45 (5% renew)[b]	0.20				
Raney Ni	50 g	50 (10% loss)	0.25				
process[a]			0.75				
isolated 0.90 · 2.55 = 2.30 mol ≈ 1.14 kg ⇒ price per kg: total costs / 1.14 = 5.90 Hfl kg^{-1}							
Acylation of bola 10							
bola 10	1.14 kg (2.30 mol)		6.71	22.81	90%	**12.00**	11.05
C_{14}-anhydride	3.02 kg (6.90 mol)	5.00	15.10				
process[b]			1.00				
isolated 0.90 · 2.30 = 2.07 mol ≈ 1.90 kg ⇒ price per kg: total costs / 1.90 = 12.00 Hfl kg^{-1}							

[a] The Raney Ni can be filtered off and the compound precipitates from the reaction solvent when cooled. The mother liquor can be reused. [b] The process includes stirring of the reaction mixture (0.30 Hfl kg^{-1}), evaporation of the reaction solvent (which can be reused, 0.50 Hfl kg^{-1}) and continuous extraction of the crude product with hexane.

[d] Reaction of 1,10-decanedicarboxylic acid with ammonia leads to the diamide and subsequent catalytic hydrogenation gives the aminodecane.

[e] Pure myristic acid costs 3.75 Hfl kg^{-1}, a mixture of fatty acids with an average chain length of 14 carbon atoms will be cheaper.

7.5 Conclusions

In Chapter 1 we formulated the aim of this research project: the synthesis of readily biodegradable, nontoxic surfactants based on renewables, by synthetic pathways that would be applicable on a large scale. We prepared *N*-acyl,*N*-alkyl-β-D-aldosylamines and *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols by straightforward reaction routes (Chapter 2). Preliminary tests indicate that the compounds are nontoxic (Chapter 4). The extent of biodegradation was insufficient, however, more extensive tests need to be performed to draw definite conclusions on the biodegradability of the compounds. Chapter 4 also shows that some of the carbohydrate-derived surfactants considerably increase the performance of a standard laundry detergent formulation. Furthermore, the estimated bulk prices show a reasonable price, especially with respect to their use as cosurfactants.

The bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)alkanes show a high oil-solubilization capacity. The syntheses of these carbohydrate-derived gemini surfactants do not imply tedious reaction steps and the price-performance ratio seems to be reasonable. Therefore, we have reached our aim, except for the ready biodegradability of the compounds.

In Chapter 2 we formulated an additional aim: insights into the structure-property relationships by introducing small structural changes in order to devise tailor-made materials. Chapters 3, 5, and 6 show that the physical and chemical properties and aggregation behavior of the *N*-acyl,*N*-alkyl-β-D-aldosylamines and *N*-acyl,*N*-alkyl-1-amino-1-deoxy-D-alditols, and of the bis(*N*-alkanoyl-1-amino-1-deoxy-D-glucityl)alkanes follow consistent trends, and the behavior can thus be predicted. Although general trends are also observed in the relationship between the structure and the practical performance of the surfactants (in detergency tests in case of the former surfactants and in oil solubilization experiments in case of the gemini surfactants), this interrelation is more complex.

7.6 Reference

1. Besemer, A. C. The Bromide-catalyzed Hypochlorite Oxidation of Starch and Inuline, Ph. D. Thesis, Delft Technical University, 1993; personal communications from researchers of various industries.

Summary

Surfactants (a contraction of the term surface active agents) are large volume chemicals; their annual production exceeds 5 million tons worldwide. They are primarily used as cleaning agents in laundry and dish-washing applications. Surfactants are also applied in cosmetics and pharmaceuticals, in manufacturing textiles and fibres, in the food industry, in paints and plastics, in the paper industry, in pesticides, and in the oil production process.

Surfactants have a dualistic character; they possess a hydrophilic headgroup and a hydrophobic tail. In water, surfactants form aggregates in which the headgroups point towards water and the tails stick together.

Classic types of surfactants are produced from petrochemical raw materials. In the long term, fossil feedstocks will be exhausted and products based on renewable materials will become more important. Growing consumer demands for "natural" products have also directed the search for new surfactants towards renewable sources.

Therefore, our aim was to synthesize new, readily biodegradable, and nontoxic surfactants starting from renewable materials by routes that should be possible on a large scale. We based our surfactants on carbohydrates, fatty amines, and anhydrides. The carboxylic anhydrides can be prepared from naturally occurring fatty acids. An additional benefit of applying carbohydrates is the creation of a new markets for the abundant agricultural (by)products they are produced from. The two starting carbohydrates used in this thesis are glucose, derived from starch, and lactose, which is obtained from whey.

In the first part of this thesis (Chapter 2-4), the straightforward syntheses of carbohydrate-derived surfactants such as shown in Figure 1 are described together with their fundamental aspects and practical applications.

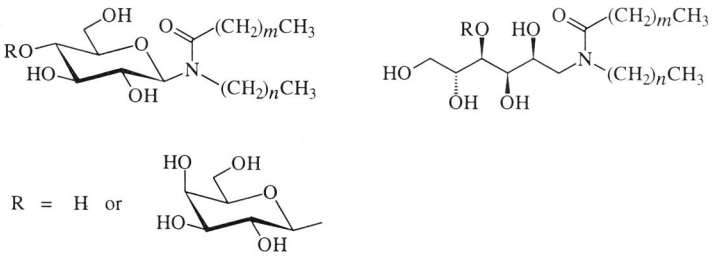


Figure 1. Carbohydrate-derived surfactants described in Chapters 2-4. (n = 7, 9, or 11; m = 0 or 1).

These surfactants show critical micelle concentrations (CMCs), standard enthalpies, standard Gibbs energies, and standard entropies of micellization, which are linear functions of alkyl chain length. The decrease in CMC is tenfold when the chain length is increased by two

methylene groups. The contribution of an additional CH_2 group to $\Delta_{mic}H°$, $\Delta_{mic}G°$, and $T\Delta_{mic}S°$ at 40°C is -2.4 kJ mol^{-1}, -3.0 kJ mol^{-1}, and 0.7 kJ mol^{-1}, respectively. The consistency of the increments per methylene group of $\Delta_{mic}H°$, $\Delta_{mic}G°$, and $T\Delta_{mic}S°$ sheds important light on the "hydrophobic" component in micelle formation of nonionic amphiphiles. The more favorable Gibbs energies (and the lower CMCs) for the longer chain analogs are caused predominantly by an exothermic shift in the enthalpy of micelle formation.

The surface tensions at the CMC are higher for the disaccharide-derived surfactants than for the monosaccharide-derived surfactants. The areas per surfactant molecule at the air-water interface are also larger for the disaccharide-derived surfactants. Increasing alkyl chain lengths leads to lower surface tensions at the CMC and smaller headgroup areas at the air-water interface.

The potential for practical application of these surfactants in the detergent industry was investigated. Three carbohydrate-derived surfactants show promising results in preliminary tests for their use as co-surfactants in laundry detergents (addition of 2.5% to a standard formulation). One of these three carbohydrate-derived surfactants stabilizes the foam formed by the standard formulation in the presence of soil.

The surfactants show low to very low biotoxicity compared to reference compounds (measured by the influence on the growth rate of micro-organisms). In preliminary biodegradability tests, extents of biodegradation of 30-45% (depending on the nature of the headgroup) were found. These percentages are insufficient to award the surfactants the specification "readily biodegradable". Further research into their biodegradability and their biodegradation pathways is clearly warranted.

In conclusion, these carbohydrate-derived surfactants have a interesting potential as co-surfactants in detergency systems.

In the second part of the thesis (Chapters 5 and 6) a simple and broadly applicable synthesis of carbohydrate-derived gemini surfactants is described. Their properties and potential for application are also described.

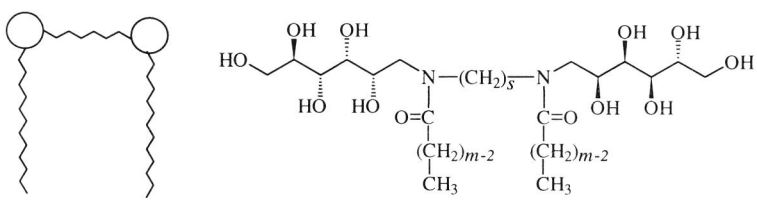


Figure 2. Simplified structure of a gemini surfactant (left) and general struture of the nonionic carbohydrate-derived gemini surfactants described in Chapters 5 and 6. The gemini surfactants are abbreviated as *m-s-m*.

Gemini surfactants (Figure 2) have two hydrophilic headgroups and two hydrophobic chains linked by a spacer. They display interesting behavior, such as lower CMCs, larger surface tension reductions, synergism in surface-active properties with conventional surfactants, better solubility in water, and good (oil) solubilization properties compared to conventional surfactants with alkyl chains with similar hydrophobicity. Almost all gemini surfactants described in the literature possess ionic headgroups.

We prepared three series of nonionic gemini surfactants based on carbohydrates. Series 14-*s*-14 (s = 6, 8, 10), series 10-*s*-10 ($2 \leq s \leq 12$) and series *m*-10-*m* ($5 \leq m \leq 16$). These nonionic carbohydrate-derived gemini surfactants show interesting aggregation behavior. Aqueous solutions were prepared by sonication and addition of 5 mol% of NaLAS (to increase solubility). Vesicles formed by the first series (visualized by using electron microscopy) become less stable and turn into thread-like micelles upon cooling when the spacer length is decreased from ten to six methylene groups. The solutions become viscous and have a viscoelastic character. Viscoelasticity disappears when the solutions are heated again. Rheology measurements showed that at 7.5°C, a 5 mM solution of the gemini surfactant 14-6-14 forms a weak gel.

Series 10-*s*-10 and *m*-10-*m* show consistent trends in their aggregation behavior. For $s \leq 10$, thread-like micelles are formed. For $s = 10$, vesicles and tubular vesicles are observed. Gemini surfactants with $5 < m < 9$ form bilayered material and when $m > 8$, vesicles are observed.

Solubilization experiments performed with these two series in which hexane and toluene were solubilized in aqueous carbohydrate-derived gemini solutions indicate that these gemini surfactants could find application as emulsifiers or oil solubilizers (in for example, enhanced oil recovery). The results agree with the trends in aggregation behavior observed by electron microscopy.

Finally, estimates of the bulk prices of the carbohydrate-derived surfactants and gemini surfactants were made (Chapter 7). The calculated prices of the carbohydrate-derived surfactants are in the range of 4.90-6.10 Hfl kg^{-1}. These prices are in the same range as those of the carbohydrate-derived surfactants which are already produced on an industrial scale. Based on the bulk prices, these carbohydrate-derived surfactants are promising co-surfactants. The price of a gemini surfactant is about twice as high as that of the monomeric surfactants.

We can conclude that we have reached our main goal, except for the ready biodegradability of the surfactants, which is an item that should be explored further. An additional aim was to gain insights into the structure-property relationships by introducing small structural changes in order to devise tailor-made materials. The physical and chemical properties and the aggregation behavior of the carbohydrate-derived (gemini) surfactants follow consistent trends, and the behavior can thus be rationalized.

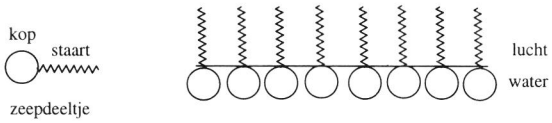
Samenvatting voor de Leek

1. Doel van het onderzoek

Tot nu toe worden de meeste zepen gemaakt uit olie. Olie is een eindige bron, op een bepaald moment zal olie opgebruikt zijn. Het doel van dit onderzoek was het maken van zepen uit *hernieuwbare materialen* die goed *afbreekbaar* en *niet giftig* zouden zijn. Met hernieuwbare of groene grondstoffen worden in het algemeen agrarische producten bedoeld waarvan elk jaar een nieuwe voorraad ter beschikking staat. Een bijkomend voordeel van het gebruik van landbouwproducten is het ontstaan van een nieuwe markt voor boeren.

2. Inleiding over zepen

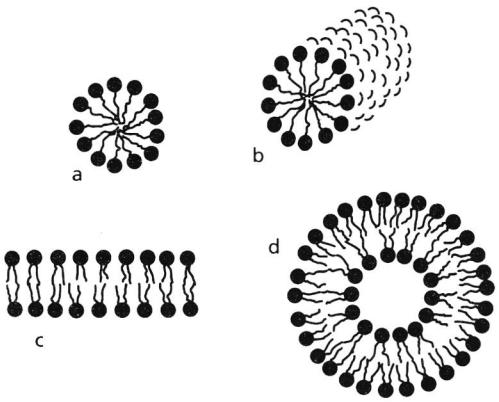
Zeep is opgebouwd uit heel kleine deeltjes die met het blote oog niet te zien zijn. In Figuur 1 is zo'n zeepdeeltje weergegeven. Het heeft een kop en een staart. De kop houdt van water, de staart is olie-achtig en heeft een hekel aan water. De kop en de staart zijn aan elkaar gezet door een chemische reactie. Een zeepdeeltje hoeft niet per se één kop en één staart te hebben, het kan ook meerdere staarten en/of koppen hebben.



Figuur 1. Als zeepdeeltjes in water worden gebracht blijven ze hangen aan het oppervlak tussen water en lucht.

Als zeep in water wordt gebracht, dan voelen de koppen zich prettig, maar de staarten niet. Daarom blijven ze hangen aan het oppervlak tussen water en lucht. De koppen zitten in het water en de staarten steken in de lucht om het contact met water te vermijden. Als er meer zeep toegevoegd wordt gaan de deeltjes op een bepaald moment in het water "samenklonteren". Hierbij kunnen verschillende soorten structuren ontstaan, afhankelijk van het soort zeep. In elke structuur zitten de koppen in het water en de staarten bijelkaar (om zo weinig mogelijk contact te hebben met water). In Figuur 2 zijn vier verschillende soorten structuren getekend. Een bolletje, een draad, een dubbellaag en een blaasje. Alleen de dwarsdoorsnede is getekend. In het geval van een bolletje of een draad zit er alleen water aan de buitenkant, de binnenkant bestaat uit staarten. In het geval van een blaasje hebben de

zeepdeeltjes een gesloten dubbellaag gevormd, met water zowel binnen als buiten, maar ook in dit geval hebben de staarten geen contact met water. Deze structuren zijn niet met het blote oog te zien.



Figuur 2. Dwarsdoorsneden van een bolletje (a), een draad (b), een dubbellaag (c) en een blaasje (d).

Olie en vet lossen niet op in water. Door nu zeep toe te voegen aan water kunnen olie en vet wel oplossen in water. Dat komt doordat de olie-achtige staarten van de zeepdeeltjes olie en vet prettig vinden. De zeepdeeltjes gaan om het vet of de olie zitten, hierbij steken de staarten in de olie en de koppen blijven in het water.

3. Suikerzepen

De zepen die in hoofdstuk 2 tot en met 4 beschreven staan hebben een kop van suiker. Als uitgangsstoffen werden glucose en melksuiker gebruikt. Glucose kan geproduceerd worden uit bijvoorbeeld aardappelzetmeel, melksuiker wordt voornamelijk gewonnen uit wei, de vloeistof die overblijft tijdens de kaasproduktie. De uitgangsstoffen die we gebruikt hebben voor de staarten kunnen gemaakt worden uit natuurlijke vetzuren.

Het koppelen van de staart aan de kop was geen probleem. Het was wel lastig om de restjes losse kop en staart die overbleven uit de zeep te verwijderen. Uiteindelijk is dit gelukt. Er zijn in totaal 24 verschillende zepen gemaakt. Ze verschillen van elkaar in soort kop en de lengte van de staart.

Een zeepdeeltje met een langere staart heeft een grotere hekel aan water dan wanneer de staart korter is. Daarom vonden we uit metingen dat een zeep met een lange staart eerder structuren vormt ("samenklontert") in water dan een zeep met een korte staart. Als de kop van

het zeepdeeltje klein is, lost het zeepdeeltje minder goed op in water. Daarom vormen de zeepdeeltjes met een kleine kop eerder structuren in water dan zeepdeeltjes met een grotere kop. Een kleine kop en een lange staart zorgen er dus voor dat een zeepdeeltje snel geneigd is een bolletje ("micel"), een draad of een blaasje ("vesicle") te vormen in water. De aanwezigheid van zulke structuren is noodzakelijk voor een goede waswerking. De zepen die het eerst structuren vormen in water werden daarom onderworpen aan wastesten.

4. Suikerzepen in waspoeder

We hebben gekeken of de suikerzepen toegepast zouden kunnen worden in waspoeder. Waspoeder bestaat niet alleen uit zeep, er zitten ook andere stoffen in die ervoor moeten zorgen dat er geen kalk op de kleding neerslaat, dat de kleuren niet verbleken etc. Het is niet realistisch om ervan uit te gaan dat de zepen die nu in waspoeder zitten volledig zullen worden vervangen door de zepen die wij gemaakt hebben. Daarvoor wassen de bestaande zepen te goed en zijn ze te goedkoop. Daarom is gekeken of door toevoeging van kleine hoeveelheden van onze zepen aan een standaard waspoeder betere wasresultaten verkregen werden.

Kleine lapjes van katoen, polyester of polyester-katoen met wijnvlekken, theevlekken, vetvlekken of moddervlekken werden in de wasmachine gewassen met een waspoeder waaraan één van de suikerzepen was toegevoegd. Acht van de suikerzepen werden getest. Drie van deze acht zorgden er bij verschillende hardheden van het water (veel of weinig kalk) voor dat de lapjes zichtbaar schoner werden.

Er werd ook gekeken of de suikerzepen goed schuimden. In een wasmachine mag zeep niet te veel schuimen, maar een wasmiddel dat voor de handwas gebruikt wordt moet wel overvloedig schuimen, omdat de consument een grote hoeveelheid schuim met een goede waswerking associeert. De meeste suikerzepen schuimden goed.

Om te kijken wat er gebeurt als het waswater vies wordt (door vuil van de kleding of door vuile borden tijdens het afwassen), werden schuimmetingen gedaan met vervuild water. Als vuil toegevoegd wordt aan het zeepwater schuimen zepen in het algemeen minder goed. Door een beetje van een bepaalde suikerzeep toe te voegen aan een standaard waspoeder, bleef het schuim veel langer goed.

5. Giftigheid en afbreekbaarheid van de suikerzepen

Zepen worden in grote hoeveelheden gemaakt en gebruikt. Ze komen dus ook in grote hoeveelheden in het milieu terecht. Daarom is het van belang dat de zepen niet giftig zijn en

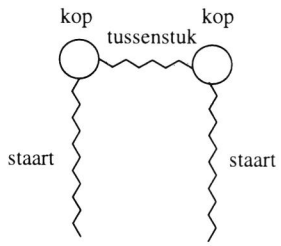
dat ze volledig en snel afgebroken worden door micro-organismen, bijvoorbeeld door bacteriën tijdens de afvalwaterzuivering.

De giftigheid van zepen kan worden bepaald door te meten hoe goed micro-organismen nog groeien als kleine hoeveelheden van de zepen worden toegevoegd. De giftigheid van de suikerzepen is vergelijkbaar met of zelfs lager dan die van de bestaande zepen.

Een probleem waar meer onderzoek voor nodig is, is de afbreekbaarheid van de suikerzepen. Voor zepen geldt dat 60% van de zeep afgebroken moet zijn na 28 dagen. De suikerzepen blijken niet te voldoen aan die maatstaf. Slechts 30 tot 45% van de suikerzepen was afgebroken door bacteriën uit een afvalwaterzuiveringsinstallatie. Dit betekent echter niet dat ze niet toegepast kunnen worden in waspoeders. Door de bacteriën te laten wennen aan de suikerzepen zou de afbreekbaarheid misschien verhoogd kunnen worden.

6. Tweelingzepen

De hoofdstukken 5 en 6 gaan over een ander soort zepen, de zogenaamde tweelingzepen. In Figuur 3 is een tweelingzeepdeeltje weergegeven. Twee zeepdeeltjes zijn verbonden door een tussenstuk, vandaar de naam. De tweelingzepen die wij gemaakt hebben, hebben ook weer een suikerkop. Er zijn in totaal 17 verschillende tweelingzepen gemaakt. Ze verschillen in de lengte van het tussenstuk en in de lengte van de staarten. We waren geïnteresseerd in het soort structuren dat ze vormen in water en of ze goed olie op zouden kunnen lossen in water.



Figuur 3. Een tweeling-zeep-deeltje.

Het soort structuur dat de tweelingzepen vormen in water blijkt afhankelijk te zijn van de lengte van het tussenstuk. Als het tussenstuk kort is, worden draden gevormd, als het tussenstuk langer is vormt de tweelingzeep blaasjes (zie ook Figuur 2). Deze structuren kunnen bekeken worden met behulp van een microscoop die de structuren tot zo'n 100.000 keer kan vergroten (een elektronenmicroscoop). Eén van de tweelingzepen vormt lange draden in water. De draden raken in elkaar verstrikt en hierdoor wordt de oplossing dikker, het wordt een gel.

Zepen kunnen ervoor zorgen dat olie op kan lossen in water. Als er veel olie oplost dan

veranderen de structuren die de zeepdeeltjes vormen in water. De zeepdeeltjes vormen dan een laag om de oliedruppeltjes in water. De staarten steken hierbij in de olie en de koppen in de waterlaag. Dit wordt een emulsie genoemd. Boter is een emulsie van water en vet: door speciale zepen (emulgatoren) worden water en vet bij elkaar gehouden. Andere emulsies zijn consumptie-ijs, mayonaise en sauzen, evenals crèmes en zalfjes voor cosmetische of medische toepassingen.

Ook de petrochemische industrie is geïnteresseerd in zepen die ervoor kunnen zorgen dat olie oplost in water. Bij de winning van aardolie bijvoorbeeld. Als olie aangeboord wordt zit er zoveel druk achter de olie dat het spontaan van de bron naar de put stroomt. Als de druk minder wordt, zorgt het in de bron pompen van water of stoom ervoor dat de druk behouden blijft en dat de olie blijft stromen. Een groot gedeelte van de olie blijft echter achter in de poriën van het gesteente. Aangezien olie niet oplost in water, is het moeilijk om deze hoeveelheid olie (zo'n 60%) te winnen. Door nu zeep toe te voegen aan water kan ervoor gezorgd worden dat de achtergebleven olie oplost in water. Deze techniek wordt nog niet toegepast, omdat er te veel zeep nodig is om de olie op te lossen: de olie zou zo veel te duur worden. En dus gaat nog veel olie verloren.

Onze metingen hebben aangetoond dat de tweelingzepen met de suikerkoppen ervoor zorgen dat olie-achtige vloeistoffen veel beter oplossen in water dan wanneer bestaande zepen gebruikt worden. Er zou dus veel minder zeep nodig zijn bij de oliewinning indien deze tweelingzepen gebruikt zouden worden, dit zou daarom een mogelijke toepassing van de tweelingzepen kunnen zijn.

7. Prijzen van de suikerzepen en de tweelingzepen

In het laatste hoofdstuk hebben we berekend hoeveel het zou kosten om de zepen op fabrieksschaal te maken. De prijs van de suikerzepen is zo'n vijf tot zes gulden per kilogram. Dat is ongeveer net zo veel als de prijs van suikerzepen die al op de markt zijn. De prijs ligt wel hoger dan die van de meest gebruikte zeep in waspoeders, die kost ongeveer f 1,50 per kilogram. Aangezien de suikerzepen maar in kleine hoeveelheden toegevoegd hoeven te worden, zal de prijs van een waspoeder niet veel stijgen terwijl er een beter wasresultaat verkregen wordt. De tweelingzepen kosten ongeveer twee keer zoveel als de suikerzepen.

8. Conclusies

De suikerzepen die gemaakt zijn kunnen toegepast worden in waspoeders. Als een beetje van een suikerzeep toegevoegd wordt aan een standaard waspoeder, wordt de was schoner. De

suikerzepen zijn niet giftig, maar de afbreekbaarheid laat nog te wensen over.

De tweelingzepen met een suikerkop zijn zeer effektief in het oplossen van olie in water. Ze zouden bijvoorbeeld toegepast kunnen worden bij het winnen van aardolie.

Stellingen

behorende bij het proefschrift van Monique Pestman, 20 november 1998

1. Wanneer een onderdeel van een artikel afgedrukt wordt op het omslag van het tijdschrift waarin het artikel gepubliceerd wordt, dient niet alleen een drukproef van het artikel, maar ook een drukproef van het omslag te worden voorgelegd aan de auteurs.

   Langmuir **1997**, volume 13, number 25.

2. Het presenteren van oppervlakte actieve eigenschappen, biodegradeerbaarheid, schuim- en antimicrobacteriële eigenschappen in water van hydrolyse gevoelige verbindingen zonder enige vermelding van de hydrolyse-gevoeligheid is curieus.

   Kawada, K.; Yago, K.; Zen, S.; Uchibori, T.; Matsumura, S. Surface activities, biodegradability, and antimicrobial properties of *N*-alkyl glycosylamines, *J. Antibact. Antifug. Agents* **1994**, *22*, 69.

3. De betekenis van het woord gemini surfactant vervaagt allengs.

   Renouf, P.; Mioskowski, C.; Lebeau, L. Hebrault, D.; Desmurs, J. R. Dimeric surfactants: First synthesis of an asymmetrical gemini compound, *Tetrahedron Letters* **1998**, *39*, 1357.

4. Deelname aan EHBO cursussen zou volledig gesubsidieerd moeten worden.

5. Door bij snelheidscontroles de limiet te scherp te stellen, wordt het verkeer niet veiliger.

6. Vrouwen worden in de voetbalwereld te vaak niet serieus genomen.

7. Het gemeenschapsgeld dat is gebruikt om vaarrecreatie in het Damsterdiep mogelijk te maken had beter benut kunnen worden voor de aanleg van een fietspad langs het Eemskanaal tussen Groningen en Delfzijl.

8. De verkoop van pepernoten in de zomer en paaseitjes in hartje winter zorgt ervoor dat tradities minder "speciaal" worden.

9. Ondanks alle commotie die vooraf ging aan het afbreken van de vijf pijpen van de Hunzecentrale, lijkt het oude gezegde 'Uit het oog, uit het hart' ook in dit geval van toepassing.