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Thermodynamics of Micellization of Nonionic Saccharide-Based *N*-Acyl-*N*-alkylaldosylamine and *N*-Acyl-*N*-alkylamino-1-deoxyalditol Surfactants

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Eight homologous series of nonionic carbohydrate-derived surfactants in which the alkyl chains are linked through *N*-acylated amine bonds were synthesized, and their critical micelle concentrations (cmc's) and standard enthalpies of micellization were determined using titration microcalorimetry. Gibbs energies of micellization ($\Delta_{\text{mic}}G^\circ$) were calculated from the critical micelle concentrations. *N*-Acyl-*N*-alkylaldosylamines (acyl = acetyl/propionyl, aldose = glucosyl/lactosyl) and *N*-acyl-*N*-alkylamino-1-deoxyalditols (acyl = acetyl/propionyl, alditol = glucitol/lactitol) with alkyl chain lengths of 8, 10, and 12 carbon atoms show a 10-fold decrease in cmc when the length of the chain is increased by two methylene groups. The enthalpograms for the C₈ analogs are more complicated than those for the C₁₀ and C₁₂ analogs. Therefore, the enthalpograms were modeled using a computer-based program which takes account of the nonideal properties of the solutions, yielding enthalpies of micelle formation. Increments in the thermodynamic parameters show satisfactory self-consistency. Each CH₂ group contributes -2.4 kJ mol^{-1} to $\Delta_{\text{mic}}H^\circ$, $\Delta_{\text{mic}}G^\circ$ -(CH₂) is -3.0 kJ mol^{-1} for each series, and $T\Delta_{\text{mic}}S^\circ$ (CH₂) is 0.7 kJ mol^{-1} at 40 °C. Although the change in entropy is the main driving force for micellization, the enthalpy of micellization may also contribute significantly to the Gibbs energy of micellization, particularly for longer alkyl chains.

Introduction

Standard enthalpies of micellization ($\Delta_{\text{mic}}H^\circ$), Gibbs energies of micellization ($\Delta_{\text{mic}}G^\circ$), and entropies of micellization ($\Delta_{\text{mic}}S^\circ$) are important in understanding micelle formation in aqueous solutions. For a given surfactant the enthalpy of micellization can in principle be determined from the temperature dependence of the cmc. But this method has a major drawback, because $\Delta_{\text{mic}}H^\circ$ is often significantly temperature dependent.^{1,2} Enthalpies of micellization can be accurately obtained using titration microcalorimetry. With this technique $\Delta_{\text{mic}}H^\circ$ can be read directly from a plot of the enthalpy of dilution versus concentration. We used the phase equilibrium model to calculate the standard Gibbs energies and entropies of micellization (mole fraction scale).³ According to this model, the standard Gibbs energy of micelle formation of a nonionic surfactant per mole of monomer is given by⁴

$$\Delta_{\text{mic}}G^\circ = RT \ln(\text{cmc} \cdot V_w^*) \quad (1)$$

Herein, V_w^* is the molar volume of water ($0.018 \text{ dm}^3 \text{ mol}^{-1}$ at 40 °C). The cmc is given in moles per cubic decimeter. The advantage of nonionic surfactants over ionic surfactants is that eq 1 can be used without having to take

account of counterion binding. The standard entropy of micelle formation per mole of monomer is calculated from

$$\Delta_{\text{mic}}S^\circ = (\Delta_{\text{mic}}H^\circ - \Delta_{\text{mic}}G^\circ)/T \quad (2)$$

In general, the entropy term is the main driving force for micelle formation by nonionic surfactants.^{5–9} As micelles are formed, the hydrophobic hydration layers around the alkyl chains are broken down. This process is accompanied by a gain in entropy and represents the driving force for hydrophobic interaction within micelles. The exact nature of this hydrophobic effect has been discussed in detail.¹⁰

Surfactants with a nonionic carbohydrate-derived head-group (Figure 1) have potential pharmaceutical (biocompatible formulation), biological (extraction of membrane proteins), and medicinal (antiviral activity) applica-

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Figure 1. Examples of the surfactant structures and abbreviations used for the names of the compounds.

tions.^{11–21} As is the case for other carbohydrate-derived surfactants (such as the alkyl polyglucosides and the aldonamides),^{22,23} the compounds described here also possess excellent detergency properties.^{24,25} We report the preparation of eight homologous series of these surfactants. The series are classified on the basis of the headgroup (either a glucose/glucitol or a lactose/lactitol headgroup) and the nature of the acyl substituent (acetyl (C_2) or propionyl (C_3)), and each series consists of three surfactant molecules with C_8 , C_{10} , and C_{12} alkyl chains. Using titration microcalorimetry, we have determined the critical micelle concentrations, $\Delta_{\text{mic}}H^\circ$, $\Delta_{\text{mic}}G^\circ$, $\Delta_{\text{mic}}S^\circ$, and hence the increments in standard enthalpies, Gibbs energies, and entropies of micellization per CH_2 for each series at 40 °C.²⁶ These results offer important insights into the relationship between the surfactant structure and the thermodynamic parameters describing aggregation.

Experimental Section

Materials. All solvents (except ethanol) were purchased from Lab-scan. Ethanol absolute GR, d(+)-glucose anhydrous, lactose (monohydrate), and the appropriate amines were purchased from Merck. Palladium on carbon (5%) was purchased from Acros. The water was doubly distilled, and all solutions were degassed before use.

Characterization. ^1H - and ^{13}C -NMR spectra were recorded using a Varian Unity Plus spectrometer (500 MHz), a Varian VXR-300 spectrometer (300 MHz), or a Varian Gemini spectrometer (200 MHz).

Titration Microcalorimetry. A Microcal Omega titration microcalorimeter (Microcal, Northampton, MA) was used. The solution in the sample cell was thermostated at 313 K and stirred (350 rpm). An aqueous surfactant solution (5–10 μL , concentration $\gg \text{cmc}$) 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 above the cmc. The crude data (Figure 2a) were analyzed using Omega software (Origin 2.9), yielding a plot of the heat per

Figure 2. Enthalpograms for dilution of a concentrated solution of $\text{NC}_2\text{nC}_{12}$ lactitol in water at 40 °C: (a) crude data, (b) enthalpy of dilution versus concentration, (c) cumulative enthalpy of dilution versus concentration: determination of the cmc.

mole of injected surfactant against surfactant concentration in the cell, the enthalpogram (Figure 2b).^{8,27,28} The measurements were performed at 40 °C to preclude possible solubility problems. All carbohydrate-derived surfactants (except $\text{NC}_3\text{nC}_{12}$ glucitol) dissolve in water at ambient temperature.

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. The values of the individual variables gave no additional information.

Synthesis. The structure of each surfactant compound was confirmed by ^1H -NMR and ^{13}C -NMR and by elemental analysis.

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N-Alkylglucosylamines. Glucose (10 g, 56 mmol) and 1 mol equiv of the appropriate alkylamine were stirred in methanol overnight. The product precipitated from the reaction mixture. The suspension was heated until it was clear and subsequently cooled slowly. The white crystals were filtered and washed with methanol and acetone (to remove unreacted alkylamine). The yields were 61–79%. The products were crystallized from methanol (yields 42% (C8), 50% (C10), 68% (C12)). NMR data indicated that the products comprised the α (about 15%) and β anomers (about 85%).

N-Dodecylglucosylamine. $^1\text{H-NMR}$ (COSY, CD_3OD , ppm): alkyl chain 0.89 (t, 3H, $^3J_{12-11} = 7.0$), 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 , $^3J_{2-1} = ^3J_{2-3} = 8.7$), 3.23 (m, H_5 , $^3J_{5-6A} = 2.3$, $^3J_{5-6B} = 5.3$), 3.28 (t (dd), H_4 , $^3J_{4-3} = ^3J_{4-5} = 8.7$), 3.35 (t (dd), H_3 , $^3J_{3-2} = ^3J_{3-5} = 8.7$), 3.66 (dd, H_{6B} , $^2J_{6B-6A} = 11.7$, $^3J_{6B-5} = 5.3$), 3.82 (d, H_1 , β product, $^3J_{1-2} = 8.7$), 3.83 (dd, H_{6B} , $^2J_{6A-6B} = 11.7$, $^3J_{6A-5} = 2.3$), 4.48 (d, H_1 , α product, $^3J_{1-2} = 4.8$), 4.71 (s, 4OH). $^{13}\text{C-NMR}$ (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-Alkylactosylamines. The *N*-alkylactosylamines were prepared according to a literature procedure.^{15,16,29}

N-Alkylamino-1-deoxyglucitols. Glucose (7 g, 39 mmol), the appropriate alkylamine (2 mol equiv), and 0.75 g of Pd/C (5%) in ethanol (75 mL) were stirred overnight in a Parr apparatus under hydrogen pressure (60 bar) at 40 °C. The carbon was filtered off, and the ethanol was removed by evaporation under reduced pressure. The white solid was twice crystallized from ethanol (overall yields 76%). $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ data have been published elsewhere.³⁰

N-Alkylamino-1-deoxylactitols. Lactose monohydrate (5 g, 13.9 mmol), the appropriate alkylamine (2 mol equiv), and 0.75 g of Pd/C (5%) in ethanol (50 mL) were stirred overnight in a Parr apparatus under hydrogen pressure (80 bar)³¹ at 70 °C. The carbon was filtered off, and the ethanol was removed by evaporation under reduced pressure. The white solid was stirred in ether to remove excess alkylamine (yields 95%) and then extracted continuously to remove residual alkylamine (yields 88%).

N-Dodecylamino-1-deoxylactitol. $^1\text{H-NMR}$ (CD_3OD , ppm): alkyl chain 0.89 (t, 3H, $^3J_{12-11} = 7.0$), 1.29 (bs, 14H), 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, 8OH). $^{13}\text{C-NMR}$ (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), 70.71, 71.60, 72.83, 72.99, 74.87, 77.15, 82.13 (C_2 – C_5 , C_2' – C_5'), 105.31 (C_1).

Acylation of the Glucose- and Lactose-Derived Compounds.³² Acetic anhydride or propionic anhydride (1.5 mol equiv) was added to the alkylated glucose or lactose derivatives and stirred overnight. The solution was neutralized with Dowex OH^- and filtered. The ethanol was removed by evaporation under reduced pressure. Yields of the crude products ranged from 85% to 95%. The compounds were purified by crystallization.

N-Acyl-*N*-alkylglucosylamines were dissolved in a small amount of acetone, and hexane was added just to the point of precipitation. The products precipitated from acetone/hexane as slightly yellow oils. The yellow impurities (not detectable by $^1\text{H-NMR}$) were also the first to crystallize from acetonitrile. The clear solution above the yellow oil was decanted and allowed to crystallize. The products precipitated as white oils/gels which

solidified after drying. The glucosylamines were solid but very hygroscopic, and therefore stock solutions were prepared for this group of compounds. NMR data indicated that the products exist exclusively as the β anomers.¹⁷

N-Acyl-*N*-alkylactosylamines were crystallized from ethanol and freeze dried. Yields were in the range 51–60%. The products contain 1 mol of water per mole of compound. NMR data indicated that the products exist exclusively as the β anomers.¹⁷

N-Acyl-*N*-alkyl-1-deoxyglucitols were crystallized from ethanol/ether (NC_2NC_8 glucitol and $\text{NC}_3\text{NC}_{12}$ glucitol, yields 78% and 86%, respectively), ethyl acetate ($\text{NC}_2\text{NC}_{10}$ glucitol, yield 60%; $\text{NC}_3\text{NC}_{10}$ glucitol, yield 84%), ethanol/ether, and subsequently ethyl acetate ($\text{NC}_2\text{NC}_{12}$ glucitol, yield 42%) or from acetonitrile (NC_3NC_8 glucitol, yield 73%).

N-Acyl-*N*-alkyl-1-deoxylactitols were crystallized once or twice from methanol/acetonitrile mixtures and yields ranged from 58% to 76%.

N-Propionyl-*N*-octylglucosylamine (NC_3NC_8 glucose). $^1\text{H-NMR}$ (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, $^3J_{3-2} = 7.3$), 2.50 (2q, 2H, $^3J_{2-3} = 7.3$), sugar moiety 3.25–3.89 (m, H_2 – H_6 , 8H, including 2H of the alkyl chain), 4.84 (d, H_1 , $^3J_{1-2} = 8.1$), 5.45 (d, H_1 , $^3J_{1-2} = 8.8$), 4.91 (s, 4OH). $^{13}\text{C-NMR}$ (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-Acetyl-*N*-octylactosylamine (NC_2NC_8 lactose). NMR data have been published previously.¹⁷

N-Propionyl-*N*-dodecylamino-1-deoxyglucitol ($\text{NC}_3\text{NC}_{12}$ glucitol). Crystallized from ethanol/ether, yield 86%. NMR data have been published elsewhere.²⁰

N-Propionyl-*N*-decylamino-1-deoxylactitol ($\text{NC}_3\text{NC}_{10}$ lactitol). $^1\text{H-NMR}$ (COSY, CD_3OD , ppm): alkyl chain 0.89 (t, 3H, $^3J_{10-9} = 6.5$), 1.29 (bs, 14H), 1.55, 1.60 (2m, 2H), 3.18–3.50 (m, 2H), acyl chain 1.09, 1.12 (2q, 3H, $^3J_{3-2} = 7.3$), 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, $\text{H}_{1'}$, $^3J_{1'-2'} = 7.8$, $^3J_{1'-2'} = 7.3$), 4.89 (s, 8OH). $^{13}\text{C-NMR}$ (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 – C_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_7), 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).³³

Results and Discussion

In the textbook case, an enthalpogram obtained by a titration microcalorimeter has a step-shaped plot identifying two concentration regions where the recorded heats per mole of injected surfactant are almost constant.³⁴ In the low-concentration region, the recorded heats are due to deaggregation and dilution of the monomers. The surfactant concentration in the sample cell is below the cmc, and the micelles of the injected aliquots deaggregate. A large change in the recorded heat (an increase or 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 is 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 van Os plot of the cumulative heats per mole of injected surfactant versus concentration of

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(31) A pressure of 20–40 bar is sufficient to accomplish complete hydrogenation.

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(33) The signals for the acetyl groups are positioned as follows. $^1\text{H-NMR}$ (CD_3OD): 2.11, 2.16 (2s, 3H). $^{13}\text{C-NMR}$ (CD_3OD): 21.34, 21.93 (C_2), 173.93, 174.21 (C_1).

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Table 1. Critical Micelle Concentrations and Thermodynamic Parameters of Micellization of Carbohydrate-Derived Surfactants at 40 °C

compound	cmc (mM)	$\Delta_{\text{mic}}H^{\circ}(\text{exp})$ (kJ mol ⁻¹)	$\Delta_{\text{mic}}H^{\circ}(\text{calc})$ (kJ mol ⁻¹)	$\Delta_{\text{mic}}G^{\circ}$ (kJ mol ⁻¹)	$T\Delta_{\text{mic}}S^{\circ}$ (kJ mol ⁻¹)
NC ₂ nC ₈ glucose	21	+ ^a	+1.4	-20.5	21.9
NC ₂ nC ₁₀ glucose	2.9	-3.0	-2.9	-25.6	22.7
NC ₂ nC ₁₂ glucose	0.26	-7.7	-7.5	-31.9	24.4
NC ₃ nC ₈ glucose	20	~ +2.7	+3.4	-20.6	24.0
NC ₃ nC ₁₀ glucose	1.8	-1.3	-1.3	-26.9	25.6
NC ₃ nC ₁₂ glucose	0.19	-5.4	-5.7	-32.8	27.1
NC ₂ nC ₈ glucitol	21	> +0.9	+1.7	-20.5	22.2
NC ₂ nC ₁₀ glucitol	2.0	-2.6	-2.5	-26.6	24.1
NC ₂ nC ₁₂ glucitol	0.18	-7.2	-7.0	-32.9	26.0
NC ₃ nC ₈ glucitol	13	≥ +2.6	+3.0	-21.8	24.7
NC ₃ nC ₁₀ glucitol	1.2	-1.9	-1.8	-27.9	26.1
NC ₃ nC ₁₂ glucitol	0.11	-7.2	-7.2	-34.3	27.1
NC ₂ nC ₈ lactose	35	+2.0	+4.3	-19.2	23.5
NC ₂ nC ₁₀ lactose	4.6	-1.4	-1.2	-24.4	23.2
NC ₂ nC ₁₂ lactose	0.45	-5.3	-5.3	-30.5	25.2
NC ₃ nC ₈ lactose	24	+5.0	+7.5	-20.1	27.6
NC ₃ nC ₁₀ lactose	2.6	+0.1	0	-25.9	25.9
NC ₃ nC ₁₂ lactose	0.31	-4.1	-4.0	-31.5	27.5
NC ₂ nC ₈ lactitol	24	> +1.1	+2.3	-20.2	22.5
NC ₂ nC ₁₀ lactitol	3.3	-1.9	-1.9	-25.3	23.5
NC ₂ nC ₁₂ lactitol	0.31	-6.6	-6.5	-31.5	25.0
NC ₃ nC ₈ lactitol	18	> +2.3	+2.9	-20.8	23.7
NC ₃ nC ₁₀ lactitol	1.8	-1.5	-1.4	-26.9	25.5
NC ₃ nC ₁₂ lactitol	0.16	-6.1	-6.2	-33.1	26.9

^a $\Delta_{\text{mic}}H^{\circ}$ is endothermic but could not be determined accurately experimentally, due to the strongly nonideal enthalpogram.

surfactant in the sample cell (Figure 2c).^{8,27,28} The thermodynamic data are summarized in Table 1.

Critical Micelle Concentrations. The critical micelle concentrations have the same order of magnitude as generally shown by nonionic surfactants. A number of trends can be identified. The cmc's decrease by a factor of 10 when the alkyl chain is increased by two methylene groups. This 10-fold decrease in cmc is also shown by polyethoxylated surfactants,³⁵ *N*-alkanoyl-*N*-methyl gluconamides,³⁶ and other nonionic surfactants.^{37,38}

The propionylated surfactants have lower cmc's than their acetylated counterparts, which is accounted for by the larger hydrophobic contents of these surfactants. 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 (10^{1/2})).

Generally speaking, the length of the alkyl chain determines the order of magnitude of the cmc. The headgroup size (monosaccharide versus 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 1 shows that, in our case, the nature of the headgroup influences the cmc within the order of magnitude determined by the chain length.^{39,40}

The glucose-derived surfactants have lower cmc's than the lactose-derived surfactants, also due to the smaller hydrophilic headgroup and the consequently relatively larger hydrophobic part. Surfactants with a reduced saccharide headgroup have smaller cmc's than those with an intact cyclic structure. Probably, the (hydrated) alditol

headgroup is smaller, but volumes of appropriate hydrated carbohydrate-derived headgroups are not known.

Enthalpies of Micellization. Standard enthalpies of micellization were directly obtained (vide supra) from the enthalpograms (Table 1, $\Delta_{\text{mic}}H^{\circ}(\text{exp})$). Derivatives with a decyl or dodecyl chain produced enthalpograms conforming to the textbook 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. This slope is accounted for in terms of nonideal thermodynamic properties of the solutions in both the syringe and the sample cell and reflects micelle–micelle, monomer–monomer, and monomer–micelle interactions.^{8,34,41} This feature was especially pronounced for the C₈ surfactants because, as a consequence of the high cmc, the concentration of surfactant in the syringe is high.

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 nonideal 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.^{12,19} 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 fits were obtained between calculated and observed enthalpograms. The calculation and method were supported by the results which produced enthalpies of micelle formation which conformed to the pattern observed for the C₁₀ and C₁₂ surfactants.

Parts a and b of Figure 3 show the experimental and fitted enthalpograms of NC₂nC₈ glucitol and NC₂nC₁₂ lactitol. Enthalpies obtained using the computer program are listed in Table 1. There are two contributions to

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Figure 3. Experimental and fitted enthalpograms of (a) NC_2nC_8 glucitol and (b) $\text{NC}_2\text{nC}_{12}$ lactitol.

$\Delta_{\text{mic}}H^\circ$: (i) an endothermic contribution from the headgroups and (ii) an exothermic contribution from the alkyl chains.^{9,42–44} For alkylpolyglycol 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 $\Delta_{\text{mic}}H^\circ$ increase correspondingly. Disaccharide derivatives have more hydroxyl groups and show an increase in $\Delta_{\text{mic}}H^\circ$ (that is more endothermic) relative to their monosaccharide counterparts.

On going from C_8 to C_{12} , the exothermic contribution of the alkyl chain increases and the enthalpy of micellization becomes more favorable. $\Delta_{\text{mic}}H^\circ$ 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, $\Delta_{\text{mic}}H^\circ$ equals zero. The temperature at which $\Delta_{\text{mic}}H^\circ = 0$ may be called the transition temperature. According to Table 1 $\text{NC}_3\text{nC}_{10}$ lactose has a transition temperature of 40 °C. The transition temperature at which $\Delta_{\text{mic}}H^\circ$ changes sign from positive to negative is lower for the analog with the longer alkyl chain.³⁶ 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.^{8,45}

Table 2. Contributions of a CH_2 Group to $\Delta_{\text{mic}}H^\circ$, $\Delta_{\text{mic}}G^\circ$, and $T\Delta_{\text{mic}}S^\circ$ at 40 °C for a Series Glucose- and Lactose-Derived Surfactants

compound	$\Delta_{\text{mic}}H^\circ$ per CH_2 (kJ mol ⁻¹)	$\Delta_{\text{mic}}G^\circ$ per CH_2 (kJ mol ⁻¹)	$T\Delta_{\text{mic}}S^\circ$ 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	<i>b</i>
NC_2nC_n lactitol	-2.2	-2.8	0.6
NC_3nC_n lactitol	-2.3	-3.1	0.8

^a The regression constants exceed 0.999, except for the results marked with * (0.98–0.99) and [†] (0.83). ^b The value of $T\Delta_{\text{mic}}S^\circ$ for NC_3nC_8 lactose does not conform to the general trend. Therefore, $T\Delta_{\text{mic}}S^\circ$ per CH_2 for this series could not be calculated.

The contribution of each methylene group to the enthalpy of micellization for each series, $\Delta_{\text{mic}}H^\circ(\text{CH}_2)$, is approximately -2.4 kJ mol⁻¹ (Table 2). This pattern is in good agreement with increments reported for other surfactants.^{36,44,46–48} In our case, the $\Delta_{\text{mic}}H^\circ(\text{CH}_2)$ values are self-consistent and do not show large deviations from the average value.

Gibbs Energy and Entropy of Micellization. All estimates of $\Delta_{\text{mic}}G^\circ$ are negative and increase with increasing chain length. The contribution of each CH_2 group to $\Delta_{\text{mic}}G^\circ$ is -3.0 kJ mol⁻¹.^{5,36,37,43,44,48–52} 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.^{5,7,53,54}

The entropy terms ($T\Delta_{\text{mic}}S^\circ$) are positive and increase with increasing chain length. Estimates of $T\Delta_{\text{mic}}S^\circ$ are large compared with those for ionic surfactants. The hydrophobic hydration of alkyl chains belonging to ionic surfactants is probably less than that 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.^{6,7,9} $T\Delta_{\text{mic}}S^\circ$ per CH_2 is 0.7 kJ mol⁻¹. The main driving force of micellization at 40 °C is provided by the entropy term supported in some cases by an exothermic enthalpy term.

Variations in the Carbohydrate-Derived Surfactants and Their Influence on the Standard Gibbs Energies. 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 $\Delta_{\text{mic}}S^\circ$ 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

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chains and is accounted for by a degree of backfolding of the chains.⁷

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 is accounted for by 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 CH₂ 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 carbohydrates are smaller.

Consequently, NC₃nC₁₂ glucitol exhibits the most favorable standard Gibbs energy of micellization.

Conclusions

The cmc's and enthalpies of micellization have been determined for a series of nonionic carbohydrate-derived surfactants using microcalorimetry. Estimates of $\Delta_{\text{mic}}H^\circ$ lead to several interesting and self-consistent patterns. The accompanying $\Delta_{\text{mic}}G^\circ$ and $T\Delta_{\text{mic}}S^\circ$ parameters are reported. Considerable insight is gained into the relationship between the structure of the surfactant and its thermodynamic variables describing aggregation.

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