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Synthesis of nonionic reduced-sugar based bola amphiphiles and gemini surfactants with an α,ω-diamino-(oxa)alkyl spacer

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Abstract—Reduced-sugar based gemini surfactants with an α,ω-diamino-(oxa)alkyl spacer exhibit a rich pH-dependent aggregation behavior and are efficient DNA carriers in gene transfection. Herein, we describe an improved synthetic procedure for these amphiphiles. First, a series of novel nonionic bolaform amphiphiles with identical headgroups and α,ω-diamino-(oxa)alkyl spacers were synthesized by reductive aminations involving α,ω-diaminoalkanes and the appropriate sugars or aldehydes. The bolaform compounds were used as starting materials for the synthesis of the corresponding reduced-sugar based gemini surfactants in a reductive alkylation reaction employing a polymer-bound cyanoborohydride. A series of new gemini surfactants have been synthesized and characterized.

1. Introduction

Gemini surfactants possess two amphiphilic groups connected to each other by a spacer bound to the headgroups or close to the headgroups.[1,2] In recent years, a large variety of bola amphiphiles and the corresponding gemini surfactants have been synthesized[1] and studied.[3,4] The geminis possess properties substantially different from those of single-headgroup surfactants, and interesting applications have emerged.[1,2] Our attention has been focused on geminis having an α,ω-diaminoalkyl or α,ω-diamino-ethylene oxide spacer, which possess an amazingly rich pH-dependent aggregation behavior.[5–10] They form cationic micelles at low pH values (pH<∼5.5) whereas at higher pH values worm-like micelles and vesicles are formed. Close to pH 7, the zeta potential has dropped to small values and the vesicles flocculate. Rather unexpectedly, a further increase of the pH leads to redispersal of the vesicles, which now carry a negative charge, most likely due to physisorption of hydroxide ions.

An interesting application involves their use in gene transfection. In the presence of DNA, lipoplexes are formed, which have been successfully used in in vitro and in vivo gene transfection.[5,11–14] Substantial structural variations in the geminis are possible and in the past we have synthesized geminis with different carbohydrate headgroups, hydrocarbon tails, and spacers.[5–7,15,16] Also, non-symmetrical bola amphiphiles based on carbohydrates are known.[17] In general, the synthesis of the bola compounds has involved a reductive amination of aldehydes with primary amines. As reductants, Pd/C or PtO_2 catalysts at ca. 9 bar (ca. 60 psi) H_2 pressure were employed.[15,18] In order to cope with the sensitivity of the two (unsaturated) chains under the reaction conditions, sodium cyanoborohydride has been used.[5–7] Often it was found difficult to remove the excess of this reagent and particularly the last traces of boron. Another problem involved the formation of boronic esters after the introduction of the carbohydrate headgroups.

In the present paper, we describe an improved and general synthetic procedure involving the use of polymer-bound cyanoborohydride in the reductive alkylation reactions and leading to the formation of the desired, analytically pure gemini surfactants in satisfactory yields.

2. Results and discussion

The synthesis leading to the bola amphiphiles and the gemini surfactants, outlined in Figure 1, involves two steps: a reductive amination and a reductive alkylation.

In general, the reductive amination of aldehydes or ketones turned out to be an efficient method for making the bola amphiphiles. There are two possibilities to carry out the reaction: either to use an excess of the aldehyde or an excess of the amine. The choice between these possibilities depended on the difficulties that were expected in purifying the reaction mixture and the availability of suitable scavengers to remove the excess of the compound that was used in

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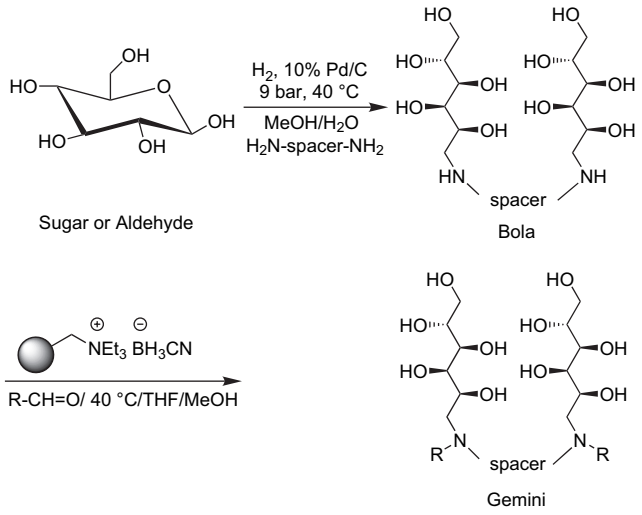

Figure 1. Synthetic scheme.

excess. In the present work, we have chosen for a general catalytic hydrogenation using Pd/C (10%) at a pressure of 9 bar in different methanol/water mixtures. The choice of the methanol/water ratio was determined by the solubility of the sugar. The purification of the bolaform was easier when the desired product was a solid. In most cases, crystallization was sufficiently effective (**B1**–**10**, **B12**–**14**, and **B17**–**19**, Table 1).

In the case of **B12** it proved difficult to remove the Pd/C. Pd/C could only be filtered off in an acidic medium (Section 3).

In the other preparations, ion-exchange materials had to be used because otherwise it was not possible to remove the excess of the sugar by crystallization (**B11**, **B15**, and **B16**). In case the product was a liquid (**B21**) or was very sticky (**B22**), purification by both crystallization and ion-exchange was required. The low yield of **B21** was caused by the complexity of the reaction mixture. Each amino moiety of the 1,6-diaminohexane reacted with 1 or 2 mol of trioxadecanaldehyde leading to the formation of mono-, di-, tri- and tetra-substituted 1,6-diaminohexanes. The different substituted products were analyzed with LC/MS.

Table 1. Bolaform amphiphiles

Compound	Headgroup	Spacer
B1	Glucitol	$-(CH_2)_2-$
B2	Glucitol	$-(CH_2)_3-$
B3	Glucitol	$-(CH_2)_4-$
B4	Glucitol	$-(CH_2)_6-$
B5	Glucitol	$-(CH_2)_8-$
B6	Glucitol	$-(CH_2)_{10}-$
B7	Glucitol	$-(CH_2)_{12}-$
B8	Glucitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$
B9	Mannitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$
B10	Galactitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$
B11	Lactitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$
B12	Galactitol	$-(CH_2)_6-$
B13	Mannitol	$-(CH_2)_6-$
B14	Talitol	$-(CH_2)_6-$
B15	Lactitol	$-(CH_2)_6-$
B16	Melibitol	$-(CH_2)_6-$
B17	Arabinitol	$-(CH_2)_6-$
B18	Erithritol	$-(CH_2)_6-$
B19	3-(1,2-Dihydroxypropyl)	$-(CH_2)_6-$
B20	Methyl	$-(CH_2)_6-$
B21	Methyl-2,5,8,11-tetraoxatridecyl-	$-(CH_2)_6-$
B22	Glucitol	$-(CH_2)_3-O-(CH_2-CH_2-O)_4-(CH_2)_3-$

As stated before, an effective synthetic procedure for the gemini surfactants (Table 2) involved a reductive alkylation of the bolaform compounds. In most cases, hydrogen gas was used with Pd/C (10%) as the catalyst.[5] But due to the sensitivity of the carbon–carbon double bond for catalytic reduction, the oleyl derivatives **GS1**–**3** were prepared by using $NaBH_3CN$.[5–7] The excess of the sodium cyanoborohydride was destroyed with dilute HCl. The gemini surfactants were isolated as the double-protonated salts. But a difficult step in this procedure was the extraction of the product with THF. Due to the long hydrocarbon chains in the gemini, often a suspension was formed and separation between the organic layer and the aqueous layer did not occur or was very slow. As a consequence, a large amount of NaCl was needed for salting out the organic layer. In addition, the salts possess a limited stability and are very hygroscopic. In the present study we have chosen for a polymer-bound cyanoborohydride (MP-cyanoborohydride, Fig. 1) in the synthesis of the geminis **GS1**–**7** and **GS9**–**25**. Gemini **GS8** was prepared by using $NaCNBH_3$ and the product was isolated as the HCl salt. A great advantage of MP-cyanoborohydride was that it could easily be filtered off. In the reductive alkylation the aldehyde was used in excess. This was necessary because traces of the corresponding alcohol were formed during the reduction depending on the pH of the reaction mixture[19] and also some alkylcyanohydrine was formed by addition of HCN to the aldehyde. However, these impurities could be easily removed by extraction either with acetone or acetonitrile or a mixture of both depending on the solubility of the gemini in these solvents. During the reaction boric esters derived from the sugar moiety were also formed, particularly in cases where the sugar moiety contained more than three hydroxyl groups. These boric esters were hydrolyzable in an acidic medium adjusted with HCl to pH ca. 1 at 40 °C in THF.

The hydrolyzes were checked with ^{11}B NMR spectroscopy. The acid was removed by stirring the reaction mixture with a basic anion-exchange material (Dowex monosphere 550A, OH^-). Even **GS10**–**12** with a 1,4 and 1,6 ether bond, respectively, and acid-sensitive in acidic medium (lactose and melibiose), were stable under these conditions. Due to the reduced-sugar headgroup the geminis **GS5**–**8**; **GS11**–**14**, and **GS22**, **23** contained 0.5–2.0 mol of water per mol of gemini. Even freeze-fracture techniques were not sufficient in making the geminis water free. This was possibly also a reason for the liquid crystalline behavior of the geminis. Only **GS21** had a sharp melting point.

In summary, we have developed a general and efficient two-step protocol for the synthesis of reduced-sugar based gemini surfactants. This straightforward route can successfully replace earlier published synthetic procedures and allows

Table 2. Reduced-sugar derived gemini surfactants

Compound	Headgroup	Spacer	Hydrocarbon tail
GS1	Glucitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$	$C_{18:1}$
GS2	Mannitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$	$C_{18:1}$
GS3	Mannitol	$-(CH_2)_6-$	$C_{18:1}$
GS4	Glucitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$	$C_{17}C{=}O$
GS5	Glucitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$	C_{18}
GS6	Mannitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$	C_{18}
GS7	Galactitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$	$C_{18:1}$
GS8	Galactitol	$-(CH_2)_6-$	$C_{18:1}$
GS9	Talitol	$-(CH_2)_6-$	$C_{18:1}$
GS10	Lactitol	$-(CH_2-CH_2-O)_2-CH_2-CH_2-$	$C_{18:1}$
GS11	Lactitol	$-(CH_2)_6-$	$C_{18:1}$
GS12	Melibitol	$-(CH_2)_6-$	$C_{18:1}$
GS13	Glucitol	$-(CH_2)_2-$	$C_{18:1}$
GS14	Glucitol	$-(CH_2)_4-$	$C_{18:1}$
GS15	Glucitol	$-(CH_2)_6-$	$C_{18:1}$
GS16	Glucitol	$-(CH_2)_8-$	$C_{18:1}$
GS17	Glucitol	$-(CH_2)_{10}-$	$C_{18:1}$
GS18	Glucitol	$-(CH_2)_{12}-$	$C_{18:1}$
GS19	Glucitol	$-(CH_2)_3-$	C_{12}
GS20	Glucitol	$-(CH_2)_3-O-(CH_2-CH_2-O)_4-(CH_2)_3-$	$C_{18:1}$
GS21	Arabinitol	$-(CH_2)_6-$	$C_{18:1}$
GS22	Erithritol	$-(CH_2)_6-$	$C_{18:1}$
GS23	3-(1,2-Dihydroxypropyl)	$-(CH_2)_6-$	$C_{18:1}$
GS24	Methyl	$-(CH_2)_6-$	$C_{18:1}$
GS25	Methyl-2,5,8,11-tetraoxatridecyl	$-(CH_2)_6-$	$C_{18:1}$

an easy access of the desired, analytically pure, gemini amphiphiles.

3. Experimental section

3.1. General

All reactions were carried out in distilled anhydrous solvents under a nitrogen atmosphere using oven-dried glassware. For the synthesis of the bola amphiphiles an autoclave was used. ^{1}H NMR and ^{13}C NMR spectra were run on a Varian VXR 300 or a Varian Gemini 200 spectrometer. Melting points (uncorrected) were determined using a Koffler melting point microscope. Several compounds displayed liquid crystalline behavior, in these cases no melting points are reported. THF was distilled over sodium/benzophenone and the possible peroxide content was checked with a peroxide-test (Merck). Elemental analyses were carried out by Mr. J. van der Velde in the Analytical Department. Mass spectra were obtained on a Waters LC/MS instrument equipped with an electrospray probe and executed by Mrs. T. D. Tiemersma-Wegman. The carbohydrates were purchased from: Merck: D-(+)-glucose; Fluka: D-(+)-mannose, D-(+)-lactose, and D-(−)-erythrose; Sigma: DL-glyceraldehyde and α-D-(+)-melibiose; Acros: D-(−)-arabinose, D-(+)-galactose, and D-(+)-talose. The α,ω-diaminoalkanes and **B20** were purchased from Aldrich. 2,2′-(Ethylenedioxy)diethylamine and oleyl alcohol (ca. 75–80% cis) were from Fluka; oleylaldehyde was prepared by a Swern oxidation,[6] 1,19-diamino-4,7,10,13,16-pentaoxanonadecane was from Brunschwig Chemie; MP-cyanoborohydride and MP (macroporous poly(styrene-*co*-divinylbenzene))-carbonate from Argonaut; ion-exchange: Dowex MAC-3 hydrogen form, Dowex monosphere 550A(OH^-) anion-exchange (Sigma–Aldrich); Amberlyst 15 was from Janssen/Chimica and 10% Pd/C from Acros.

3.2. Bola compounds

The ^{13}C NMR spectra were recorded in D_2O, the second solvent mentioned was used as an internal reference.

3.2.1. 1,2-Bis(1-deoxy-D-glucitol-1-ylamino)ethane (B1).[15,16] Mp: 138–139 °C. ^{1}H NMR (D_2O, 300 MHz) δ 3.86–3.46 (m, 12H), 2.70–2.60 (m, 8H); ^{13}C NMR (D_2O/DMSO-d_6, 50.3 MHz) δ 72.7, 72.5, 72.3, 64.5, 52.0, 49.2, 39.5. Anal. Calcd for $C_{14}H_{32}N_2O_{10}$: C, 43.29; H, 8.30; N, 7.21. Found: C, 43.4; H, 8.35; N, 7.25.

3.2.2. 1,3-Bis(1-deoxy-D-glucitol-1-ylamino)propane (B2).[15,16] Mp: 154–155 °C. ^{1}H NMR (D_2O, 200 MHz) δ 3.75–3.41 (m, 12H), 2.61–2.41 (m, 8H), 1.55–1.47 (quint, $J_{H,H}$=7.2, 2H); ^{13}C NMR (D_2O/CD_3OD, 50.3 MHz) δ 72.1, 71.9, 71.7, 63.9, 51.3, 47.5, 29.3. Anal. Calcd for $C_{15}H_{38}N_2O_{10}$: C, 44.77; H, 8.52; N, 6.96. Found: C, 44.8; H, 8.57; N, 7.00.

3.2.3. 1,4-Bis(1-deoxy-D-glucitol-1-ylamino)butane (B3).[5,15] Mp: 150–151 °C. ^{1}H NMR (D_2O/DMSO-d_6, 300 MHz) δ 3.74–3.46 (m, 12H), 2.57–2.46 (m, 8H), 1.36 (br s, 4H); ^{13}C NMR (D_2O/DMSO-d_6, 75.4 MHz) δ 72.6, 72.5, 72.4, 72.2, 64.4, 51.8, 49.8, 27.8. Anal. Calcd for $C_{18}H_{40}N_2O_{10}$: C, 46.14; H, 8.71; N, 6.73. Found: C, 46.4; H, 8.79; N, 6.79.

3.2.4. 1,6-Bis(1-deoxy-D-glucitol-1-ylamino)hexane (B4). See Ref. 15.

3.2.5. 1,8-Bis(1-deoxy-D-glucitol-1-ylamino)octane (B5). See Refs. 15,18.

3.2.6. 1,10-Bis(1-deoxy-D-glucitol-1-ylamino)decane (B6). See Refs. 15,18.

3.2.7. 1,12-Bis(1-deoxy-D-glucitol-1-ylamino)dodecane (B7). See Refs. 15,18.

3.2.8. 1,8-Bis(1-deoxy-D-glucitol-1-ylamino)-3,6-dioxaoctane (B8). See Ref. 6.

3.2.9. 1,8-Bis(1-deoxy-D-mannitol-1-ylamino)-3,6-dioxaoctane (B9). See Ref. 7.

3.2.10. 1,8-Bis(1-deoxy-D-galactitol-1-ylamino)-3,6-dioxaoctane (B10). A mixture of D-(+)-galactose (9.314 g, 51.7 mmol), 1,8-diamino-3,6-dioxaoctane (3.334 g, 22.5 mmol), and Pd/C (10%, 0.800 g) in MeOH/H_2O (60% v/v, 63 mL) was stirred at 40 °C for 24 h under a hydrogen atmosphere (9 bar). Water (100 mL) was added to the reaction mixture. The mixture was heated to 60 °C, filtrated at this temperature to prevent crystallization, and cooled slowly to 5 °C. The precipitate was filtered off by suction and dried above P_2O_5 in vacuo, giving **B10** (7.96 g, 74%) as a white solid, mp: 164 °C (dec). ^{1}H NMR (D_2O, 300 MHz) δ 3.94–3.83 (m, 4H), 3.59–3.46 (m, 16H), 2.77–2.59 (m, 8H); ^{13}C NMR (D_2O/CH_3OH, 50.3 MHz) δ 71.5, 70.8, 70.1, 69.0, 63.9, 52.1, 48.1. Anal. Calcd for $C_{18}H_{40}N_2O_{12}\cdot 0.5H_2O$: C, 44.53; H, 8.51; N, 5.77. Found: C, 44.8; H, 8.92; N, 5.68.

3.2.11. 1,8-Bis(1-deoxy-D-lactitol-1-ylamino)-3,6-dioxaoctane (B11). A mixture of D-(+)-lactose (11.16 g, 31.0 mmol), 1,8-di-amino-3,6-dioxa-octane (1.66 g, 11.2 mmol), and Pd/C (10%, 0.5 g) in MeOH/H_2O (50% v/v, 60 mL) was stirred at 40 °C for 24 h under a hydrogen atmosphere (9 bar). Filtration and freeze-drying gave the crude product, which was purified over an ion-exchange column (125 g, MAC-3). Elution with water and NH_4OH (0.5 M in water), respectively, gave **B11** (7.8 g, 87%) as a white solid, mp: 98 °C (dec). ^{1}H NMR (D_2O, 300 MHz) δ 4.39 (d, $J_{H,H}$=7.3, 2H), 3.92–3.40 (m, 32H), 2.76–2.71 (m, 6H), 2.60–2.53 (m, 2H); ^{13}C NMR (D_2O/CD_3OD, 50.3 MHz) δ 101.3, 77.32, 73.7, 70.9, 69.5, 69.4, 69.3, 69.0, 67.9, 67.7, 67.1, 60.4, 59.4, 49.2, 46.0. Anal. Calcd for $C_{30}H_{60}O_{22}N_2\cdot 2.5H_2O$: C, 42.60; H, 7.75; N, 3.31. Found: C, 42.40; H, 7.46; N, 3.54.

3.2.12. 1,6-Bis(1-deoxy-D-galactitol-1-ylamino)hexane (B12). A mixture of D-(+)-galactose (9.314 g, 51.7 mmol), 1,6-diaminohexane (2.614 g, 22.5 mmol), and Pd/C (10%, 0.8 g) in MeOH/H_2O (60% v/v, 125 mL) was stirred at 40 °C for 24 h under a hydrogen atmosphere (9 bar). Filtration of the reaction mixture to remove the Pd/C was difficult. Dilution with water and elevation of the temperature facilitated the filtration. Alternatively, the mixture was acidified with HCl (1 M) to pH 2–3 and filtrated, followed by adjusting the pH to 10–11 with NaOH (1 M). Filtration and drying of the precipitate gave **B12** (5.0 g, 50%), mp: 197–198 °C. ^{1}H NMR (D_2O, 300 MHz) δ 3.94–3.83 (m, 4H), 3.56–3.46 (m, 8H), 2.76–2.50 (m, 8H), 1.41 (br s, 4H), 1.24 (m, br s, 4H); ^{13}C NMR (D_2O/DMSO-d_6/65 °C, 75.4 MHz) δ 72.7, 71.8, 71.4, 70.1, 64.7, 52.8, 49.8, 29.7, 27.6. Anal. Calcd for $C_{18}H_{40}N_2O_{10}$: C, 48.64; H, 9.07; N, 6.30. Found: C, 48.6; H, 9.18; N, 6.14.

3.2.13. 1,6-Bis(1-deoxy-D-mannitol-1-ylamino)hexane (B13). See Ref. 7.

3.2.14. 1,6-Bis(1-deoxy-D-talitol-1-ylamino)hexane (B14). A mixture of D-(+)-talose (0.72 g, 4.0 mmol), 1,6-diaminohexane (0.220 g, 1.9 mmol), and Pd/C (10%, 75 mg) in MeOH/H_2O (70% v/v, 5 mL) was stirred for 24 h at 40 °C and 40 bar pressure (autoclave) in a hydrogen atmosphere. The precipitate was diluted with reaction solvent (9 mL) and filtrated at 65 °C. Evaporation of the solvent gave the crude product (0.900 g). Purification by crystallization (MeOH/H_2O, 70% v/v) gave pure **B14** (0.453 g, 54%) as a white solid, mp: 150 °C (dec). ^{1}H NMR (D_2O, 300 MHz) δ 3.91–3.80 (m, 4H), 3.69–3.65 (m, 2H), 3.56–3.49 (m, 6H), 2.71–2.49 (m, 8H), 1.4 (br t, $J_{H,H}$=6.2, 4H), 1.24 (br s, 4H). Anal. Calcd for $C_{18}H_{40}N_2O_{10}\cdot H_2O$: C, 46.74; H, 9.15; N, 6.06. Found: C, 46.6; H, 9.15; N, 6.06.

3.2.15. 1,6-Bis(1-deoxy-D-lactitol-1-ylamino)hexane (B15). A mixture of D-(+)-lactose (10.8 g, 30 mmol), 1,6-diaminohexane (1.16 g, 10 mmol), and Pd/C (10%, 0.355 g) in MeOH/H_2O (60% v/v, 115 mL) was stirred at 40 °C for 24 h under a hydrogen atmosphere (9 bar). The reaction mixture was filtrated and freeze-dried, which gave **B15** (10.7 g of the crude compound). This material (4.0 g) was purified on an ion-exchange column (25.5 g Dowex 50×8, H^+) using H_2O and NH_4OH (0.2 M) as the eluant giving **B15** (1.0 g, 35%) as a white solid. ^{1}H NMR (D_2O, 300 MHz) δ 4.38 (d, $J_{H,H}$=7.7, 2H), 3.96–3.39 (m, 24H), 2.78–2.73 (m, 2H), 2.58–2.51 (m, 6H), 1.41 (br s, 4H), 1.24 (br s, 4H); ^{13}C NMR (D_2O/CD_3OD, 50.3 MHz) δ 101.2, 77.1, 73.7, 70.9, 69.4, 69.2, 68.4, 67.1, 60.4, 59.4, 49.0, 46.9, 26.0, 24.5.

3.2.16. 1,6-Bis(1-deoxy-α-D-melibitol-1-ylamino)hexane (B16). A mixture of D-(+)-melibiose (4.621 g, 13.5 mmol), 1,6-diaminohexane (0.580 g, 5 mmol), and Pd/C (10%, 0.250 g) was stirred at 40 °C for 24 h. under a H_2 atmosphere (9 bar). Filtration, evaporation of the solvent, and freeze-drying gave the crude compound. Purification on a MAC-3 ion-exchange column with a H_2O/NH_4OH gradient gave **B16** (3.24 g, 84%) as a white solid, mp: 99 °C (dec). ^{1}H NMR (D_2O, 300 MHz) δ 4.97 (d, $J_{H,H}$=3.3, 2H), 3.98–3.66 (m, 24H), 2.81–2.67 (m, 8H), 1.53 (m, 4H), 1.35 (br s, 8H); ^{13}C NMR (D_2O/CD_3OD, 50.3 MHz) δ 98.9, 71.6, 71.5, 71.4, 70.9, 70.1, 69.9, 69.8, 69.3, 69.1, 61.7, 50.9, 49.1, 28.1, 26.8. Anal. Calcd for $C_{30}H_{60}N_2O_{20}\cdot 2H_2O$: C, 44.77; H, 8.02; N, 3.48. Found: C, 44.7; H, 7.78; N, 3.47.

3.2.17. 1,6-Bis(1-deoxy-D-arabinitol-1-ylamino)hexane (B17). D-(−)-arabinose (3.45 g, 23 mmol), 1,6-diaminohexane (1.16 g, 10 mmol), and Pd/C (10%, 0.4 g) were mixed in MeOH/H_2O (50% v/v, 22 mL) and stirred for 24 h in a hydrogen atmosphere at 40 °C and at 9 bar pressure. After the reaction was complete, H_2O (15 mL) was added at 40 °C, and the precipitate (A) was filtered off. The solvent was removed by freeze-drying, giving a white solid. Crystallization (MeOH/H_2O, 90% v/v) gave 0.959 g of **B17**. The former precipitate (A) was stirred in H_2O (25 mL) and filtered again. The mixture was freeze-dried and the residue was purified on an ion-exchange column (MAC-3) and eluted with a H_2O/NH_4OH (0.5 M) gradient to afford **B17** (0.676 g). Total yield 1.635 g (42.5%), mp: 166–167 °C. ^{1}H NMR (D_2O, 300 MHz) δ 3.90–3.85 (m, 2H), 3.74–3.70 (m, 2H), 3.65–3.51 (m, 4H), 3.39–3.35 (m, 2H), 2.71–2.47 (m, 8H), 1.40 (br t, $J_{H,H}$=6.2, 4H), 1.24 (br s, 4H); ^{13}C NMR (D_2O/CD_3OD, 50.3 MHz) δ 70.4, 69.4, 66.8, 61.4, 49.6, 46.8,

26.6, 24.6. Anal. Calcd for $C_{16}H_{36}N_2O_8$: C, 49.98; H, 9.44; N, 7.29. Found: C, 49.9; H, 9.29; N, 7.15.

3.2.18. 1,6-Bis(1-deoxy-D-erithritol-1-ylamino)hexane (B18). A mixture of D-(−)-erythrose (1.0 g, 8.33 mmol), 1,6-diaminohexane (0.464 g, 4 mmol), and Pd/C (10%, 0.160 g) dissolved in 15 mL of MeOH/H_2O (70% v/v) was stirred at 40 °C and 9 bar H_2 pressure, for 24 h. The Pd/C was filtered off and the freeze-dried residue was crystallized from methanol to yield **B18** (0.611 g, 47%) as a white solid, mp 154–155 °C. ^{1}H NMR (D_2O, 300 MHz) δ 3.65–3.60 (m, 4H), 3.50–3.46 (m, 4H), 2.72–2.67 (m, 2H), 2.54–2.48 (m, 6H), 1.39 (br s, 4H), 1.22 (br s, 4H); ^{13}C NMR (D_2O/CD_3OD, 50.3 MHz) δ 74.4, 70.8, 63.0, 51.2, 49.0, 28.9, 26.9. Anal. Calcd for $C_{14}H_{32}N_2O_6$: C, 51.83; H, 9.94; N, 8.63. Found: C, 51.8; H, 9.97; N, 8.35.

3.2.19. *N,N′*-DL-Glyceryl-1,6-hexanediamine (B19). DL-Glyceraldehyde (1.98 g, 22.0 mmol), 1,6-diaminohexane (1.16 g, 10 mmol), and Pd/C (10%, 0.4 g) in MeOH/H_2O (40% v/v, 15 mL) were stirred at 40 °C and under 9 bar H_2 pressure for 5 h. After filtration the mixture was purified by crystallization from MeOH/MeCN (33% v/v) giving **B19** (0.650 g, 25%) as a light yellow solid, mp: 99–125 °C (dec). ^{1}H NMR (D_2O, 300 MHz) δ 3.70–3.66 (m, 2H), 3.48–3.35 (m, 4H), 2.56–2.42 (m, 8H), 1.36 (br t, $J_{H,H}$=6.8, 4H), 1.19 (br s, 4H); ^{13}C NMR (D_2O/CD_3OD, 75.4 MHz) δ 71.2, 65.0, 51.7, 49.5, 29.1, 27.2. Anal. Calcd for $C_{12}H_{28}N_2O_4$: C, 54.52; H, 10.68; N, 10.60. Found: C, 53.9; H, 10.32; N, 10.29.

3.2.20. *N,N′*-Dimethyl-1,6-hexanediamine (B20). Compound **B20** was a commercial product.

3.2.21. *N,N′*-Methyl-2,5,8,11-tetraoxatridecyl-1,6-hexanediamine (B21). 3,6,9-Trioxadecanaldehyde (3.09 g, 15 mmol),[20] 1,6-diaminohexane (0.783 g, 6.75 mmol), and Pd/C (10%, 0.3 g) were added to MeOH/H_2O (70% v/v, 10 mL) and stirred at 40 °C under a H_2 pressure (9 bar) for 24 h. Filtration, evaporation of the solvent, and purification on a ion-exchange column (MAC-3) gave an impure viscous oil (1.546 g). Purification on Dowex (50×8, H+) using H_2O/NH_4OH (2.5 M) as a gradient gave **B21** (0.134 g, 4%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.70–3.46 (m, 28H), 3.33 (s, 6H), 2.75 (t, $J_{H,H}$=4.5, 4H), 2.53 (t, $J_{H,H}$=6.1, 4H), 1.45 (m, 4H), 1.29 (br s, 4H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 71.7, 70.4, 70.35, 70.3, 70.1, 58.8, 49.8, 49.1, 29.9, 27.2; LC/MS (ionspray); M+1: 497.4 $[C_{24}H_{53}N_2O_8]^+$; M+1/2: 249.2 $[C_{24}H_{53}N_2O_8]^{2+}$.

3.2.22. 1,19-Bis(1-deoxy-D-glucitol-1-ylamino)-4,7,10,16-pentaoxanonadecane (B22). 1,19-Diamino-4,7,10,13,16-pentaoxanonadecane (1.0 g, 3.24 mmol) and D-(+)-glucose (6.81 mmol, 1.226 g) were dissolved in MeOH/H_2O (70% v/v, 10 mL) and Pd/C (10%, 0.109 g) was added. The mixture was stirred at 40 °C and 40 bar hydrogen for 24 h. Filtration (by suction), evaporation of the solvent, and freeze-drying gave a colorless sticky residue (1.882 g). Purification on an ion-exchange column, MAC-3 (H_2O/NH_4OH gradient, 0.2, 0.5, and 1.0 mol, respectively), gave **B22** (1.477 g, 72%) as a sticky white solid. ^{1}H NMR (D_2O, 300 MHz) δ 3.76–3.46 (m, 32H), 2.66–2.54 (m, 8H), 1.66–1.64 (m, 4H); ^{13}C NMR (D_2O/DMSO-d_6, 50.3 MHz) δ 72.6, 72.5, 72.4, 72.3, 71.2, 70.8, 70.7, 64.4, 51.9, 47.3, 29.7. Anal. Calcd for $C_{26}H_{56}N_2O_{15}$: C, 49.04; H, 8.86; N, 4.40. Found: C, 48.6; H, 8.84; N, 4.26.

3.3. Reduced-sugar based gemini surfactants

3.3.1. General procedure. To the corresponding bola (1 mmol) dissolved or suspended in methanol (10 mL) were added acetic acid (2 mmol), MP-cyanoborohydride (900 mg), and aldehyde (2.2 mmol) in THF (5 mL). The mixture was gently stirred and heated at 40 °C for 20 h. MP-cyanoborohydride was filtered off and the solvent was evaporated. The residue was treated with a mixture of acetone/acetonitrile (50:50% v/v, 20–40 mL). The solid was filtered off and dissolved in *peroxide free* THF (10–20 mL) and HCl (1 M, 5 mL) was added. This mixture was stirred at 40 °C for 2 days to hydrolyze the boric esters (followed by ^{11}B NMR) and then the mixture was neutralized with Dowex OH^- (8 g, washed before with THF). The ion-exchange material was filtered off and washed with THF. The combined fractions were collected and evaporated to dryness in vacuo, or freeze-dried and in some cases crystallized. In this way the geminis **GS1–3**, **GS5–7**, **GS9–21** were synthesized.

3.3.1.1. 1,8-Bis(*N-cis*-octadecene-9-yl-1-deoxy-glucitol-1-ylamino)-3,6-dioxaoctane (GS1).[6] Recrystallization from THF/acetonitrile gave **GS1** (0.688 g, 70%) as a waxy white solid, mp: 50 °C (dec). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.36–5.33 (m, 4H), 3.82–3.59 (m, 20H), 2.78–2.58 (m, 12H), 2.03 (m, 8H), 1.50 (m, 4H), 1.31 (chain, 44H), 0.91 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 131.5, 130.9, 74.0, 72.9, 72.4, 71.9, 71.0, 69.9, 64.8, 58.7, 56.4, 54.9, 33.7, 33.1, 30.8, 30.6, 30.5, 30.4, 28.7, 28.2, 27.4, 23.8, 14.5. Anal. Calcd for $C_{54}H_{108}N_2O_{12}$: C, 66.36; H, 11.14; N, 2.87. Found: C, 66.3; H, 11.22; N, 2.82.

3.3.1.2. 1,8-Bis(*N-cis*-octadecene-9-yl-1-deoxy-mannitol-1-ylamino)-3,6-dioxaoctane (GS2).[7] Neutralization, evaporation of the THF, and freeze-drying gave **GS2** (0.750 g, 77%) as a white solid, mp: 50 °C (dec). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.35 (m, 4H), 3.82–3.59 (m, 20H), 2.90–2.53 (m, 12H), 2.03 (m, 8H), 1.24 (m, 4H), 1.30 (m, 44H), 0.91 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 131.5, 130.8, 74.9, 72.8, 71.6, 71.3, 70.0, 68.3, 65.2, 60.2, 56.5, 54.9, 33.7, 30.9, 30.6, 30.5, 30.4, 28.6, 28.2, 27.5, 23.8, 14.4. Anal. Calcd for: $C_{54}H_{108}N_2O_{12}$: C, 66.36; H, 11.14; N, 2.87. Found: C, 65.9; H, 11.08; N, 2.95.

3.3.1.3. 1,6-Bis(*N-cis*-octadecene-9-yl-1-deoxy-mannitol-1-ylamino)hexane (GS3).[7] Crystallization from THF/acetonitrile gave **GS3** (0.700 g, 74%) as a white solid, mp: 40–90 °C (liquid crystalline). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.35 (m, 4H), 3.84–3.59 (m, 12H), 2.87–2.80 (m, 12H), 2.60–2.47 (m, 10H), 2.02 (m, 8H), 1.52 (br s, 8H), 1.32 (chain, 50H), 0.90 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 131.5, 130.9, 75.3, 72.7, 71.6, 67.7, 65.2, 60.0, 55.6, 55.4, 33.7, 33.1, 30.9, 30.7, 30.5, 30.4, 30.2, 28.3, 28.2, 27.4, 23.8, 14.6. Anal. Calcd for $C_{54}H_{108}N_2O_{10}$: C, 68.60; H, 11.51; N, 2.96. Found: C, 68.3; H, 11.79; N, 2.87.

3.3.1.4. 1,8-Bis(*N-cis*-octadecene-9-oyl-1-deoxy-glucitol-1-ylamino)-3,6-dioxaoctane (GS4). See Ref. 7.

3.3.1.5. 1,8-Bis(*N*-octadecyl-1-deoxy-D-glucitol-1-ylamino)-3,6-dioxaoctane (GS5). After evaporation of the THF, the residue was freeze-dried (to remove traces of THF and H_2O) to give **GS5** (0.426 g, 43%, recrystallized from MeOH) as a white solid, mp: 50 °C (dec). ^{1}H NMR ($CD_3OD/CDCl_3$, 300 MHz) δ 4.84–3.57 (m, 20H), 2.74–2.59 (m, 12H), 1.50 (br s, 4H), 1.29 (chain, 60H), 0.90 (t, $J_{H,H}$=6.6, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 73.8, 72.8, 72.5, 71.9, 71.3, 70.3, 64.9, 58.8, 66.6, 55.0, 33.0, 30.8, 30.4, 28.5, 27.8, 23.7, 14.5. Anal. Calcd for $C_{54}H_{112}N_2O_{12}\cdot 1H_2O$: C, 64.89; H, 11.50; N, 2.80. Found: C, 64.7; H, 11.23; N, 2.93.

3.3.1.6. 1,8-Bis(*N*-octadecyl-1-deoxy-D-mannitol-1-ylamino)-3,6-dioxaoctane (GS6). Crystallization from MeOH gave **GS6** (0.660 g, 67%) as a white solid, mp: 50–103 °C (liquid crystalline). ^{1}H NMR (CD_3OD, 300 MHz) δ 3.84–3.59 (m, 20H), 2.92–2.54 (m, 12H), 1.52 (br s, 4H), 1.29 (chain, 60H), 0.90 (t, $J_{H,H}$=6.6, 6H); ^{13}C NMR (CD_3OD/55 °C, 75.4 MHz) δ 75.0, 73.2, 72.0, 71.5, 70.2, 68.7, 65.3, 60.3, 56.7, 55.1, 33.0, 30.7, 30.3, 28.5, 27.7, 23.6, 14.3. Anal. Calcd for $C_{54}H_{112}N_2O_{12}\cdot 0.5H_2O$: C, 65.48; H, 11.50; N, 2.83. Found: C, 65.7; H, 11.35; N, 2.86.

3.3.1.7. 1,8-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-galactitol-1-ylamino)-3,6-dioxaoctane (GS7). Neutralization, evaporation of THF, and freeze-drying gave **GS7** (0.800 g, 82%) as a white solid, mp: 93 °C (liquid crystalline). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.36–5.33 (m, 4H), 3.99–3.90 (m, 4H), 3.69–3.54 (m, 16H), 2.82–2.60 (m, 12H), 2.04–2.00 (m, 8H), 1.51 (br s, 4H), 1.32–1.29 (m, chain, 44H), 0.90 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 131.5, 130.8, 72.7, 71.9, 71.6, 71.4, 70.4, 68.5, 65.0, 59.3, 55.0, 50.3, 33.7, 33.1, 30.8, 30.6, 30.5, 30.4, 30.3, 28.6, 28.2, 27.9, 23.8, 14.5. Anal. Calcd for $C_{54}H_{108}N_2O_{12}\cdot 0.5H_2O$: C, 65.75; H, 11.14; N, 2.84. Found: C, 65.6; H, 10.81; N, 2.85.

3.3.1.8. 1,6-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-galactitol-1-ylamino)hexane (GS8). This compound was prepared by a method described before[7] and isolated as the double HCl salt. Neutralization with $NaOCH_3$ in methanol, evaporation, and crystallization from methanol/acetone gave **GS8** (0.744 g, 72%) as a white solid, mp: 30–110 °C (liquid crystalline). ^{1}H NMR ($CD_3OD/CDCl_3$, 300 MHz) δ 5.33–5.29 (m, 4H), 3.87–3.45 (m, 12H), 2.67–2.44 (m, 12H), 1.98–1.96 (m, 8H), 1.42 (br s, 8H), 1.23 (chain, 50H), 0.84 (t, $J_{H,H}$=6.6, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 130.7, 130.3, 130.1, 72.3, 71.5, 70.9, 76.4, 64.4, 57.9, 55.0, 54.5, 32.9, 30.1, 29.7, 27.9, 27.5, 26.8, 23.0, 14.3. Anal. Calcd for $C_{54}H_{108}N_2O_{10}\cdot 2H_2O$: C, 66.08; H, 11.50; N, 2.85. Found: C, 66.4; H, 11.45; N, 2.83.

3.3.1.9. 1,6-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-talitol-1-ylamino)hexane (GS9). Yield (0.658 g, 70%) as a white sticky solid, mp: 150 °C (dec). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.39–5.32 (m, 4H), 3.88–3.86 (m, 4H), 3.75 (t, $J_{H,H}$=6.4, 2H), 3.65–3.63 (m, 6H), 2.82–2.76 (m, 2H), 2.63–2.49 (m, 10H), 2.13–1.95 (m, 8H), 1.51 (br s, 8H), 1.30 (chain, 48H), 0.90 (t, $J_{H,H}$=6.6, 6H); ^{13}C NMR (CD_3OD, 75.4 MHz) δ 130.8, 130.7, 76.2, 73.5, 72.1, 69.1, 64.6, 59.0, 55.6, 55.5, 33.5, 33.0, 30.7, 30.6, 30.5, 30.4, 30.2, 28.5, 28.3, 28.1, 27.4, 23.7, 14.5. Anal. Calcd for $C_{54}H_{108}N_2O_{10}$: C, 68.60; H, 11.51; N, 2.96. Found: C, 68.2; H, 11.74; N, 2.95.

3.3.1.10. 1,8-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-lactitol-1-ylamino)-3,6-dioxaoctane (GS10). Crystallization from methanol/acetonitrile gave **GS10** (1.157 g, 89%) as a white solid, mp: 25–210 °C (liquid crystalline, slow dec from 170 °C). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.35–5.32 (m, 4H), 4.46 (d, $J_{H,H}$=7.3, 2H), 3.90–3.47 (m, 32H), 2.79–2.57 (m, 8H), 2.02 (br s, 4H), 1.31–1.29 (chain, 48H), 0.89 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 130.7, 105.4, 83.5, 79.6, 79.0, 78.3, 76.8, 74.6, 73.1, 72.7, 72.5, 71.2, 70.3, 70.0, 69.8, 63.5, 62.3, 58.6, 56.6, 54.7, 50.3, 33.5, 32.9, 30.7, 30.5, 30.3, 28.5, 28.0, 27.8, 23.6, 14.5. Anal. Calcd for $C_{66}H_{128}N_2O_{22}$: C, 60.90; H, 9.91; N, 2.15. Found: C, 60.90; H, 9.99; N, 2.19.

3.3.1.11. 1,6-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-lactitol-1-ylamino)hexane (GS11). Freeze-drying gave **GS11** (0.863 g, 63%) as a white solid, mp: 50–200 °C (liquid crystalline, dec from 200 °C). ^{1}H NMR ($CD_3OD/CDCl_3$, 300 MHz) δ 5.37–5.32 (m, 4H), 4.60 (d, $J_{H,H}$=7.3, 2H), 3.89–3.69 (m, 18H), 5.60–3.47 (m, 6H), 2.64–2.50 (m, 12H), 1.48 (br s, 8H), 1.31–1.29 (chain, 48H), 0.89 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 131.3, 130.7, 105.4, 83.3, 76.7, 74.3, 73.1, 72.6, 70.0, 69.9, 63.5, 62.3, 58.4, 55.8, 55.9, 55.5, 47.7, 33.5, 32.9, 30.7, 30.6, 30.5, 30.3, 30.2, 28.6, 28.4, 28.0, 27.6, 23.6, 14.5. Anal. Calcd for $C_{66}H_{128}N_2O_{20}\cdot 0.5H_2O$: C, 61.99; H, 10.17; N, 2.19. Found: C, 61.9; H, 10.03; N, 2.29.

3.3.1.12. 1,6-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-melibitol-1-ylamino)hexane (GS12). Crystallization from THF/acetonitrile gave **GS12** (0.838 g, 66%) as a white solid, mp: 50 °C (dec). ^{1}H NMR ($CD_3OD/CDCl_3$, 300 MHz) δ 5.38–5.32 (m, 4H), 4.86 (d, $J_{H,H}$=1.3, 2H), 3.97–3.60 (m, 24H), 2.64–2.52 (m, 12H), 2.52–2.02 (m, 8H), 1.49 (m, 8H), 1.30 (chain, 48H), 0.89 (t, $J_{H,H}$=6.6, 6H); ^{13}C NMR (CD_3OD, 75.4 MHz) δ 131.4, 130.8, 130.7, 100.3, 79.4, 79.0, 78.6, 73.2, 72.4, 71.8, 71.6, 71.2, 71.0, 70.5, 70.3, 62.7, 58.5, 55.7, 55.5, 33.5, 32.9, 30.7, 30.6, 30.5, 30.4, 30.3, 30.2, 28.5, 28.4, 27.6, 23.6, 14.4. Anal. Calcd for $C_{66}H_{128}N_2O_{20}\cdot 1H_2O$: C, 61.56; H, 10.18; N, 2.18. Found: C, 61.4; H, 10.00; N, 2.19.

3.3.1.13. 1,2-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-glucitol-1-ylamino)ethane (GS13). Crystallization from acetone/THF gave **GS13** (0.664 g, 74%) as a white solid, mp: recrystallization at 115 °C followed by melting at 168 °C. ^{1}H NMR (CD_3OD, 300 MHz) δ 5.35 (m, 4H), 3.87–3.32 (m, 12H), 2.79–2.49 (m, 12H), 2.02 (m, 8H), 1.51 (br s, 4H), 1.30 (chain, 44H), 0.89 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 131.3, 130.7, 130.6, 73.9, 72.6, 72.0, 64.7, 58.1, 56.2, 52.9, 33.5, 32.9, 30.6, 30.4, 30.3, 28.5, 28.0, 27.5, 23.6, 14.5. Anal. Calcd for $C_{50}H_{100}N_2O_{10}\cdot 0.5H_2O$: C, 66.85; H, 11.33; N, 3.12. Found: C, 66.9; H, 11.25; N, 3.11.

3.3.1.14. 1,4-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-glucitol-1-ylamino)butane (GS14). Crystallization from

acetone/THF gave **GS14** (0.633 g, 69%) as a white solid, mp: 45–113 °C (liquid crystalline). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.35–5.31 (m, 4H), 3.81–3.60 (m, 12H), 2.61–2.55 (m, 12H), 2.02 (br s, 8H), 1.49 (br s, 8H), 1.29 (chain, 44H), 0.89 (t, $J_{H,H}$=5.7, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 131.3, 130.7, 73.7, 72.7, 72.5, 71.7, 64.7, 58.3, 55.7, 55.3, 33.5, 32.9, 30.7, 30.6, 30.2, 28.5, 28.0, 27.6, 25.6, 23.6, 14.5. Anal. Calcd for $C_{52}H_{104}N_2O_{10}$: C, 68.08; H, 11.43; N, 3.05. Found: C, 68.0; H, 11.45; N, 2.99.

3.3.1.15. 1,6-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-glucitol-1-ylamino)hexane (GS15). Crystallization from THF/acetone gave **GS15** (0.736 g, 78%) as a white solid, mp: 30–63 °C. ^{1}H NMR ($CD_3OD/CDCl_3$, 300 MHz) δ 5.34–5.31 (m, 4H), 3.82–3.61 (m, 12H), 2.61–2.48 (m, 12H), 2.02–2.00 (m, 8H), 1.49 (br s, 8H), 1.30–1.27 (m, chain, 50H), 0.88 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 130.63, 130.57, 73.6, 72.6, 71.5, 64.7, 58.2, 55.5, 55.3, 33.5, 32.9, 30.7, 30.5, 30.3, 30.2, 28.4, 28.2, 28.0, 27.4, 23.6, 14.5. Anal. Calcd for $C_{54}H_{108}N_2O_{10}$: C, 68.60; H, 11.51; N, 2.96. Found: C, 68.5; H, 11.58; N, 2.87.

3.3.1.16. 1,8-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-glucitol-1-ylamino)octane (GS16). Crystallization from acetone/THF gave **GS16** (0.656 g, 67%) as a sticky white solid, mp: 25–50 °C. ^{1}H NMR ($CD_3OD/CDCl_3$, 200 MHz) δ 5.35–5.31 (m, 4H), 3.82–3.60 (m, 12H), 2.62–2.48 (m, 12H), 1.48 (m, 4H), 1.29 (chain, 56H), 0.89 (t, $J_{H,H}$=6.3, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 131.3 (trans), 130.7, 130.6, 73.5, 72.6, 71.5, 64.7, 58.3, 55.4, 33.5, 32.9, 30.7, 30.68, 30.58, 30.52, 30.5, 30.3, 30.2, 30.0, 28.5, 28.4, 28.0, 27.4, 23.6, 14.5. Anal. Calcd for $C_{56}H_{112}N_2O_{10}$: C, 69.09; H, 11.60; N, 2.88. Found: C, 69.1; H, 11.62; N, 2.91.

3.3.1.17. 1,10-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-glucitol-1-ylamino)decane (GS17). The glassy and sticky white solid was dissolved in acetone (40 mL) and cooled at −20 °C. The precipitate was collected by suction giving **GS17** (0.719 g, 72%) as a white solid, mp: 43–65 °C (liquid crystalline). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.37–5.31 (m, 4H), 3.81–3.59 (m, 12H), 2.61–2.45 (m, 12H), 1.02 (br s, 8H), 1.47 (br s, 8H), 1.29 (chain, 56H), 0.89 (t, $J_{H,H}$=6.6, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 131.2, 130.7, 130.6, 73.6, 72.6, 71.5, 64.7, 58.3, 55.4, 33.4, 32.9, 30.6, 30.5, 30.3, 30.2, 28.4, 28.0, 27.4, 23.6, 14.5. Anal. Calcd for $C_{58}H_{116}N_2O_{10}$: C, 69.55; H, 11.67; N, 2.80. Found: C, 69.5; H, 11.70; N, 2.82.

3.3.1.18. 1,12-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-glucitol-1-ylamino)dodecane (GS18). If necessary, **GS18** can be crystallized from acetone at low temperature (−20 °C). Yield **GS18** (0.833 g, 81%) as a white solid, mp: 65 °C (liquid crystalline). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.34–5.31 (m, 4H), 3.82–3.59 (m, 12H), 2.61–2.45 (m, 12H), 2.17 (br s, 8H), 1.47 (br s, 8H), 1.30 (chain, 60H), 0.89 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR ($CD_3OD/CDCl_3$, 50.3 MHz) δ 131.2, 130.7, 130.6, 73.5, 72.5, 71.5, 64.7, 58.3, 55.4, 33.5, 32.8, 30.6, 30.5, 30.2, 30.1, 28.4, 28.0, 27.4, 23.5, 14.5. Anal. Calcd for $C_{60}H_{120}N_2O_{10}$: C, 69.99; H, 11.75; N, 2.72. Found: C, 70.1; H, 11.82; N, 2.76.

3.3.1.19. 1,3-Bis(*N*-dodecyl-1-deoxy-D-glucitol-1-ylamino)propane (GS19). Two times of the quantities as described in Section 3.3.1 have been used. Crystallization from MeOH/acetone gave **GS19** (1.147 g, 78%) as a white solid, mp: 30–175 °C (liquid crystalline). ^{1}H NMR (CD_3OD, 200 MHz) δ 3.80–3.60 (m, 12H), 2.61–2.51 (m, 12H), 1.66–1.28 (chain, 42H), 0.89 (t, $J_{H,H}$=6.6, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 73.7, 72.7, 72.4, 71.8, 64.7, 58.2, 55.8, 53.5, 33.0, 30.7, 30.4, 28.6, 27.5, 24.7, 23.6, 14.5. Anal. Calcd for $C_{39}H_{82}N_2O_{10}\cdot 0.5H_2O$: C, 62.62; H, 11.18; N, 3.74. Found: C, 62.6; H, 10.94; N, 3.79.

3.3.1.20. 1,19-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-glucitol-1-ylamino)-4,7,10,16-pentaoxanonadecane (GS20). Crystallization from acetone/THF gave **GS20** (0.646 g, 57%) as a waxy white solid, mp: 20–53 °C (liquid crystalline). ^{1}H NMR (CD_3OD, 300 MHz) δ 5.35–5.32 (m, 4H), 3.82–3.50 (m, 32H), 2.66–251 (m, 12H), 2.03–2.01 (m, 8H), 1.77–1.73 (m, 4H), 1.49 (br s, 4H), 0.89 (t, $J_{H,H}$=6.2, 6H); ^{13}C NMR (CD_3OD, 75.4 MHz) δ 131.4, 130.5, 73.5, 72.4, 72.1, 71.4, 71.2, 70.8, 70.1, 64.5, 58.0, 55.4, 52.0, 33.2, 32.7, 30.4, 30.3, 30.2, 30.0, 29.9, 28.2, 27.8, 27.5, 27.3, 23.3, 14.2. Anal. Calcd for $C_{62}H_{124}N_2O_{15}$: C, 65.46; H, 10.99; N, 2.46. Found: C, 65.2; H, 11.11; N, 2.40.

3.3.1.21. 1,6-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-arabinitol-1-ylamino)hexane (GS21). Crystallization from methanol/acetone gave **GS21** (0.675 g, 76%) as a white solid, mp: 68–70 °C. ^{1}H NMR (CD_3OD, 300 MHz) δ 5.39–5.33 (m, 4H), 3.94 (m, 2H), 3.82–3.78 (m, 2H), 3.69–3.60 (m, 4H), 3.43–3.40 (m, 2H), 2.68–2.49 (m, 12H), 2.03 (m, 8H), 1.50 (br s, 8H), 0.91 (t, $J_{H,H}$=7.0, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 131.5, 130.9, 74.0, 73.3, 68.6, 65.1, 59.0, 55.9, 33.6, 33.1, 30.9, 30.8, 30.7, 30.6, 30.5, 30.3, 28.6, 28.5, 27.8, 23.7, 14.5. Anal. Calcd for $C_{52}H_{104}N_2O_8$: C, 70.54; H, 11.84; N, 3.16. Found: C, 70.3; H, 11.81; N, 3.13.

3.3.1.22. 1,6-Bis(*N-cis*-octadecene-9-yl-1-deoxy-D-erithritol-1-ylamino)hexane (GS22). The reaction mixture was filtrated (removal of the MP-cyanoborohydride) and the solvent was evaporated. The residue was dissolved in THF and added to Amberlyst 15 (H^+) (8 g, washed before with THF), stirred for 1 h, and filtrated. The Amberlyst was washed again with THF (two times 10 mL) to remove the impurities. THF was added to the Amberlyst and NH_3 gas was passed through till a basic pH was obtained. Filtration and evaporation gave **GS22** (0.597 g; a part of it stayed on the Amberlyst) as a viscous light yellow oil. Purification by column chromatography (SiO_2, $CHCl_3$/MeOH 60:40 v/v) gave **GS22** (0.357 g, 45%) as a colorless oil. ^{1}H NMR (CD_3OD, 300 MHz) δ 5.40–5.33 (m, 4H), 3.73–3.54 (m, 8H), 2.78 (d, $J_{H,H}$=6.6, 1H), 2.73 (d, $J_{H,H}$=6.6, 1H), 2.62–2.49 (m, 10H), 2.04 (m, 8H), 1.51 (br s, 8H), 1.33 (chain, 48H), 0.91 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 131.5, 131.4, 130.83, 130.78, 77.1, 68.3, 64.5, 59.9, 55.7, 55.5, 33.6, 33.1, 30.8, 30.7, 30.6, 30.5, 30.3, 30.2, 28.5, 28.4, 28.2, 27.7, 27.6, 23.7, 14.5. Anal. Calcd for $C_{50}H_{100}N_2O_6\cdot 0.5H_2O$: C, 71.98; H, 12.20; N, 3.36. Found: C, 72.0; H, 12.09; N, 3.49.

3.3.1.23. *N,N′*-Di-DL-1-glyceryl-*N,N′*-di-octadecene-9-yl-1,6-diaminohexane (GS23). Formed from bola **B19**

(0.79 mmol, 0.209 g). The same procedure as in the synthesis of **GS22** was employed yielding **GS23** (0.348 g, 58%) as a colorless viscous liquid. ^{1}H NMR (CD_3OD, 300 MHz) δ 5.39–5.33 (m, 4H), 3.75–3.71 (m, 2H), 3.59–3.49 (m, 4H), 2.54–2.45 (m, 12H), 2.05–2.01 (m, 8H), 1.49 (br s, 8H), 1.31 (chain, 48H), 0.91 (t, $J_{H,H}$=6.4, 6H); ^{13}C NMR (CD_3OD, 50.3 MHz) δ 131.4, 130.8, 69.8, 66.6, 59.1, 55.9, 55.8, 33.6, 33.0, 30.8, 30.6, 30.4, 30.3, 28.5, 28.4, 28.1, 27.8, 23.7, 14.5. Anal. Calcd for $C_{48}H_{96}N_2O_4\cdot 0.5H_2O$: C, 74.46; H, 12.63; N, 3.62. Found: C, 74.6; H, 12.53; N, 3.77.

3.3.1.24. 1,6-Bis(*N*-methyl-*N*-*cis*-octadecene-9-yl)diaminohexane (GS24). The crude material was purified by chromatography (SiO_2, MeOH/CH_2Cl_2, 40:60 v/v) to afford **GS24** (0.540 g, 84%) as a colorless viscous liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.33 (m, 4H), 2.29 (m, 8H), 2.17 (s, 6H), 1.99 (m, 8H), 1.41 (br s, 8H), 1.26 (chain, 48H), 0.82 (t, $J_{H,H}$=6.2, 6H); ^{13}C NMR ($CDCl_3$, 75.MHz) δ 129.8, 129.7, 57.9, 57.8, 42.3, 32.5, 31.8, 29.7, 29.5, 29.4, 29.2, 29.1, 27.5, 27.3, 27.1, 22.6, 14.0. Anal. Calcd for $C_{44}H_{88}N_2$: C, 81.92; H, 13.75; N, 4.34. Found: C, 81.4; H, 13.97; N, 4.35.

3.3.1.25. *N*,*N*′-Di-*cis*-octadecene-9-yl-*N*,*N*′-2,5,8,11-tetraoxatridecyl-1,6-diaminohexane (GS25). Bola **B21** (0.56 mmol, 0.262 g) was dissolved in methanol (10 mL) and acetic acid (adjust to pH ca. 6), oleylaldehyde (1.17 mmol, 0.311 g), and MP-cyanoborohydride (0.510 g) were added successively. The mixture was gently stirred at room temperature for 20 h. After filtration, the material was dissolved in methanol (10 mL) and neutralized with MP-carbonate (0.500 g). Filtration and evaporation of the solvent gave a light yellow liquid (0.513 g), which was purified by chromatography (SiO_2, DCM/10–30% methanol) giving **GS25** (0.279 g, 50%) as a slightly yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.31–5.27 (m, 4H), 3.61–3.48 (m, 28H), 3.32 (s, 6H), 2.59 (m, 4H), 2.37 (m, 8H), 1.96–1.92 (m, 8H), 1.36–1.21 (chain, 56H), 0.85 (t, $J_{H,H}$=6.6, 6H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 129.8, 129.7, 71.8, 70.5, 70.4, 70.3, 69.6, 58.9, 54.7, 53.1, 32.5, 31.8, 29.6, 29.5, 29.4, 29.2, 27.4, 27.1, 26.9, 22.6, 14.0. Anal. Calcd for $C_{60}H_{120}N_2O_8$: C, 72.24; H, 12.12; N, 2.81. Found: C, 71.8; H, 12.05; N, 2.71.

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