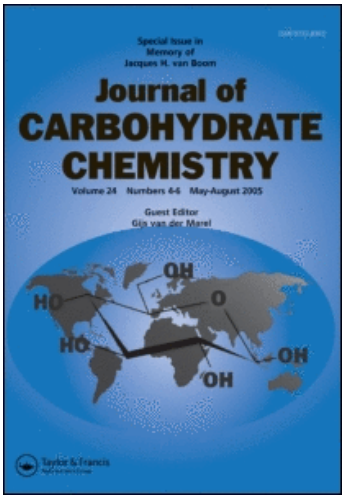


Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Synthesis of Novel α,ω-Type 1-Glucosamide and 1-Galactosamide Bolaamphiphiles

Mitsutoshi Masuda[a]; Toshimi Shimizu[a]
[a] Department of Organic Materials, National Institute of Materials and Chemical Research, Tsukuba, Ibaraki, Japan

To cite this Article Masuda, Mitsutoshi and Shimizu, Toshimi(1998) 'Synthesis of Novel α,ω-Type 1-Glucosamide and 1-Galactosamide Bolaamphiphiles', Journal of Carbohydrate Chemistry, 17: 3, 405 — 416
To link to this Article: DOI: 10.1080/07328309808002902
URL: http://dx.doi.org/10.1080/07328309808002902

J. CARBOHYDRATE CHEMISTRY, 17(3), 405-416 (1998)

SYNTHESIS OF NOVEL α,ω-TYPE 1-GLUCOSAMIDE AND 1-GALACTOSAMIDE BOLAAMPHIPHILES

Mitsutoshi Masuda* and Toshimi Shimizu

Department of Organic Materials
National Institute of Materials and Chemical Research
1-1 Higashi, Tsukuba, Ibaraki 305, Japan

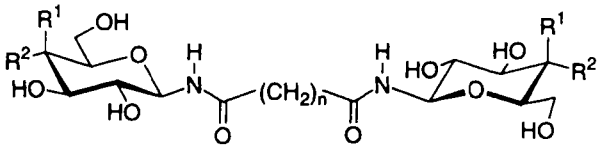
Received July 10, 1997 - Final Form November 24, 1997

ABSTRACT

A new family of bolaamphiphiles in which two glucosylamine or galactosylamine moieties are linked via a β-*N*-glycosidic bond to an α,ω-dicarboxylic acid has been described. The 1-D-glucosamide and 1-D-galactosamide bolaamphiphiles were obtained in good yield by the condensation of the dicarboxylic acid dichloride with the corresponding 1-aldopyranosylamine.

INTRODUCTION

The bolaamphiphiles can be designated as a bola-form α,ω-amphiphile in which two hydrophilic groups are linked to each other by one or more hydrophobic chains. They self-assemble in aqueous solutions to form a wide variety of supramolecular structures.[1-5] In particular, sugar-based bolaamphiphiles may be expected to form stable and chiral assemblies via stereoselective hydrogen bonds between sugar hydroxyl groups. However, there has been little investigation into their self-assembling properties except for acyclic gluconamide-based bolaamphiphiles.[6] We have recently demonstrated that aldopyranose-based bolaamphiphiles provide intriguing fibrous assemblies as well as single crystals stabilized by two- or three-dimensional networks of hydrogen bonds



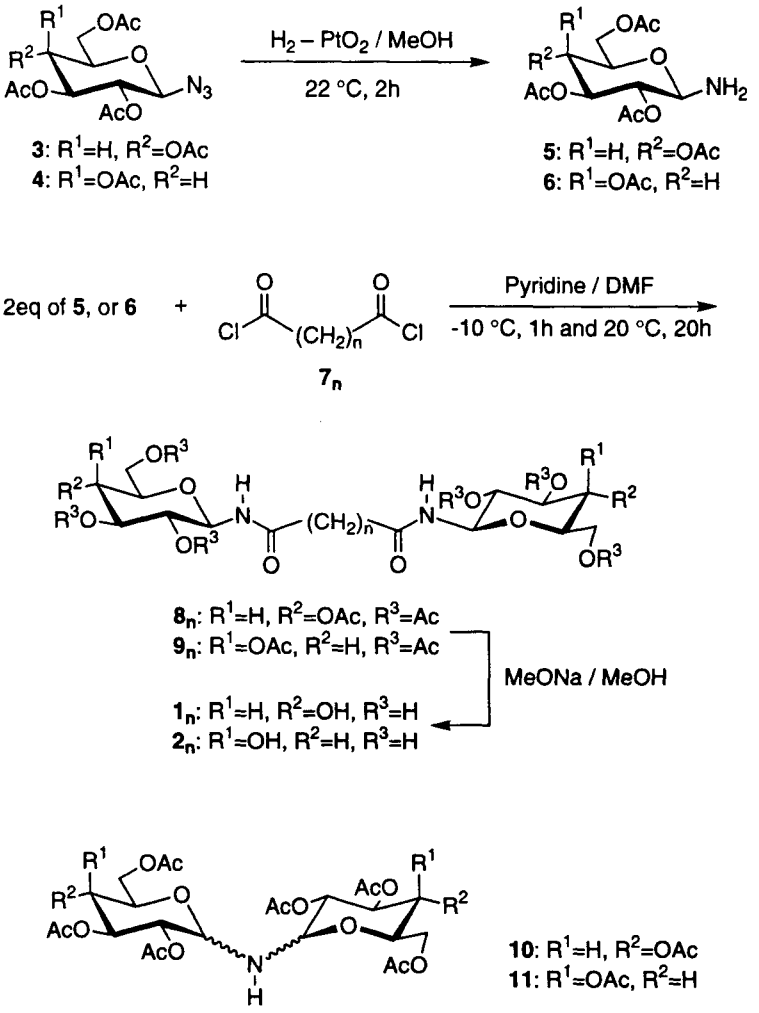
$\mathbf{1_n}$: R^1=H, R^2=OH, n = 6, 9, 10, 11, 12, 13, 14, and 18
$\mathbf{2_n}$: R^1=OH, R^2=H, n = 10, 11, and 12

Scheme 1

between amide and sugar hydroxyl groups.[7–10] We report here a simple and efficient synthetic method to prepare stereochemically pure β-1-D-glucosamide ($\mathbf{1_n}$) and β-1-D-galactosamide bolaamphiphiles ($\mathbf{2_n}$) (Scheme 1). To date, the syntheses of sugar-based bolaamphiphiles with *O*- or *S*-glycosidic linkage have been only reported.[11–14]

RESULTS AND DISCUSSION

The synthetic route to $\mathbf{1_n}$ and $\mathbf{2_n}$ is shown in Scheme 2. Tetraacetylated β-1-azide derivatives **3** and **4** were hydrogenolyzed to afford the β-1-D-aldopyranosylamines **5** and **6** in 82 and 52% yields, respectively.[15–16] The 1-aldosamide bolaamphiphile octaacetates $\mathbf{8_n}$ and $\mathbf{9_n}$ were obtained by condensation of an α,ω-dicarboxylic acid dichloride $\mathbf{7_n}$ with **5** or **6**. The *O*-acetyl β-1-aldopyranosylamines **5** and **6** easily undergo self-condensation to afford the secondary amines **10** and **11**, respectively.[17] Therefore, the 1-aldopyranosylamine has to be used for the subsequent amide coupling reaction without isolation. The yields from the coupling reaction between **5** and $\mathbf{7_n}$, and **6** and $\mathbf{7_n}$ are listed in Table 1. The difference in the sugar moieties and the length of the hydrocarbon link have little influence on the coupling yields (41–65%). Stereochemical purities were checked by ^{1}H NMR. The vicinal $J_{1,2}$ coupling constants of each anomeric proton for the octaacetylated bolaamphiphiles $\mathbf{8_n}$ and $\mathbf{9_n}$ are also summarized in Table 1. The magnitude of the coupling constants $J_{1,2}$ indicates the existence of 100% β-configuration for all the bolaamphiphiles. The acetylated crude products were easily purified using column chromatography. The acetyl groups of $\mathbf{8_n}$ and $\mathbf{9_n}$ can be quantitatively deprotected with methanol containing a catalytic amount of sodium methoxide. The deacetylated bolaamphiphiles $\mathbf{1_n}$ and $\mathbf{2_n}$ precipitated during the



Scheme 2

deacetylation. The reaction mixture was then neutralized by treatment with an ion-exchange resin (H^+ form). The final products were purified using column chromatography. Evaporation of the solvent yielded a white powder. The final stereochemical purities and the structural identification were checked by ^1H NMR spectroscopy. The chromatographic purities were checked by thin-layer chromatography on silica gel plates and MALD-TOFMS using sinapinic acid as a matrix. All the intermediates and final products gave satisfactory elemental analysis as shown in the

Table 1. Yields for the preparation of $\mathbf{8_n}$ and $\mathbf{9_n}$, and ^{1}H NMR coupling constants of their anomeric protons ($J_{1,2}$).

Acetylated bolaamphiphiles	Yield (%)	$J_{1,2}$ (Hz)[a]
$\mathbf{8_6}$	52	9.6
$\mathbf{8_9}$	53	9.6
$\mathbf{8_{10}}$	60	9.6
$\mathbf{8_{11}}$	49	9.6
$\mathbf{8_{12}}$	52	9.6
$\mathbf{8_{13}}$	45	9.6
$\mathbf{8_{14}}$	54	9.6
$\mathbf{8_{18}}$	41	9.6
$\mathbf{9_{10}}$	65	9.2
$\mathbf{9_{11}}$	57	9.2
$\mathbf{9_{12}}$	60	9.2

a. The coupling constants were calculated from ^{1}H NMR spectra of $\mathbf{8_n}$ and $\mathbf{9_n}$ in $CDCl_3$ at 22 °C.

experimental part. The magnitude of coupling constants ($J_{1,2}$) of the anomeric proton and X-ray single crystal analyses revealed that the β-configuration was retained in the deacetylated bolaamphiphiles $\mathbf{1_n}$ and $\mathbf{2_n}$.[8–10]

In contrast to this acid chloride method, the use of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) and 1-hydroxybenzotriazole (HOBt) as a coupling reagent gave low yields (22% for $\mathbf{8_{10}}$ and 19% for $\mathbf{8_{11}}$) in *N*-glycosidic bond formation. These low yields are ascribable to the self-condensation of the aldopyranosylamine. Direct coupling of unprotected aldopyranosylamines with long-chain fatty-acid derivatives is known to afford sugar surfactants.[18–20] However, this methodology is not common and only applicable to limited sugars. In addition, the unprotected aldopyranosylamines[16] are unstable and purification of the unprotected surfactants is difficult. In general the preparation and isolation of the unprotected aldosylamine require careful treatment owing to its browning-[21] and Lobry de Bruyn–

van Ekenstein reactions[22] in acidic and basic conditions. We were not able to obtain the target bolaamphiphiles via this direct-coupling method. Purification of the crude bolaamphiphiles using a silica gel column and gel permeation chromatography was unsuccessful due to the formation of many by-products. In contrast, the use of protected aldopyranosylamines[16] will be favorable for the preparation of additional sugar-based bolaamphiphiles with a β-*N*-glycosidic bond.

CONCLUSIONS

1-Glucosamide and 1-galactosamide bolaamphiphiles have been efficiently synthesized in three steps from conventionally protected β-glycosyl azides.

EXPERIMENTAL

General methods and materials. ^{1}H NMR spectra were recorded on a JEOL GSX-270 (270 MHz) spectrometer unless otherwise specified. All the protons were assigned by two-dimensional ^{1}H NMR spectroscopy (^{1}H-^{1}H COSY). MALD-TOFMS spectra were recorded on a Shimadzu/KRATOS KOMPACT MALDI-III with sinapinic acid as a matrix. Preparative column chromatography was performed using silica gel (Silica gel 60, Merck). The chromatographic purities of the intermediates were monitored by TLC (Kiesel gel 60 F254, Merck). Compounds were visualized by spraying the plates with 5% sulfuric acid in methanol and by charring them on a hot plate.

2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl azide (3). A commercially available 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (10.0 g, 24.3 mmol) was mixed with sodium azide (15.8 g, 243 mmol) in DMF (250 mL) at room temperature. This solution was stirred for 24 h. The reaction mixture was poured into water (500 mL) and extracted with dichloromethane (200 mL) three times. The combined extracts were dried (Na_2SO_4) and concentrated, giving a solid, which was recrystallized from 2-propanol. The azide derivative **3** was obtained (7.44 g, 82.0%) as white needle crystals: mp 131.8–135 °C; R_f = 0.50 (chloroform/methanol = 95:5, *v/v*); $[\alpha]_D$ -37.4° (*c* 1.0, methanol); ^{1}H NMR ($CDCl_3$, 22 °C) δ 5.23 (t, J = 9.2 and 8.9 Hz, 1H, H-3), 5.11 (t, J = 9.6 and 9.2 Hz, 1H, H-4), 4.97 (t, J = 9.9 and 9.6 Hz, 1H, H-4), 4.66 (d, J = 8.9 Hz, 1H, H-1), 4.28 (dd, J = 12.5 and 4.6 Hz, 1H, H-6a), 2.17, 2.10, 2.07 and 1.99 (s, 12H, CH_3-CO).

Anal. Calcd for $C_{14}H_{19}N_3O_9$: C, 45.04; H, 5.13; N, 11.26. Found: C, 45.44; H, 5.11; N, 11.16.

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl azide (4). The synthetic procedure was the same as that for **3**: Yield 58.4%, white prismatic crystals; mp 90.9 °C; R_f = 0.63 (chloroform/methanol = 95:5, *v/v*); $[\alpha]_D$ -13.8° (*c* 1.0, methanol); ^{1}H NMR ($CDCl_3$, 22 °C) δ 5.43 (dd, J = 1.0 and 3.3 Hz, 1H, H-4), 5.17 (dd, J = 8.6 and 10.2 Hz, 1H, H-2), 5.04 (dd, J = 3.3 and 10.2 Hz, 1H, H-3), 4.61 (d, J = 8.6 Hz, 1H, H-1), 4.19 (dd, J = 6.9 and 12.3 Hz, 1H, H-6a), 4.14 (dd, J = 6.3 and 12.3 Hz, 1H, H-6b), 4.02 (ddd, J = 6.9, 6.3 and 1.0 Hz, 1H, H-5), 2.18, 2.10, 2.07 and 1.99 (s, 12H, CH_3-CO).

Anal. Calcd for $C_{14}H_{19}N_3O_9 \cdot$ 1/10 *i*-PrOH: C, 45.28; H, 5.26; N, 11.08. Found: C, 45.36; H, 5.08; N, 10.90.

General synthetic method for α,ω-dicarboxylic acid dichlorides (7_n). A mixture of octanedioic acid (0.174 g, 1 mmol), thionyl chloride (0.475 g, 4 mmol) and DMF (1 drop) was refluxed for 2 h. The residual thionyl chloride was removed *in vacuo*. The resulting diacid dichloride 7_6 was directly used for the coupling reaction without further purification.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)hexane-1,6-dicarboxamide (8_6).** Platinum (IV) oxide (90.8 mg, 0.4 mmol) was added to a solution of the azide **3** (0.523 g, 2.0 mmol) in methanol (130 mL) under a nitrogen atmosphere. Hydrogen was introduced to the solution for 3 h. After filtration and evaporation of methanol, the residue was dissolved in DMF (20 mL) containing pyridine (0.198 g, 2.5 mmol). To the mixture was added a dichloromethane (5 mL) solution of 7_6 (0.190 g, 0.90 mmol) at -10 °C. The reaction mixture was stirred at -10 °C for 1 h and at 20 °C for 20 h. The solvent was removed under reduced pressure. To the residue was added chloroform (200 mL) and the organic layer was washed with 5% sodium hydrogen carbonate aqueous solution (100 mL), 5% citric acid (100 mL) and water (100 mL). The organic layer was separated, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was subjected to column chromatography. Elution with a chloroform/methanol mixture (1% methanol in chloroform to 8% methanol in chloroform) gave octaacetylated bolaamphiphile 8_6, which was recrystallized from ethyl acetate/hexane to afford needle crystals (0.390 g, 52%): mp 181.5 °C; R_f = 0.64 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.53 (d, J = 9.6 Hz, 2H, N-H), 5.31 (t, J = 9.6 and 9.2 Hz, 2H, H-3), 5.28 (dd, J = 9.6Hz, 2H, H-1), 5.06 (t, J = 10.2

and 9.2 Hz, 2H, H-4), 4.93 (dd, J = 9.6 Hz, 2H, H-2), 4.31 (dd, J = 12.5 and 4.3 Hz, 2H, H-6a), 4.09 (dd, J = 12.5 and 2.0 Hz, 2H, H-6b), 3.84 (ddd, J = 10.2, 4.3 and 2.0 Hz, 2H, H-5), 2.18 (m, 4H, CH_2-CONH), 2.08, 2.04, 2.03 and 2.02 (s, 6H, CH_3-CO), 1.59 (m, 4H, -CH_2-CH_2-CONH), 1.29 (m, 4H, -CH_2-).

Anal. Calcd for $C_{36}H_{52}N_2O_{20}$: C, 51.92; H, 6.29; N, 3.36. Found: C, 51.98; H, 6.27; N, 3.47.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)nonane-1,9-dicarboxamide (8_9).** The purified substance 8_6 can undergo gelation in ethyl acetate/hexane. Filtration with suction and drying of the gel gave a xerogel. Yield 53%, as a xerogel; mp 163.7 °C; R_f = 0.71 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.27 (d, J = 9.6 Hz, 2H, N-H), 1.26 (m, 10H, -CH_2-); otherwise similar data as for 8_6.

Anal. Calcd for $C_{39}H_{58}N_2O_{20}$: C, 53.54; H, 6.68; N, 3.20. Found: C, 53.95; H, 6.65; N, 3.44.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)decane-1,10-dicarboxamide (8_{10}).** Yield 60%, as a xerogel; mp 156.8 °C; R_f = 0.67 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.23 (d, J = 9.2 Hz, 2H, N-H), 1.25 (m, 12H, -CH_2-); otherwise similar data as for 8_6.

Anal. Calcd for $C_{40}H_{60}N_2O_{20}$: C, 54.05; H, 6.80; N, 3.15. Found: C, 54.19; H, 6.76; N, 3.09.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)undecane-1,11-dicarboxamide (8_{11}).** Yield 49%, as a xerogel; mp 149.0 °C; R_f = 0.69 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 20 °C) δ 6.23 (d, J = 9.2 Hz, 2H, N-H), 1.25 (m, 14H, -CH_2-); otherwise similar data as for 8_6.

Anal. Calcd for $C_{41}H_{62}N_2O_{20}$: C, 54.54; H, 6.92; N, 3.10. Found: C, 54.49; H, 6.89; N, 3.18.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dodecane-1,12-dicarboxamide (8_{12}).** Yield 52%, as a xerogel; mp 100.6–106.9 °C;[23] R_f = 0.67 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.21 (d, J = 9.2 Hz, 2H, N-H), 1.24 (m, 16H, -CH_2-); otherwise similar data as for 8_6.

Anal. Calcd for $C_{42}H_{64}N_2O_{20}$: C, 55.01; H, 7.03; N, 3.05. Found: C, 54.70; H, 6.95; N, 2.97.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)tridecane-1,13-dicarboxamide (8_{13}).** Yield 45%, as a xerogel; mp 84.0–93.0 °C;[23] R_f = 0.71 (chloro-

form/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.21 (d, J = 9.2 Hz, 2H, N-H), 1.24 (m, 18H, -CH_2-); otherwise similar data as for **8_6**.

Anal. Calcd for $C_{43}H_{66}N_2O_{20}$: C, 55.98; H, 7.15; N, 3.01. Found: C, 56.15; H, 7.28; N, 2.91.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)tetradecane-1,14-dicarboxamide (8_{14}).** Yield 55%, as a xerogel; mp 98.9–103.9 °C[23]; R_f = 0.76 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.20 (d, J = 9.6 Hz, 2H, N-H), 1.24 (m, 20H, -CH_2-); otherwise similar data as for **8_6**.

Anal. Calcd for $C_{44}H_{68}N_2O_{20}$: C, 55.92; H, 7.25; N, 2.96. Found: C, 55.85; H, 7.23; N, 2.89.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)octadecane-1,18-dicarboxamide (8_{18}).** Yield 41%, as a xerogel; mp 128.1–132.0 °C[23]; R_f = 0.76 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.20 (d, J = 9.6 Hz, 2H, N-H), 1.24 (m, 20H, -CH_2-); otherwise similar data as for **8_6**.

Anal. Calcd for $C_{48}H_{76}N_2O_{20}$: C, 57.59; H, 7.65; N, 2.80. Found: C, 57.61; H, 7.63; N, 2.74.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)decane-1,10-dicarboxamide (9_{10}).** Yield 65%, as an amorphous solid; R_f = 0.35 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.28 (d, J = 9.2 Hz, 2H, N-H), 5.44 (dd, J = 2.0 and 0.9 Hz, 2H, H-4), 5.25 (t, J = 9.2 Hz, 2H, H-1), 5.14 (dd, J = 9.6 and 2.0 Hz, 2H, H-3), 5.10 (dd, J = 9.6 and 9.2 Hz, 2H, H-2), 4.13 (dd, J =10.7 and 7.3 Hz, 2H, H-6a), 4.07 (dd, J = 10.7 and 5.7 Hz, 2H, H-6b), 4.03 (ddd, J = 7.3, 5.7 and 0.9 Hz, 2H, H-5), 2.16 (m, 4H, -*CH_2*-CONH), 2.15, 2.05, 2.04 and 2.00 (s, 24H, *CH_3*-CO), 1.58 (m, 4H, -*CH_2*-CH_2-CONH), 1.26(m, 12H, -CH_2-).

Anal. Calcd for $C_{40}H_{60}N_2O_{20}$: C, 54.05; H, 6.80; N, 3.15. Found: C, 53.80; H, 6.80; N, 3.05.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)undecane-1,11-dicarboxamide (9_{11}).** Yield 57%, as an amorphous solid; R_f = 0.35 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22 °C) δ 6.20 (d, J = 9.2 Hz, 2H, N-H), 1.26(m, 14H, -CH_2-); otherwise similar data as for **9_{10}**.

Anal. Calcd for $C_{41}H_{62}N_2O_{20}\cdot 1/2H_2O$: C, 54.00; H, 6.96; N, 3.07. Found: C, 54.04; H, 6.87; N, 2.98.

***N,N'*-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)dodecane-1,12-dicarboxamide (9_{12}).** Yield 60%, as an amorphous solid; R_f = 0.33 (chloroform/methanol = 95:5, *v/v*); ^{1}H NMR ($CDCl_3$, 22°C) δ 6.29 (d, J = 9.2 Hz, 2H, N-H), 1.26 (m, 16H, -CH_2-); otherwise similar data as for 8_6.

Anal. Calcd for $C_{42}H_{64}N_2O_{20}\cdot 1/2H_2O$: C, 54.48; H, 7.08; N, 3.03. Found: C, 54.58; H, 7.07; N, 2.94.

***N,N'*-Bis(β-D-glucopyranosyl)hexane-1,6-dicarboxamide (1_6).** The octaacetylated bolaamphiphile 8_6 (4 mmol) in methanol (16 mL) was treated with 0.05 M sodium methoxide (0.4 mL) at room temperature for 5 h with monitoring by TLC. The reaction mixture was neutralized with ion-exchange resin (Amberlite IR-120, H^+ form), filtered and concentrated. The resulting crude bolaamphiphile was purified using silica gel column chromatography (eluent: chloroform/methanol/water = 64:31:5, *v/v*). The final products were obtained by concentration of the aqueous solution and drying the residue at room temperature at 5 mm Hg for 12 h to give needle crystals (1.95 g, 98%): mp 219.6 °C; R_f = 0.17 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (D_2O, 23 °C) δ 4.80 (d, J = 9.2 Hz, 2H, H-1), 3.72 (dd, J = 11.9 and 2.0 Hz, 2H, H-6b), 3.57 (dd, J = 11.9 and 5.2 Hz, 2H, H-6a), 3.39 (dd, J = 9.3 and 9.1 Hz, 2H, H-3), 3.37 (m, J = 8.8, 5.2, and 2.0 Hz, 2 Hz, 2H, H-5), 3.26 (dd, J = 9.3 and 8.8 Hz, 2H, H-4), 3.22 (dd, J = 9.1 and 9.1 Hz, 2H, H-2), 2.17 (t, J = 7.3 and 7.3 Hz, 4H, -*CH*$_2$-CONH-), 1.47 (m, 4H, -*CH*$_2$-CH_2-CONH), 1.20 (m, 4H, -CH_2-).

Anal. Calcd for $C_{20}H_{36}N_2O_{12}\cdot 5/3H_2O$: C, 45.62; H, 7.53; N, 5.32. Found: C, 45.55; H, 7.48; N, 5.21.

***N,N'*-Bis(β-D-glucopyranosyl)nonane-1,9-dicarboxamide (1_9).** Crystalline powder; yield 95%; mp 213.1 °C; R_f = 0.26 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (D_2O, 24 °C) δ 4.95 (d, J = 9.1 Hz, 2H, H-1), 3.88 (dd, J = 11.9 and 2.0 Hz, 2H, H-6b), 3.72 (dd, J = 11.9 and 5.2 Hz, 2H, H-6a), 3.55 (dd, J = 9.3 and 9.1 Hz, 2H, H-3), 3.50 (m, J = 8.8, 5.2, and 2.0 Hz, 2 Hz, 2H, H-5), 3.42 (dd, J = 9.3 and 8.8 Hz, 2H, H-4), 3.40 (dd, J = 9.1 and 9.1 Hz, 2H, H-2), 2.32 (t, J = 7.3 and 7.4 Hz, 4H, -*CH*$_2$-CONH-), 1.61 (m, 4H, -*CH*$_2$-CH_2-CONH), 1.30 (m, 10H, -CH_2-).

Anal. Calcd for $C_{23}H_{42}N_2O_{12}\cdot 2/3H_2O$: C, 50.17; H, 7.93; N, 5.09. Found: C, 50.41; H, 7.96; N, 4.80.

***N,N'*-Bis(β-D-glucopyranosyl)decane-1,10-dicarboxamide (1_{10}).** Xerogel; yield 92%; mp 219.6 °C; R_f = 0.29 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR

(D_2O, 24 °C) δ 4.95 (d, J = 9.1 Hz, 2H, H-1), 3.91 (dd, J = 11.9 and 2.0 Hz, 2H, H-6b), 3.86 (dd, J = 11.9 and 5.2 Hz, 2H, H-6a), 3.55 (dd, J = 9.3 and 9.1 Hz, 2H, H-3), 3.50 (m, J = 8.8, 5.2, and 2.0 Hz, 2Hz, 2H, H-5), 3.42 (dd, J = 9.3 and 8.8 Hz, 2H, H-4), 3.39 (dd, J = 9.1 and 9.1 Hz, 2H, H-2), 2.32 (t, J = 7.6 and 7.3 Hz, 4H, -*CH*$_2$-CONH-), 1.61 (m, 4H, -*CH*$_2$-CH_2-CONH), 1.30 (m, 12H, -CH_2-).

Anal. Calcd for $C_{24}H_{44}N_2O_{12}\cdot 3H_2O$: C, 47.52; H, 8.31; N, 4.62. Found: C, 47.56; H, 8.10; N, 4.56.

***N,N'*-Bis(β-D-glucopyranosyl)undecane-1,11-dicarboxamide (1_{11}).** Platelet crystals; yield 95%; mp 220.4 °C; R_f = 0.29 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (300MHz, D_2O, 25 °C) δ 4.96 (d, J = 9.1 Hz, 2H, H-1), 3.89 (dd, J = 12.2 and 2.0 Hz, 2H, H-6b), 3.73 (dd, J = 12.2 and 5.2 Hz, 2H, H-6a), 3.55 (dd, J = 9.2 and 9.1 Hz, 2H, H-3), 3.52 (m, J = 9.3, 5.2, and 2.0 Hz, 2Hz, 2H, H-5), 3.42 (dd, J = 9.3 and 9.2 Hz, 2H, H-4), 3.39 (dd, J = 9.1 and 9.1 Hz, 2H, H-2), 2.33 (t, J = 7.8 and 6.9 Hz, 4H, -*CH*$_2$-CONH-), 1.62 (m, 4H, -*CH*$_2$-CH_2-CONH), 1.29 (m, 14H, -CH_2-).

Anal. Calcd for $C_{25}H_{46}N_2O_{12}$: C, 52.99; H, 8.18; N, 4.94. Found: C, 53. 04; H, 8.20; N, 4.89.

***N,N'*-Bis(β-D-glucopyranosyl)dodecane-1,12-dicarboxamide (1_{12}).** Fibrous crystals; yield 98%; mp 219.2 °C; R_f = 0.32 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (D_2O, 80 °C) δ 4.95 (d, J = 8.9 Hz, 2H, H-1), 3.88 (dd, J = 12.2 and 2.3 Hz, 2H, H-6b), 3.72 (dd, J = 12.2 and 5.0 Hz, 2H, H-6a), 3.56 (dd, J = 9.2 and 8.9 Hz, 2H, H-3), 3.52 (m, J = 9.6, 5.0, and 2.3 Hz, 2Hz, 2H, H-5), 3.42 (dd, J = 9.6 and 8.9 Hz, 2H, H-4), 3.39 (dd, J = 9.2 and 8.9 Hz, 2H, H-2), 2.32 (t, J = 7.6 and 7.3 Hz, 4H, -*CH*$_2$-CONH-), 1.61 (m, 4H, -*CH*$_2$-CH_2-CONH), 1.29 (m, 16H, -CH_2-).

Anal. Calcd for $C_{26}H_{48}N_2O_{12}$: C, 53.78; H, 8.33; N, 4.82. Found: C, 53.90; H, 8.33; N, 4.77.

***N,N'*-Bis(β-D-glucopyranosyl)tridecane-1,13-dicarboxamide (1_{13}).** Crystalline powder; yield 95%; mp 225.7 °C; R_f = 0.34 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (D_2O, 80 °C) δ 4.95 (d, J = 9.1 Hz, 2H, H-1), 3.88 (dd, J = 11.9 and 2.0 Hz, 2H, H-6b), 3.72 (dd, J = 11.9 and 5.2 Hz, 2H, H-6a), 3.55 (dd, J = 9.3 and 9.1 Hz, 2H, H-3), 3.50 (m, J = 8.8, 5.2, and 2.0 Hz, 2Hz, 2H, H-5), 3.42 (dd, J = 9.3 and 8.8 Hz, 2H, H-4), 3.40 (dd, J = 9.1 and 9.1 Hz, 2H, H-2), 2.32 (t, J = 7.3 and 7.4 Hz, 4H, -*CH*$_2$-CONH-), 1.61 (m, 18H, -*CH*$_2$-CH_2-CONH), 1.30(m, 4H, -CH_2-).

Anal. Calcd for $C_{27}H_{50}N_2O_{12}\cdot 2/3H_2O$: C, 53.45; H, 8.53; N, 4.62. Found: C, 53.32; H, 8.33; N, 4.55.

***N,N'*-Bis(β-D-glucopyranosyl)tetradecane-1,14-dicarboxamide (1_{14}).** Platelet crystals; yield 97%; mp 225.7 °C; R_f = 0.38 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (DMSO-d_6 and D_2O one drop, 60 °C) δ 4.71 (d, J =8.9 Hz, 2H, H-1), 3.64 (dd, J = 11.9 and 2.0 Hz, 2H, H-6b), 3.43 (dd, J = 11.9 and 5.0 Hz, 2H, H-6a), 3.21 (dd, J = 8.6 and 8.2 Hz, 2H, H-3), 3.14 (m, J = 8.9, 5.0, and 2.0 Hz, 2Hz, 2H, H-5), 3.10 (dd, J = 8.9 and 8.2 Hz, 2H, H-4), 3.08 (dd, J = 8.9 and 8.6 Hz, 2H, H-2), 2.10 (t, J = 7.6 and 7.3 Hz, 4H, -CH_2-CONH-), 1.50 (m, 4H, -CH_2-CH_2-CONH), 1.25 (m, 20H, -CH_2-).

Anal. Calcd for $C_{28}H_{52}N_2O_{12}$: C, 55.25; H, 8.61; N, 4.60. Found: C, 55.15; H, 8.57; N, 4.56.

***N,N'*-Bis(β-D-glucopyranosyl)octadecane-1,18-dicarboxamide (1_{18}).** Crystalline powder; yield 100%; mp 220.8–222.8 °C; R_f = 0.45 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (DMSO-d_6 and D_2O one drop, 60 °C) δ 1.25 (m, 20H, -CH_2-); otherwise similar data as for $\mathbf{1_{14}}$.

Anal. Calcd for $C_{32}H_{60}N_2O_{12}$: C, 57.81; H, 9.10; N, 4.21. Found: C, 57.90; H, 9.08; N, 4.14.

***N,N'*-Bis(β-D-galactopyranosyl)decane-1,10-dicarboxamide (2_{10}).** Needle crystals; yield 92%; mp 213.7–215.0 °C; R_f = 0.18 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (D_2O, 50 °C) δ 4.91 (d, J = 8.6 Hz, 2H, H-1), 3.99 (dd, J = 3.0 and 0.9 Hz, 2H, H-4), 3.76—3.71 (m, 6H, H-6a, b and H-5), 3.71 (dd, J =9.9 and 3.0 Hz, 2H, H-3), 3.64 (dd, J = 9.9 and 8.6 Hz, 2H, H-2), 2.33 (t, J = 7.6 and 7.3 Hz, 4H, -CH_2-CONH-), 1.62 (m, 4H, -CH_2-CH_2-CONH), 1.30 (m, 12H, -CH_2-).

Anal. Calcd for $C_{24}H_{44}N_2O_{12}\cdot H_2O$: C, 49.48; H, 8.18; N, 4.81. Found: C, 49.32; H, 8.02; N, 4.72.

***N,N'*-Bis(β-D-galactopyranosyl)undecane-1,11-dicarboxamide (2_{11}).** Crystalline powder; yield 94%; mp 202.1–206.5 °C; R_f = 0.38 (chloroform/methanol/water = 64:31:5, *v/v*); ^{1}H NMR (D_2O, 50 °C) δ 1.30 (m, 14H, -CH_2-); otherwise similar data as for $\mathbf{2_{10}}$.

Anal. Calcd for $C_{25}H_{46}N_2O_{12}\cdot 4/3H_2O$: C, 50.84; H, 8.30; N, 4.74. Found: C, 51.01; H, 8.28; N, 4.52.

***N,N'*-Bis(β-D-galactopyranosyl)dodecane-1,12-dicarboxamide (2_{12}).** Needle crystals; yield 91%; mp 194.9–200.0 °C; R_f = 0.25 (chloroform/methanol/water =

64:31:5, *v/v*); ^{1}H NMR (D_2O, 50 °C) δ1.30 (m, 12H, -CH_2-); otherwise similar data as for **2_{10}**.

Anal. Calcd for $C_{26}H_{48}N_2O_{12}\cdot 4/3H_2O$: C, 51.64; H, 8.45; N, 4.63. Found: C, 51.67; H, 8.34; N, 4.56.

REFERENCES AND NOTES

1. Y. Okahata and T. Kunitake, *J. Am. Chem. Soc.*, **101**, 5231 (1979).
2. J. -H. Fuhrhop and D. Fritsch, *Acc. Chem. Res.*, **19**, 130 (1986).
3. G. R. Newkome, G. R. Baker, S. Arai, M. J. Saunders, P. S. Russo, K. J. Theriot, C. N. Moorefield, L. E. Rogers, J. E. Miller, T. R. Lieux, M. E. Murray, B. Philips and L. Pascal, *J. Am. Chem Soc.*, **112**, 8458 (1990).
4. J. -H. Fuhrhop, D. Spiroski and C. Boettcher, *J. Am. Chem. Soc.*, **115**, 1600 (1993).
5. G. H. Escamilla and G. R. Newkome, *Angew. Chem. Int. Ed. Eng.*, **33**, 1937 (1994).
6. A. M. Fahrnow, W. Saenger, D. Fritsch, P. Schnieder and J. -H. Fuhrhop, *Carbohydr. Res.*, **242**, 11 (1993).
7. T. Shimizu and M. Masuda, *J. Am. Chem. Soc.*, **119**, 2812 (1997).
8. M. Masuda and T. Shimizu, *Chem. Commun.*, 1057 (1996).
9. T. Shimizu, M. Masuda and M. Shibakami, *Chem. Lett.*, 267 (1997).
10. M. Masuda and T. Shimizu, *Carbohydr. Res.*, **302**, 139 (1997)
11. J. -H. Fuhrhop, H. H. David, J. Mathieu, U. Liman, H. -J. Winter and E. Boekema, *J. Am. Chem. Soc.*, **108**, 1785 (1986).
12. P. Stangier, V. Vill, S. Rohde, U. Jeschke and J. Thiem, *Liq. Cryst.*, **17**, 589 (1994).
13. P. Gouéth, A. Ramiz, G. Ronco, G. Mackenzie and P. Villa, *Carbohydr. Res.*, **266**, 171 (1995).
14. D. Lafont, P. Boullanger and Y. Chevalier, *J. Carbohydr. Chem.*, **14**, 533 (1995).
15. F. Micheel and A. Klemer, *Adv. Carbohydr. Chem. Biochem.*, **16**, 85 (1961).
16. H. G. Garg and R. W. Jeanloz, *Adv. Carbohydr. Chem. Biochem.*, **43**, 135 (1985).
17. B. Paul and W. Korytnyk, *Carbohydr. Res.*, **67**, 457 (1978).
18. P. Plusquellec, C. Benner-Hénaff, P. Léon-Ruaud, S. Duquenoy, M. Lefeuvre and H. Wróblewski, *J. Carbohydr. Chem.*, **13**, 737 (1994).
19. A. Lubineau, J. Augé and B. Drouillat, *Carbohydr. Res.*, **266**, 211 (1995).
20. Y. Inouye, K. Onodera, S. Kitaoka and S. Hirano, *J. Am. Chem. Soc.*, **78**, 4722 (1956).
21. G. P. Ellis, *Adv. Carbohydr. Chem.*, **14**, 565 (1959).
22. J. C. Speck, Jr. *Adv. Carbohydr. Chem.*, **13**, 63 (1958).
23. The broad melting point ranges for **8_{12}**, **8_{13}**, **8_{14}**, and **8_{18}** are ascribable to the low crystallinity which strongly depends on the alkylene chain length.