Design and Synthesis of Glycoside Inhibitors of Glioma and Melanoma Growth

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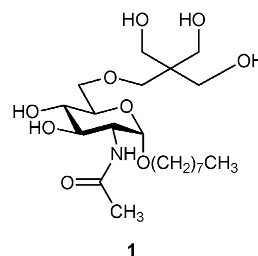
An *N*-acetylglucosaminide derivative with a pentaerythritol substituent at position C-6 was previously synthesized and shown to inhibit neural tumor growth. Now, we report the preparation of a series of new synthetic compounds introducing systematic changes in the nature, polarity, and size of the sugar substituents. The antimitotic activity of the new compounds was tested on cultured rat (C6) and human (U-373) glioma lines and on a human melanoma line (A-375). The antimitotic and antitumoral activity of the new compounds on glioma cell lines increased up to 2 orders of magnitude with respect to the parent compound or was abolished, permitting a detailed structure−function analysis of the new antitumorals. One of the glycosides inhibited melanoma division with an ID_{50} below the micromolar range.

Introduction

Glioblastoma and melanoma are two types of tumors with a high proliferative potential and poor prognosis. Only half of the patients receiving standard treatment for brain tumor in the United States survived 1 year after diagnosis.[1] Melanoma survival rate often depends on the severity of the melanoma and whether or not metastases have occurred. Brain metastases are a common feature of malignant melanoma, making the prognosis of melanoma patients exceedingly poor.[2] Therefore, the development of new drugs able to control the proliferation of glioblastoma and melanoma cells is essential for the treatment of the diseases.

We have described the presence in brain extracts of inhibitors of astroblast and astrocytoma division.[3−5] The inhibitor had glycidic epitopes immunologically related to those of the epidermal growth factor receptor and of blood groups A, H, or Lewix X.[6] On the basis of these observations we synthesized a family of oligosaccharides with Lewis X-type structure and tested their activities as inhibitors of normal and transformed neural cells division.[7] The tetrasaccharide α-D-GalNAc(1,3)-β-D-Gal(1,4)[α-L-Fuc(1,3)]-D-GlcNAc inhibited the proliferation of rat C6 glioma cells in culture and the growth of brain tumors formed after intracerebral transplantation of C6 cells.[8] From the results obtained with the oligosaccharide tested, the practical synthesis of a second generation of differently substituted mono- and disaccharides was carried out.[9,10] We showed that an octyl *N*-acetylglucosaminide with a pentaerythritol chain at position 6 (compound **1**, Chart 1) inhibited the growth of a neuroectodermic tumor implanted in rats.[10] Compound **1** inhibited the division of human glioma U-373 cells in culture, although with a modest ID_{50} value (43 ± 14 μM). We report here the synthesis of a new series of derivatives with improved antimitotic activity, by systematic modifications of the substituents at positions 1, 2, 3, and 6 of the glucosamine backbone, and their effects on inhibition of proliferation on rat (C6) and human (U-373) glioma and human melanoma (A-375).

Chart 1. Glycoside **1** Inhibited the Division of Human Glioma U-373 Cells in Culture[10]



Results and Discussion

Chemistry. By acylation of the amine group of D-glucosamine with acetic anhydride, pent-4-enoyl chloride, or oleoyl chloride, the corresponding *N*-acylglucosamines (**2**−**4**, Scheme 1) were obtained. Subsequent Fischer-type glycosidation with a variety of alcohols furnished the α-glycosides **5**−**13**.

Compounds with a pentaerythritol chain were synthesized from **10** and **11** by the sequence of reactions shown in Scheme 2. Thus, selective tritylation at HO-6 followed by benzylation at HO-3 and HO-4 and detritylation afforded alcohols **14** and **15**. Alkylation of **14** and **15** with cyclic sulfate **16** gave **17** and **18**, which were submitted to hydrogenolysis of benzyl and benzylidene groups to give sulfates **19** and **20**. Finally, acid hydrolysis of the sulfate group in **19** and **20** furnished **21** and **22**.

In a similar manner, alcohols **14** and **15** were treated with (*R*/*S*)-2,3-isopropylideneglyceryl tosylate to give **23** and **24** (Scheme 3), as a 1:1 mixture of epimers at C-2 of the glyceryl chain. After acid hydrolysis and hydrogenolysis, compounds **27** and **28** were obtained. We also worked with pure epimers **(*R*)-24** and **(*S*)-24** obtained from **(*R/S*)-24** after column chromatography, which after deprotection led to **(*R*)-28** and **(*S*)-28**. The *R* configuration at C-2 of the glyceryl chain in **(*R*)-24** could be deduced by the alkylation of **14** with the pure enantiomer (*R*)-2,3-isopropylideneglyceryl tosylate, which gave a compound identical to **(*R*)-24**.

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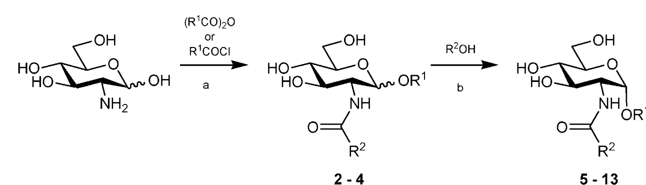
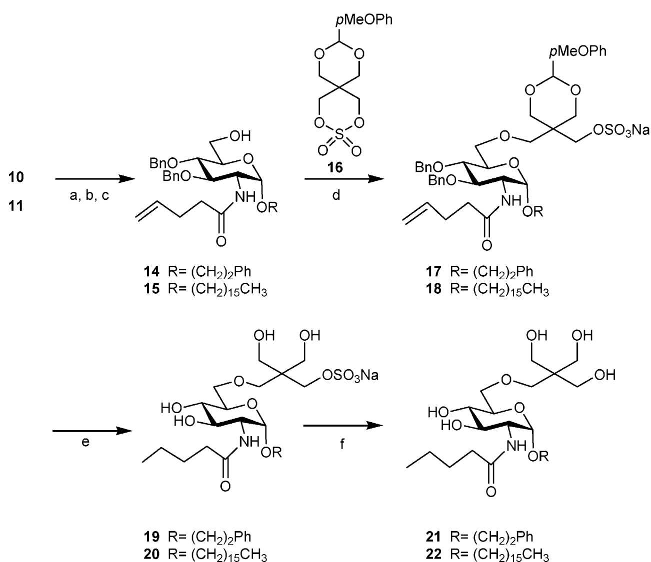
Scheme 1[a]



compound	R^1	R^2
2	H	CH_3
3	H	$(CH_2)_2CH{=}CH_2$
4	H	$(CH_2)_7CH{=}CH(CH_2)_7CH_3$
5	CH_2Ph	CH_3
6	$(CH_2)_2Ph$	CH_3
7	$(CH_2)_4Ph$	CH_3
8	$(CH_2)_7CH_3$	CH_3
9	$(CH_2)_{15}CH_3$	CH_3
10	$(CH_2)_2Ph$	$(CH_2)_2CH{=}CH_2$
11	$(CH_2)_{15}CH_3$	$(CH_2)_2CH{=}CH_2$
12	$(CH_2)_8CH{=}CH(CH_2)_7CH_3$	CH_3
13	$(CH_2)_7CH_3$	$(CH_2)_7CH{=}CH(CH_2)_7CH_3$

Reagents and conditions: (a) Na, MeOH or 1 N NaOH, (b) $BF_3{\cdot}OEt_2$, 130−165 °C.

Scheme 2[a]

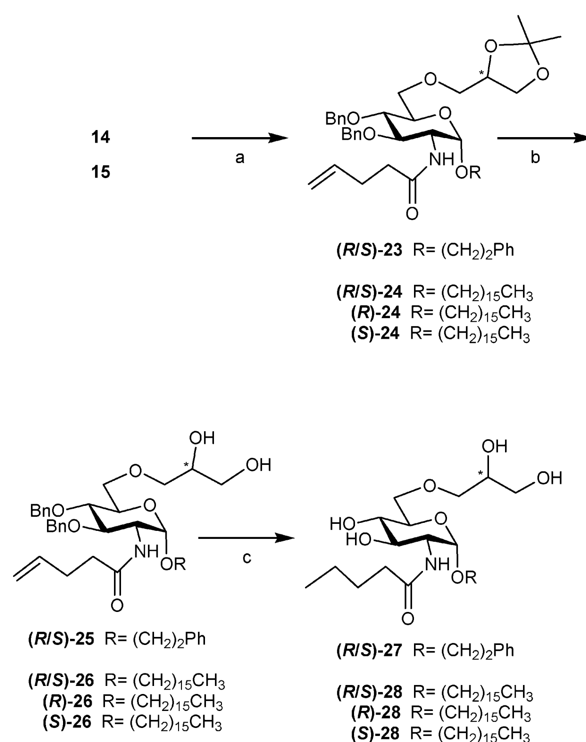


Reagents and conditions: (a) $(Ph)_3CCl$, Py, 75 °C, (b) NaH, THF, Bu_4NI, BnBr, 80 °C, (c) *p*-TsOH, 1:2 CH_2Cl_2−MeOH, rt, (d) NaH, THF−DMF, **16**, 90 °C, (e) 10% Pd/C, H_2, MeOH, (f) 1 M H_2SO_4, 3:1 dioxane−MeOH.

Modifications at C-2 were also achieved by acyl exchange at the amido group of some of the synthesized glycosides using different procedures. Thus, the treatment[11] of **8** with $Ba(OH)_2$ gave the amine, which after benzoylation afforded the benzoyl glucosamine derivative **29** (Scheme 4), although in low overall yield (45%). Alternatively, the pent-4-enoyl group in compound **26** was removed by treatment[12] with iodine to give amine **30**, which was reacted with palmitoyl chloride to give **31**, also in low overall yield (30%), which after deprotection gave **32**. Better results were obtained in the *N*-transacylation reaction[13] on **33**, previously prepared by peracetylation of **1**, by treatment with oleoyl chloride and DMAP under reflux in pyridine, affording **34** in 58% yield. Deprotection step on **34** led to **35**.

Compounds bearing a sulfate group at C-3 position were obtained as follows (Scheme 5). Glycosides **10**−**13** were treated with 2,2-dimethoxypropane to give the 4,6-*O*-isopropylidene

Scheme 3[a]



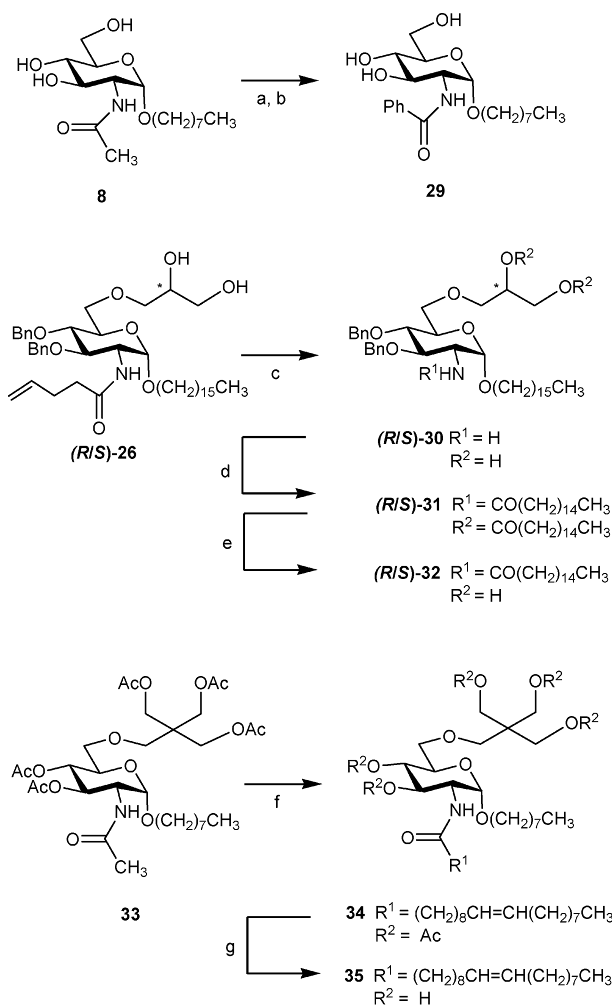
Reagents and conditions: (a) NaH, DMF, (*R*/*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethyl *p*-toluenesulfonate, 90 °C, (b) trifluoroacetic acid, MeOH, rt, (c) 10% Pd/C, H_2, MeOH.

derivatives **36**−**39**, respectively, which were reacted with SO_3−pyridine complex leading, after neutralization with KOH, to the targets **40**−**43** in excellent yields. It is worth noting that the hydrolysis of the isopropylidene group took place during the sulfation reaction probably through an intramolecular catalysis by the recently introduced bisulfate group. Similarly, compounds with a sulfate group at C-6 were synthesized by sulfation of the acetals **44**, **45**, **46**, obtained by reaction of glycosides **10**, **12**, and **13** with butane-2,3-dione. Acid hydrolysis of **47**, **48**, and **49** led to **50**, **51**, and **52**, respectively.

Biological Activity. The antimitotic activity of compounds with substitutions at positions C-1 and C-2 of the glucosamine backbone was tested on rat (C6) and human (U-373) glioma and human melanoma (A-375) in cell culture. The results, summarized in Table 1, show that compounds bearing a phenyl ring at position C-1 (**5**−**7**, **10**) or C-2 (**29**) were inactive in all cell types. Much more encouraging were the inhibition results of compounds with aliphatic chains at those positions, although their activity depended on the chain length of the substituent and the absence or presence of a double bond in the chain. Thus, the octyl glycoside **8** was inactive in all cell types, the hexadecanoyl derivative **9** was inhibitory for C6 and A-375 cell lines, and the oleyl glycoside **12** showed the best antimitotic activity of this family. Compound **13** with an *N*-oleoyl substitution at C-2 exhibited also good inhibitory activity, although with higher ID_{50} values than **12**.

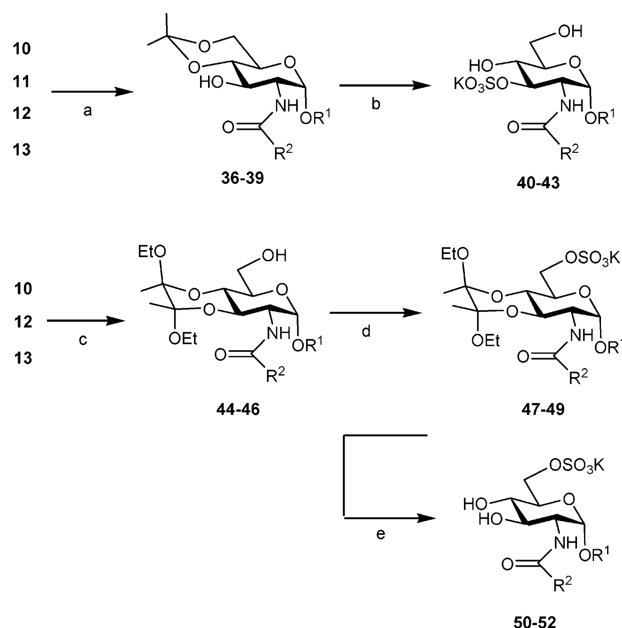
Table 2 summarizes the antimitotic activities of the glycosides substituted with a hydroxylated alkyl group at position C-6 of the sugar. As previously discussed, an alkyl group was preferred to a phenyl ring as indicated by the ID_{50} values of the related pairs of compounds **20**/**19**, **22**/**21**, and **28**/**27**. Interestingly, the presence of a sulfate group at the pentaerythritol substituent in **19** and **20** improved efficacy with respect to the nonsulfated derivatives **21** and **22**. Similarly, the compound substituted with a glyceryl chain **28** showed better antimitotic activity than the

Scheme 4[a]



Reagents and conditions: (a) $Ba(OH)_2$, 1:2 H_2O−MeOH, 90 °C, (b) benzoic anhydride, Et_3N, MeOH, rt, (c) I_2, 1:1 H_2O−THF, sodium thiosulfate, (d) palmitoyl chloride, Py, CH_2Cl_2, rt, (e) 10% Pd/C, H_2, THF, rt, (f) oleoyl chloride, Py, 4-(dimethylamino)pyridine, reflux, (g) 1 M NaOMe−MeOH, rt.

Scheme 5[a]



compound	R[1]	R[2]
10, 36, 40, 44, 47, 50	$(CH_2)_2Ph$	$(CH_2)_2CH{=}CH_2$
11, 37, 41	$(CH_2)_{15}CH_3$	$(CH_2)_2CH{=}CH_2$
12, 38, 42, 45, 48, 51	$(CH_2)_8CH{=}CH(CH_2)_7CH_3$	CH_3
13, 39, 43, 46, 49, 52	$(CH_2)_7CH_3$	$(CH_2)_7CH{=}CH(CH_2)_7CH_3$

Reagents and conditions: (a) 2,2-dimethoxypropane, *p*-TsOH, DMF, rt, (b) SO_3−pyridine complex, Py, rt, (c) butane-2,3-dione, camphorsulfonic acid, triethylorthoformate, EtOH, 60 °C, (d) SO_3−pyridine complex, Py, rt, (e) 2:1 acetic acid−H_2O, 70 °C.

parent with a pentaerythritol group **22**. The configuration of the chiral center of the glyceryl chain has little effect on the activity against U-373 and A-375 cell lines, since the epimers **(*R*)-28** or **(*S*)-28** showed similar ID_{50} values.

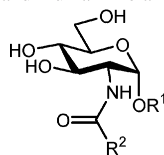
The influence of a sulfate group at position C-3 or C-6 of the pyranoid ring on the antimitotic activity was next studied (Table 3). No significant differences in efficacy were observed between the regioisomeric pairs **40**/**50**, **42**/**51**, and **43**/**52**. However, when comparing the activity of the oleyl glycoside **12** (Table 1) with the sulfated analogues **42** and **51**, it was observed that while the negatively charged group was detrimental for the antimitotic activity against C6 and U-373 glioma cells, it led to an increase in activity on A-375 melanoma cell cultures. It is worth noting that **51** was effective on the melanoma cell line at a concentration below micromolar.

Normal stromal cells derived from rat bone marrow were less sensitive to inhibition than glioma and melanoma cells after exposure to the best inhibitors, **12** and **51**. The growth of stromal cells was inhibited at slightly higher concentration of **12** ($ID_{50} = 10\ \mu M$) and at higher concentration of **51** ($ID_{50} = 40\ \mu M$) than glioma and melanoma cells (see Tables 1 and 3, respectively). Therefore, some concentration-dependent selectivity toward tumoral cells versus nontumoral cells was shown by the glycosides.

The mechanism of growth inhibition by the new compounds is still unknown. It has been recently shown that substituted aryl glycopyranosides cause selective inhibition of the DNA synthesis that precedes induction of apoptosis and growth inhibition of human glioblastoma cells.[14] However, our results show that the glycosides containing a phenyl ring were inactive against the cell lines tested. An alternative mode of action for the new glycosides to exert their effects could be by altering the biosynthesis of tumor-associated gangliosides.[15] This type of glycosphingolipid has been shown to have crucial regulatory roles in tumor onset and progression.[16] The initial step of all glucosylceramide (GlcCer)-based sphingolipids, including gangliosides, is the coupling of ceramide and glucose catalyzed by the enzyme glucosylceramide synthase. In this context, two imino-sugars substituted with an alkyl substituent[17,18] (NB-DNJ[17] and OGT-2378[18]) inhibit melanoma tumor growth by inhibiting glucosylceramide synthase, and NB-DNJ has also been proposed for brain cancer treatment.[19] The chemical structures of our compounds resemble that of GlcCer and, therefore, they could be operating by inhibiting GlcCer formation or, alternatively, by competing with GlcCer for the galactosyltransferase that synthesizes lactosylceramide. On the other hand, imino sugars derived from functionalized pyrrolidines that inhibit α-mannosidase activity have been shown to have inhibitory properties for human glioblastoma and melanoma cells.[20]

In conclusion, we have evaluated a series of new substituted *N*-acyl-α-D-glucoamininide derivatives as inhibitors of proliferation of glioma and melanoma cell lines. The results obtained indicate that the most inhibitory molecules have an oleyl group or a long alkyl chain at position C-1 of the

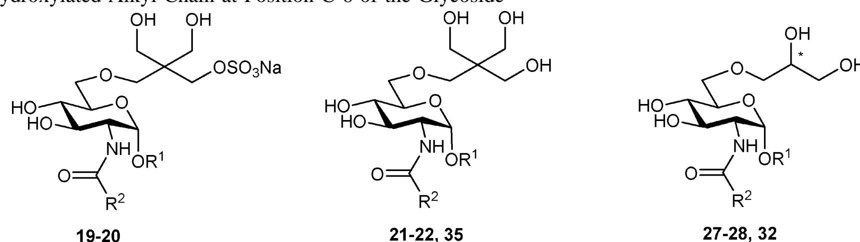
Table 1. Inhibition of Rat Glioma (C6), Human Glioma (U-373), and Human Melanoma (A-375) Cell Cultures by Compounds **5**−**13**, **29**



compd	R^1	R^2	ID_{50} (μM) C6	U-373	A-375
5	CH_2Ph	CH_3	>50	>50	>50
6	$(CH_2)_2Ph$	CH_3	>50	>50	>50
7	$(CH_2)4Ph$	CH_3	>50	>50	>50
8	$(CH_2)_7CH_3$	CH_3	>50	>50	>50
9	$(CH_2)_{15}CH_3$	CH_3	13.0 ± 3.7	>50	29.3 ± 5.2
10	$(CH_2)_2Ph$	$(CH_2)_2CH{=}CH_2$	>50	>50	>50
11	$(CH_2)_{15}CH_3$	$(CH_2)_2CH{=}CH_2$	>50	>50	>50
12	$(CH_2)_8CH{=}CH(CH_2)_7CH_3$[a]	CH_3	1.3 ± 0.8	4.6 ± 2.2	4.8 ± 2.7
13	$(CH_2)_7CH_3$	$(CH_2)_7CH{=}CH(CH_2)_7CH_3$[a]	12.0 ± 4.6	13.3 ± 4.1	6.0 ± 1.0
29	$(CH_2)_7CH_3$	Ph	>50	>50	>50

[a] The central double bond is cis-configured.

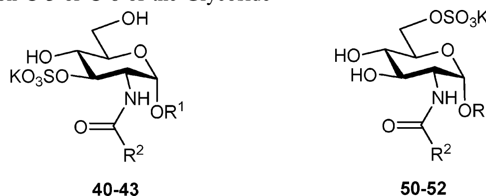
Table 2. Influence of a Hydroxylated Alkyl Chain at Position C-6 of the Glycoside



compd	R^1	R^2	ID_{50} (μM) C6	U-373	A-375
19	$(CH_2)_2Ph$	$(CH_2)_3CH_3$	8.6 ± 5.6	6.7 ± 0.7	9.3 ± 1.7
20	$(CH_2)_{15}CH_3$	$(CH_2)_3CH_3$	11.0 ± 6.0	3.2 ± 0.2	2.3 ± 0.3
21	$(CH_2)_2Ph$	$(CH_2)_3CH_3$	>50	>50	>50
22	$(CH_2)_{15}CH_3$	$(CH_2)_3CH_3$	18.3 ± 7.2	27.3 ± 3.7	17.0 ± 2.0
27	$(CH_2)_2Ph$	$(CH_2)_3CH_3$	>50	>50	>50
28	$(CH_2)_{15}CH_3$	$(CH_2)_3CH_3$	ND[a]	4.6 ± 0.3	3.0 ± 0.5
(*R*)-28	$(CH_2)_{15}CH_3$	$(CH_2)_3CH_3$	ND[a]	4.9 ± 0.6	2.2 ± 0.2
(*S*)-28	$(CH_2)_{15}CH_3$	$(CH_2)_3CH_3$	ND[a]	5.6 ± 1.7	3.4 ± 0.3
32	$(CH_2)_{15}CH_3$	$(CH_2)_{14}CH_3$	2.6 ± 1.2	3.3 ± 0.8	9.3 ± 0.6
35	$(CH_2)_7CH_3$	$(CH_2)_7CH{=}CH(CH_2)_7CH_3$[b]	11.9 ± 4.6	20.6 ± 5.2	13.3 ± 3.3

[a] ND means not determined. [b] The central double bond is cis-configured.

Table 3. Influence of a Sulfate Group at Position C-3 or C-6 of the Glycoside



compd	R^1	R^2	ID_{50} (μM) C6	U-373	A-375
40	$(CH_2)_2Ph$	$(CH_2)_2CH{=}CH_2$	>50	>50	>50
41	$(CH_2)_{15}CH_3$	$(CH_2)_2CH{=}CH_2$	22.6 ± 3.7	33.0 ± 3.5	7.2 ± 6.3
42	$(CH_2)_8CH{=}CH(CH_2)_7CH_3$[a]	CH_3	12.3 ± 0.3	9.6 ± 1.2	2.1 ± 0.6
43	$(CH_2)_7CH_3$	$(CH_2)_7CH{=}CH(CH_2)_7CH_3$[a]	5.4 ± 2.5	15.6 ± 4.3	16.0 ± 2.0
50	$(CH_2)_2Ph$	$(CH_2)_2CH{=}CH_2$	>50	>50	>50
51	$(CH_2)_8CH{=}CH(CH_2)_7CH_3$[a]	CH_3	13.0 ± 3.5	13.0 ± 3.0	0.6 ± 0.3
52	$(CH_2)_7CH_3$	$(CH_2)_7CH{=}CH(CH_2)_7CH_3$[a]	5.6 ± 1.7	12.6 ± 7.7	15.6 ± 2.8

[a] The central double bond is cis-configured.

glucosamine backbone. Additionally, the activity can be modulated, making the compounds more inhibitory on some of the cell lines tested, by introducing a hydroxylated alkyl chain or a sulfate group at position C-6. The present work has provided some compounds exhibiting ID_{50} values below micromolar concentration.

Experimental Section

Chemistry. General Methods. Chemicals were purchased puriss p.A. from commercial suppliers or purified by standard techniques. Solvents were distilled over drying agents: dimethylformamide, BaO; dichloromethane, CaH_2; tetrahydrofuran, sodium/benzophenone ketyl; acetonitrile, CaH_2; and pyridine, BaO. Thin-layer chromatography (TLC) was performed on aluminum sheets (60 F_{254} Merck silica gel) and compounds were visualized by irradiation with UV light and/or by treatment with a solution of Ce_2MoO_4 or 5% H_2SO_4 in EtOH, followed by heating. Flash column chromatography was performed using thick-walled columns, employing silica gel (Merck 60, 0.040−0.063 mm). The eluent used is indicated, and solvent ratios refer to volume. Melting points are not corrected. Optical rotations were recorded on a Perkin-Elmer 241 Polarimeter (λ = 589 nm, 1-dm cell). ^{1}H NMR spectra were registered at 400, 300, or 200 MHz, and ^{13}C NMR were obtained at 100, 75, or 50 MHz using $CDCl_3$, CD_3OD, D_2O, or DMSO as solvent at room temperature. Chemical shift values are reported in parts per million (δ). Coupling constant values (J) are reported in hertz (Hz), and spin multiplicities are indicated by the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Mass spectroscopy spectra were registered on a HP series 1100 MSD spectrometer.

2-Amino-2-deoxy-2-*N*-(pent-4-enoyl)-α,*β*-D-glucopyranose (3). To a solution of Na (1.95 g, 0.08 mmol) in methanol (40 mL) was added D-glucosamine hydrochloride (18.45 g, 85.5 mmol). The mixture was slowly stirred for 3 min and the solid was filtered off. The filtrate was treated with 4-pentenoic anhydride (15 mL, 82.1 mmol) for 3 min and the solid was filtered and washed with Et_2O−methanol (1:1) to give **3** (17.69 g, 79%).

2-Amino-2-deoxy-2-*N*-oleoyl-α,*β*-D-glucopyranose (4). Oleyl chloride was added dropwise to a cooled solution (−10 °C) of D-glucosamine hydrochloride (10 g, 50 mmol) in 1 N NaOH (51 mL). The temperature was allowed to gradually rise to room temperature with stirring for 2 h. After this time, the mixture was filtered off and the filtrate was washed with ethanol and ether. The solid was crystallized from ethanol to give **4** (15.4 g, 70%) as a solid. Mp: 159−161 °C. ^{1}H NMR (300 MHz, DMSO): δ 7.63 (d, <1H, J = 8.1 Hz), 7.48 (d, <1H, J = 7.8 Hz), 6.44 (d, <1H, J = 6.6 Hz), 6.37 (d, <1H, J = 4.6 Hz), 5.4−5.3 (m, 2H), 4.53 (dd, 1H, J = 5.4 Hz, J = 6.6 Hz), 4.41 (t, 1H, J = 5.4 Hz), 3.7−3.2 (m, 4H), 3.1−3.0 (m, 1H), 2.1−1.9 (m, 7H), 1.5−1.4 (m, 2H), 1.3−1.1 (m, 20H), 0.84 (t, 3H, J = 6.3 Hz). ^{13}C NMR (75 MHz, CD_3OD): δ 130.37, 130.33, 130.29, 91.32, 72.72, 71.90, 71.17, 61.88, 54.93,39.36, 35.98, 31.95, 29.86, 29.78, 29,51, 29.46, 29.35, 29.35, 29.27, 29.16, 27.33, 27.26, 25.99, 22.76, 14.61. MS (ES) m/z (calcd 443.3): 444.4 (M + 1).

Benzyl 2-*N*-Acetyl-2-amino-2-deoxy-α-D-glucopyanoside (5). To a mixture of **2** (752 mg, 3.39 mmol) and benzyl alcohol (2.80 mL, 27.04 mmol) was added $BF_3{\cdot}OEt_2$ (75 μL) under inert atmosphere. The mixture was stirred at 130 °C for 40 min, cooled at room temperature, and purified by column chromatography (CH_2Cl_2−methanol, 10:0→10:1) to give **5** (402 mg, 38%). $[\alpha]_D$: +203° (c 1.12, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.4−7.3 (m, 5H), 5.44 (d, 1H, J = 2.4 Hz), 4.8−4.7 (m, 2H), 4.70 (dd, 1H, J = 2.2 Hz, J = 12.2 Hz), 4.45 (dd, 1H, J = 2.4 Hz, J = 12.2 Hz), 3.9−3.8 (m, 2H), 3.7−3.6 (m, 3H), 3.4−3.3 (m, 1H), 1.90 (s, 3H). ^{13}C NMR (75 MHz, CD_3OD): δ 172.45, 137.85, 128.24, 128.09, 127.69, 96.40, 72.91, 71.55, 71.26, 69.02, 61.58, 54.26, 21.43. MS (ES) m/z (calcd 311.2): 312.2 (M + 1), 313.2 (M + 2). Anal. ($C_{15}H_{21}NO_6$) C, H, N.

Phenylethyl 2-*N*-Acetyl-2-amino-2-deoxy-α-D-glucopyranoside (6). To a mixture of **2** (500 mg, 2.26 mmol) and 2-phenylethanol (1.35 g, 22.60 mmol) was added $BF_3{\cdot}OEt_2$ (50 μL). The mixture was heated at 165 °C under Ar for 5 min, cooled at room temperature, and purified by column chromatography (CH_2Cl_2−methanol, 10:1) to give **6** (360 mg, 49%). $[\alpha]_D$: +153° (c 1.16, MeOH). ^{1}H NMR (200 MHz, CD_3OD): δ 7.3−7.2 (m, 5H), 4.74 (d, 1H, J = 3.7 Hz), 3.9−3.5 (m, 6H), 3.4−3.3 (m, 2H), 2.88 (t, 2H, J = 6.6 Hz), 1.89 (s, 3H). ^{13}C NMR (50 MHz, CD_3OD): δ 172.42, 139.27, 128.84, 128.25, 126.10, 97.28, 72.64, 71.73, 71.09, 68.47, 61.49, 54.30, 35.66, 21.56. MS (ES) m/z (calcd 325.2): 326.3 (M + 1), 327.2 (M + 2). Anal. ($C_{16}H_{23}NO_6$) C, H, N.

Phenylbutyl 2-*N*-Acetyl-2-amino-2-deoxy-α-D-glucopyranoside (7). To a mixture of **2** (500 mg, 2.26 mmol) and 4-phenyl-1-butanol (1.5 mL, 9.73 mmol) was added $BF_3{\cdot}OEt_2$ (50 μL) under Ar. The mixture was stirred at 165 °C for 10 min, cooled at room temperature, and purified by column chromatography (CH_2Cl_2−methanol, 10:1) to provide **7** (380 mg, 47%) as a white solid. Mp: 161−162 °C. $[\alpha]_D$: +135° (c 1.04, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.2−7.1 (m, 5H), 4.73 (d, 1H, J = 3.4 Hz), 3.8−3.5 (m, 6H), 3.4−3.3 (m, 2H), 2.60 (t, 2H, J = 7.3 Hz), 1.90 (s, 3H), 1.7−1.6 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD): δ 172.48, 142.49, 128.29, 128.18, 125.62, 97.29, 72.60, 71.64, 71.25, 67.59, 61.60, 54.40, 35.46, 28.95, 28.95, 28.08, 21.51. MS (ES) m/z (calcd 353.2): 354.2 (M + 1), 355.2 (M + 2). Anal. ($C_{18}H_{27}NO_6$) C, H, N.

Octyl 2-*N*-Acetyl-2-amino-2-deoxy-α-D-glucopyranoside (8). To a solution of **2** (10 g, 45.2 mmol) in nitromethane (350 mL) were added octanol (21.3 mL, 135 mmol) and $BF_3{\cdot}OEt_2$ (0.91 mL) under Ar. The mixture was heated at 100 °C for 2 h and then cooled at room temperature until a precipitate appeared. The solid was filtered off, the filtrate was concentrated, and the residue was purified by column chromatography (EtOAc−methanol, 10:1→6:1) to give **8** (3.43 g, 40%). $[\alpha]_D$: +142° (c 1.05, MeOH). ^{1}H NMR (200 MHz, CD_3OD): δ 4.74 (d, 1H, J = 3.5 Hz), 3.9−3.5 (m, 8H), 3.4−3.3 (m, 5H), 1.94 (s, 3H), 1.6−1.5 (m, 2H), 1.4−1.3 (m, 12H), 0.87 (t, 3H, J = 6.6 Hz). ^{13}C NMR (50 MHz, CD_3OD): δ 172.42, 97.27, 72.57, 71.64, 71.24, 61.58, 54.40, 48.46, 31.85, 29.37, 29.30, 29.27, 26.13, 22.55, 21.49, 13.29. MS (ES) m/z (calcd 333.2): 334.2 (M + 1), 334.2 (M + 2). Anal. ($C_{16}H_{31}NO_6$) C, H, N.

Hexadecanoyl 2-*N*-Acetyl-2-amino-2-deoxy-α-D-glucopyranoside (9). A mixture of **2** (1.0 g, 4.52 mmol) and 1-hexadecanol (5.48 g, 22.60 mmol) was heated at 160 °C under Ar and $BF_3{\cdot}OEt_2$ (100 μL) was added. The reaction was stirred at 160 °C for 15 min, cooled at room temperature, and diluted with CH_2Cl_2 (25 mL). Hexane was added, and the precipitate was collected and crystallized from Et_2O to give **9** (271.9 mg, 14%) as a white solid. Mp: 159−161 °C. $[\alpha]_D$: +108° (c 1.01, MeOH). ^{1}H NMR (200 MHz, CD_3OD): δ 4.86 (d, 1H, J = 3.5 Hz), 4.0−3.6 (m, 8H), 3.5−3.4 (m, 3H), 2.06 (s, 3H), 1.7−1.6 (m, 2H), 1.5−1.4 (m, 26H), 0.98 (t, 3H, J = 6.2 Hz). ^{13}C NMR (50 MHz, CD_3OD): δ 173.49, 98.30, 73.57, 72.66, 72.22, 68.84, 62.60, 55.41, 32.99, 30.72, 30.53, 30.48, 30.40, 27.23, 23.66, 22.61, 14.65. MS (ES) m/z (calcd 445.3): 446.5 (M + 1), 447.5 (M + 2). Anal. ($C_{24}H_{47}NO_6$) C, H, N.

Phenylethyl 2-Amino-2-deoxy-2-*N*-(pent-4-enoyl)-α-D-glucopyranoside (10). A mixture of **3** (7.5 g, 28.7 mmol), 2-phenylethanol (20.6 mL, 168 mmol), and $BF_3{\cdot}OEt_2$ (0.75 mL) was heated at 100 °C under Ar for 10 min, cooled at room temperature, and purified by column chromatography (CH_2Cl_2−methanol, 10:1) to give **10** (5.5 g, 52%). $[\alpha]_D$: +131° (c 1.05, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.3−7.1 (m, 5H), 5.8−5.7 (m, 1H), 5.0−4.9 (m, 2H), 4.70 (d, 1H, J = 3.4 Hz), 3.9−3.5 (m, 6H), 3.4−3.3 (m, 2H), 2.9−2.8 (m, 2H), 2.3−2.1 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD): δ 174.94, 139.25, 137.19, 128.33, 128.27, 126.13, 114.61, 97.38, 72.65, 71.69, 71.09, 68.59, 61.46, 54.20, 35.72, 35.10, 29.65. MS (ES) m/z (calcd 365.2): (M + 1), (M + 2). Anal. ($C_{19}H_{27}NO_6$) C, H, N.

Hexadecanoyl 2-Amino-2-deoxy-2-*N*-(pent-4-enoyl)-α-D-glucopyranoside (11). A mixture of **3** (7 g, 28.7 mmol), hexadecanol (32.47, 140 mmol), and $BF_3{\cdot}OEt_2$ (0.64 mL) was heated at 120 °C under Ar for 30 min, cooled at room temperature, and purified by column chromatography (CH_2Cl_2−methanol, 1:0→10:1) to give **11** (4.40 g, 34%) as a white solid after recrystallization from methanol. Mp: 160−166 °C. $[\alpha]_D$: +99° (c 1.03, MeOH). ^{1}H NMR (400 MHz, CD_3OD): δ 6.0−5.8 (m, 1H), 5.1−4.8 (m, 2H), 4.79 (d, 1H, J = 3.9 Hz), 3.9−3.6 (m, 4H), 3.4−3.3 (m, 4H), 2.4−2.3 (m, 4H), 1.7−1.6 (m, 2H), 1.4−1.3 (m, 26H), 0.92 (t, 3H, J = 5.9

Hz). MS (ES) *m/z* (calcd 485.3): 486.3 (M + 1). Anal. ($C_{27}H_{51}NO_6$) C, H, N.

Oleyl 2-Amino-2-*N*-acetyl-2-deoxy-α-D-glucopyranoside (12). To a mixture of **2** (1 g, 4.52 mmol) and 85% oleyl alcohol (6 mL) was added BF_3·OEt_2 (0.91 mL, 7.2 mmol). The reaction mixture was stirred at 100 °C under Ar for 2 h, cooled at room temperature, and concentrated under reduce pressure. The crude was purified by column chromatography (EtOAc−methanol, 10:0→10:1) to give **12** (200 mg, 10%). $[\alpha]_D$: +103.1° (*c* 0.95, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 5.4−5.3 (m, 2H), 4.74 (d, 1H, *J* = 3.5 Hz), 3.9−3.8 (m, 2H), 3.7−3.5 (m, 4H), 3.4−3.3 (m, 2H), 2.0−1.9 (m, 4H), 1.94 (s, 3H), 1.6−1.5 (m, 2H), 1.3−1.2 (m, 22H), 0.86 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75 MHz, CD_3OD): δ 172.41, 129.70, 129.66, 97.29, 72.55, 71.65, 71.22, 67.79, 61.56, 54.39, 32.63, 32.07, 31.92, 31.86, 31.81, 31.71, 31.62, 31.45, 31.41, 31.36, 31.30, 29.19, 28.33, 22.56, 21.49, 13.33. MS (ES) *m/z* (calcd 471.4): 472.4 (M + 1), 473.4 (M + 2). Anal. ($C_{26}H_{49}NO_6$) C, H, N.

Octyl 2-Amino-2-deoxy-2-*N*-(oleoyl)-α-D-glucopyranoside (13). To a mixture of **4** (500 mg, 1.13 mmol) and octanol (21.3 mL, 135 mmol) was added BF_3·OEt_2 (30 μL). The reaction mixture was heated at 110 °C under Ar for 5 min, cooled at room temperature, and purified by column chromatography (EtOAc−methanol, 1:0→10:1) to give **13** (308 g, 50%). $[\alpha]_D$: +85.1° (*c* 1.37, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 5.4−5.3 (m, 2H), 4.78 (d, 1H, *J* = 3.4 Hz), 3.9−3.5 (m, 5H), 3.4−3.3 (m, 3H), 2.3−2.2 (m, 2H), 2.1−2.0 (m, 4H), 1.7−1.5 (m, 4H), 1.3−1.2 (m, 30H), 0.9−0.8 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD): δ 178.61, 130.90, 130.81, 98.44, 73.78, 72.70, 72.47, 69.02, 62.78, 55.53, 37.10, 33.11, 33.10, 30.92, 30.88, 30.83, 30.67, 30.54, 30.50, 30.47, 30.39, 30.36, 30.29, 28.23, 28.20, 27.43, 27.16, 23.79, 23.70, 14.52, 14.50. MS (ES) *m/z* (calcd 555.4): 556.5 (M + 1). Anal. ($C_{32}H_{61}NO_6$) C, H, N.

Phenylethyl 2-Amino-3,4-di-*O*-benzyl-2-deoxy-2-*N*-(pent-4-enoyl)-α-D-glucopyranoside (14). A solution of **10** (1.20 g, 3.31 mmol) in pyridine (7.5 mL) was heated at 75 °C under Ar and triphenylmethyl chloride (2.77 g, 9.93 mmol) was added. The reaction mixture was stirred at this temperature for 30 min and then cooled at room temperature. Evaporation of the solvent and purification by silica gel column chromatography (EtOAc−methanol, 1:0→10:1) gave a residue (2 g) which was dissolved in anhydrous THF (18 mL) and cooled at 0 °C. Then, NaH (253 mg, 10.56 mmol) was added under Ar and the temperature was allowed to gradually rise to room temperature with stirring over 15 min. When H_2 evolution had ceased, tetrabutylamonium iodide (0.60 g, 1.62 mmol) and benzyl bromide (0.87 mL, 6.92 mmol) were added. The reaction mixture was stirred at 80 °C for 2 h and then cooled at room temperature. The excess of NaH was removed by addition of methanol (0.5 mL). Then, CH_2Cl_2 (100 mL) was added and the mixture was washed with water (40 mL × 3). The organic layer was separated, dried (Na_2SO_4), filtered, and concentrated, affording a brown crude. The crude product without purification was dissolved in a mixture of CH_2Cl_2−methanol (1:2, 40 mL), and *p*-toluenesulfonic acid (160 mg, 0.84 mmol) was added. The reaction mixture was stirred at room temperature for 3 h and then neutralized with triethylamine, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (EtOAc−hexane, 1:1) to give **14** (64%, three steps) as a white solid after recrystallization from EtOAc (minimum volume) and hexane. $[\alpha]_D$: +73.1° (*c* 1.00, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.6−7.2 (m, 15H), 5.8−5.7 (m, 1H), 4.8−4.6 (m, 2H), 5.0−4.9 (m, 5H), 4.10 (dd, 1H, *J* = 10.5 Hz, *J* = 3.9 Hz), 3.9−3.5 (m, 6H), 3.5−3.4 (m, 1H), 2.92 (t, 2H, *J* = 6.3 Hz), 2.3−2.2 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD): δ 175.32, 140.45, 140.09, 139.81, 138.27, 130.07, 129.48, 129.37, 129.33, 128.82, 128.69, 128.60, 127.35, 115.83, 98.67, 81.47, 79.57, 75.82, 75.75, 73.16, 69.66, 62.02, 54.60, 36.88, 36.35, 30.79.

Hexadecanoyl 2-Amino-3,4-di-*O*-benzyl-2-deoxy-2-*N*-(pent-4-enoyl)-α-D-glucopyranoside (15). Compound **11** was reacted under similar conditions as described for **10**, to give **15** (73%). $[\alpha]_D$: +49.9° (*c* 1.00, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.4−7.3 (m, 10H), 5.8−5.7 (m, 1H), 5.4−5.3 (m, 2H), 5.1−4.7 (m, 5H), 3.8−3.6 (m, 8H), 2.4−2.1 (m, 4H), 1.6−1.5 (m, 2H), 1.3−1.2 (m, 26H), 0.9−0.8 (t, 3H, *J* = 6.1 Hz).

Phenylethyl 2-Amino-3,4-di-*O*-benzyl-2-deoxy-6-*O*-(2-(*p*-methoxybenzilidene)-3-hydroxy-3-*O*-(oxosulfonyl)propyl)-2-*N*-(pent-4-enoyl)-α-D-glucopyranoside (17). To a solution of **14** (850 mg, 1.56 mmol) in a mixture of THF (34 mL) and DMF (3 mL) was added NaH (77 mg, 3.21 mmol) under Ar, with stirring for 10 min. When H_2 evolution had ceased, **16** (761 mg, 2.41 mmol) was added. The reaction mixture was stirred at 90 °C for 80 min and then cooled at room temperature. The excess of NaH was quenched by addition of methanol (0.5 mL), and then the solvent was removed and the residue purified by column chromatography (EtOAc−methanol, 1:0→10:1) to give **17** (1.31, 95%). $[\alpha]_D$: +61.34° (*c* 1.00, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.88 (s, 1H), 7.3−7.2 (m, 15H), 7.1−7.0 (m, 2H), 6.77 (d, 2H, *J* = 8.8 Hz), 5.8−5.6 (m, 1H), 5.2−5.1 (m, 1H), 4.9−4.5 (m, 12 H), 4.27 (s, 2H), 4.0−3.9 (m, 2H), 3.8−3.7 (m, 1H), 3.6−3.2 (m, 6H), 2.9−2.8 (m, 3H), 2.7−2.6 (m, 2H), 2.2−2.1 (m, 4H).

Phenylethyl 2-Amino-2-deoxy-6-*O*-[2,2-bis(hydroxymethyl)-3-hydroxy-3-*O*-(oxosulfonyl)propyl)]-2-*N*-penthanoyl-α-D-glucopyranoside (19). **17** (310 mg, 0.35 mmol) was dissolved in methanol (14 mL), and 10% Pd/C (150 mg) was added. The suspension was stirred under H_2 for 3 h. After this time, the solution was filtered through Celite and washed with EtOAc. Removal of the solvent gave **19** (180 mg, 87%). $[\alpha]_D$: +77° (*c* 1.39, MeOH). ^{1}H NMR (200 MHz, CD_3OD): δ 7.3−7.2 (m, 5H), 4.74 (d, 1H, *J* = 3.5 Hz), 4.1−4.4 (m, 2H), 3.9−3.8 (m, 2H), 3.6−3.3 (m, 12H), 2.89 (t, 2H, *J* = 7.1 Hz), 2.18 (t, 2H, *J* = 7.9 Hz), 1.6−1.5 (m, 2H), 1.4−1.2 (m, 2H), 0.91 (t, 3H, *J* = 7.5 Hz). ^{13}C NMR (75 MHz, CD_3OD): δ 176.80, 140.42, 130.00, 129.41, 127.27, 98.48, 72.81, 72.59, 72.10, 71.68, 71.50, 69.88, 68.15, 62.47, 62.38, 55.13, 46.57, 36.83, 36.74, 29.06, 23.31, 14.19. MS (ES) *m/z* (calcd 587.2): 605.2, 604.2. Anal. ($C_{24}H_{38}NNaO_{12}S$) C, H, N, S.

Hexadecanoyl 2-Amino-2-deoxy-6-*O*-[3-hydroxy-2,2-bis(hydroxymethyl)-3-*O*-(oxosulfonyl)propyl]-2-*N*-penthanoyl-α-D-glucopyranoside (20). Compound **15** was reacted under similar conditions as described for **14**, to give **18** (87%). **18** (550 mg, 0.55 mmol) was dissolved in a mixture of methanol−EtOAc (8:1, 45 mL), and 10% Pd/C (230 mg) was added. The suspension was then stirred under H_2 for 3 h. After this time, the solution was filtered through Celite and washed with EtOAc. Removal of the solvent and purification of the residue by column chromatography (CH_2Cl_2−methanol, 5:1) gave **20** (280 mg, 72%). $[\alpha]_D$: +78.6° (*c* 1.03, MeOH). ^{1}H NMR (200 MHz, CD_3OD): δ 4.77 (d, 1H, *J* = 3.5 Hz), 4.06 (s, 2H), 3.90 (dd, 1H, *J* = 3.5 Hz, *J* = 10.6 Hz), 3.8−3.4 (m, 11H), 2.26 (t, 2H, *J* = 7.5 Hz), 1.7−1.2 (m, 32H), 1.0−0.8 (m, 6H). MS (ES) *m/z* (calcd 707.3): 724.3, 725.3. Anal. ($C_{32}H_{62}NNaO_{12}S$) C, H, N, S.

Phenylethyl 2-*N*-Penthanoyl-2-amino-2-deoxy-6-*O*-(2,2-bis-(hydroxymethyl)-3-hydroxypropyl)-α-D-glucopyranoside (21). **19** (180 mg, 0.31 mmol) was dissolved in a mixture of dioxane−methanol (3:1, 12 mL) and a solution of 1 M H_2SO_4 (30 μL) was added. The reaction mixture was stirred for 7 h. After this time, the mixture was neutralized by addition of saturated $NaHCO_3$ solution. Removal of the solvent under reduced pressure and purification of the residue by column chromatography (CH_2Cl_2−methanol, 5:1) gave **21** (95 mg, 66%). $[\alpha]_D$: +89° (*c* 0.82, MeOH). ^{1}H NMR (400 MHz, D_2O): δ 7.2−7.1 (m, 5H), 4.74 (d, 1H, *J* = 3.5 Hz), 3.8−3.2 (m, 16H), 2.8−2.7 (t, 2H, *J* = 5.9 Hz), 2.1−2.0 (t, 2H, *J* = 7.7 Hz), 1.4−1.3 (m, 2H), 1.2−1.0 (m, 2H), 0.72 (t, 2H, *J* = 7.1 Hz). ^{13}C NMR (50 MHz, CD_3OD): δ 176.65, 140.42, 130.05 (2C), 129.47 (2C), 127.34, 98.58, 72.66 (2C), 72.40, 72.34, 71.90, 69.96, 63.20 (2C), 55.35, 46.99, 36.94, 36.77, 29.12, 23.38, 14.24. MS (ES) *m/z* (calcd 485.3): 486.3 (M + 1). Anal. ($C_{24}H_{39}NO_9$) C, H, N.

Hexadecanoyl 2-Amino-2-deoxy-2-*N*-penthanoyl-6-*O*-(2,2-bis-(hydroxymethyl)-3-hydroxypropyl)-α-D-glucopyranoside (22). **20** (147 mg, 0.21 mmol) was dissolved in a mixture of dioxane−methanol (1:1, 4 mL), and a solution of 1 M H_2SO_4 (30 μL) was added. The reaction mixture was stirred for 20 h. After this time,

the solution was neutralized by addition of saturated $NaHCO_3$ solution. Removal of the solvent and purification of the residue by column chromatography (CH_2Cl_2−methanol, 10:1→5:1) gave **22** (126 mg, 100%). $[\alpha]_D$: +108° (*c* 1.01, MeOH). ^1H NMR (200 MHz, CD_3OD): δ 4.77 (d, 1H, J = 3.5 Hz), 3.86 (dd, 1H, J = 3.5 Hz, J = 10.6 Hz), 3.8−3.3 (m, 13H), 2.24 (t, 2H, J = 7.5 Hz), 1.7−1.2 (m, 32H), 1.1−0.9 (m, 6H). MS (ES) *m/z* (calcd 605.5): 606.3 (M + 1), 607.5 (M + 2). Anal. ($C_{32}H_{63}NO_9$) C, H, N.

Phenylethyl 2-Amino-3,4-di-*O*-benzyl-2-deoxy-6-*O*-(2,2-dimethyl-1,3-dioxolan-4(*R*/*S*)-ylmethyl)-2-*N*-(pent-4-enoyl)-α-D-glucopyranoside ((*R*/*S*)-23). To a solution of **14** (100 mg, 0.18 mmol) in anhydrous DMF (1.53 mL) was added NaH (18 mg, 0.75 mmol) under Ar, with stirring for 10 min. When H_2 evolution had ceased, (*R*/*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethyl *p*-toluenesulfonate (761 mg, 2.41 mmol) was added. The reaction mixture was stirred at 90 °C for 80 min and then cooled at room temperature. The excess of NaH was quenched by addition of methanol (0.5 mL). Removal of the solvent and purification of the residue by column chromatography (EtOAc−methanol, 2:1) gave **(*R*/*S*)-23** (85 mg, 70%). ^1H NMR (300 MHz, $CDCl_3$): δ 7.4−7.2 (m, 13H), 7.2−7.1 (m, 2H), 5.8−5.7 (m, 1H), 5.0−4.6 (m, 7H), 4.4−3.9 (m, 3H), 3.8−3.4 (m, 10H), 2.9−2.8 (m, 2H), 2.2−1.9 (m, 4H), 1.58 (s, 6H).

Hexadecanoyl 2-Amino-3,4-di-*O*-benzyl-2-deoxy-6-*O*-(2,2-dimethyl-1,3-dioxolan-4(*R*/*S*)-ylmethyl)-2-*N*-(pent-4-enoyl)-α-D-glucopyranoside ((*R*/*S*)-24). To a solution of **15** (1 g, 1.50 mmol) in anhydrous DMF (12 mL) was added NaH (200 mg, 8.33 mmol), stirring under Ar for 10 min. When H_2 evolution had ceased, (*R*/*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethyl *p*-toluenesulfonate (1.3 g, 4.54 mmol) was added. The reaction mixture was stirred at 90 °C for 30 min and then cooled at room temperature. The excess of NaH was quenched by addition of methanol (0.5 mL), the solvent was removed, and the residue was purified by column chromatography (hexane−EtOAc, 3:2) to give **(*S*)-24** (160 mg), **(*R*)-24** (150 mg), and **(*R*/*S*)-24** (260 mg). ^1H NMR (200 MHz, $CDCl_3$): δ 7.3−7.1 (m, 10H), 5.8−5.7 (m, 1H), 5.4−4.5 (m, 8H), 3.5−3.3 (m, 12H), 2.3−2.1 (m, 4H), 1.6−0.9 (m, 37H).

Hexadecanoyl 2-Amino-3,4-di-*O*-benzyl-2-deoxy-6-*O*-(2(*R*/*S*),3-dihydroxypropyl)-2-*N*-(pent-4-enoyl)-α-D-glucopyranoside ((*R*/*S*)-26). To a solution of **(*R*/*S*)-24** (520 mg, 0.67 mmol) in methanol (5 mL) was added trifluoroacetic acid (7.4 μL, 0.1 mmol). The reaction mixture was stirred at room temperature for 1 h. After this time the solvent was evaporated and the residue (580 mg) was purified by column chromatography (hexane−EtOAc, 1:1→0:1) to give **(*R*/*S*)-26** (389 mg, 79%). ^1H NMR (200 MHz, CD_3OD): δ 7.5−7.3 (m, 10H), 5.9−5.8 (m, 1H), 5.2−4.7 (m, 9H), 4.3−4.2 (m, 1H), 3.9−3.4 (m, 10H), 2.5−2.3 (m, 4H), 1.7−1.3 (m, 28H), 0.92 (t, 3H, J = 6.7 Hz).

Phenylethyl 2-Amino-2-deoxy-6-*O*-(2(*R*/*S*),3-dihydroxypropyl)-2-*N*-penthanoyl-α-D-glucopyranoside ((*R*/*S*)-27). To a solution of **(*R*/*S*)-23** (82 mg, 0.12 mmol) in methanol (2 mL) was added trifluoroacetic acid (5 μL, 0.07 mmol). The reaction mixture was stirred at room temperature for 2 h. After this time, the solvent was evaporated, the residue was purified by column chromatography (hexane−EtOAc, 1:1) (78 mg) and dissolved in methanol (10 mL), and 10% Pd/C (35 mg) was added, with stirring under H_2 for 3 h. After this time, the solution was filtered through Celite and the filtrate concentrated to give **(*R*/*S*)-27** (41 mg, 74%). $[\alpha]_D$: +97.5° (*c* 1.02, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 7.4−7.1 (m, 5H), 4.77 (d, 1H, J = 3.8 Hz), 3.9−3.3 (m, 13H), 2.89 (t, 2H, J = 7.0 Hz), 2.17 (t, 2H, J = 8.1 Hz), 1.6−1.5 (m, 2H), 1.4−1.3 (m, 2H), 0.92 (t, 3H, J = 7.9 Hz). MS (ES) *m/z* (calcd 441.2): 442.3 (M + 1), 443.3 (M + 2). Anal. ($C_{22}H_{35}NO_8$) C, H, N.

Hexadecanoyl 2-Amino-2-deoxy-6-*O*-(2(*R*/*S*),3-dihydroxypropyl)-2-*N*-pentanoyl-α-D-glucopyranoside ((*R*/*S*)-28). To a solution of **(*R*/*S*)-26** (260 mg, 0.33 mmol) in methanol (18 mL) were added trifluoroacetic acid (13 μL) and 10% Pd/C (97 mg). The suspension was then stirred under H_2 for 2.5 h. After this time, the solution was filtered through Celite, and the filtrate concentrated to give **(*R*/*S*)-28** (190 mg, 100%) as a white solid. Mp: 91−97 °C. $[\alpha]_D$: +82° (*c* 1, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 4.97 (d, 1H, J = 3.7 Hz), 4.05 (dd, 1H, J = 11.0 Hz, J = 3.5 Hz), 4.0−3.8 (m, 6H), 3.8−3.5 (m, 6H), 2.44 (t, 2H, J = 6.2 Hz), 1.8−1.7 (m, 4H), 1.6−1.4 (m, 28H), 1.2−1.0 (m, 6H). MS (ES) *m/z* (calcd 561.4): 562.3 (M + 1), 563.3 (M + 2). Anal. ($C_{30}H_{59}NO_8$) C, H, N.

Compound **(*R*)-28** and **(*S*)-28** were prepared from **(*R*)-26** and **(*S*)-26**, respectively, using the same procedure as described above for the preparation of **(*R*/*S*)-28** from **(*R*/*S*)-26.**

(*S*)-Hexadecanoyl 2-Amino-2-deoxy-6-*O*-(2,3-dihydroxypropyl)-2-*N*-pentanoyl-α-D-glucopyranoside ((*S*)-28). Yield: 100%. $[\alpha]_D$: +50° (*c* 0.93, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 4.97 (d, 1H, J = 3.7 Hz), 4.05 (dd, 1H, J = 11.0 Hz, J = 3.5 Hz), 4.0−3.8 (m, 6H), 3.8−3.5 (m, 6H), 2.44 (t, 2H, J = 6.2 Hz), 1.8−1.7 (m, 4H), 1.6−1.4 (m, 28H), 1.2−1.0 (m, 6H). MS (ES) *m/z* (calcd 561.4): 562.3 (M + 1), 563.3 (M + 2). Anal. ($C_{30}H_{59}NO_8$) C, H, N.

(*R*)-Hexadecanoyl 2-Amino-2-deoxy-6-*O*-(2,3-dihydroxypropyl)-2-*N*-pentanoyl-α-D-glucopyranoside ((*R*)-28). Yield: 100%. Mp 91−97 °C. $[\alpha]_D$: +82° (*c* 1, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 4.97 (d, 1H, J = 3.7 Hz), 4.05 (dd, 1H, J = 11.0 Hz, J = 3.5 Hz), 4.0−3.8 (m, 6H), 3.8−3.5 (m, 6H), 2.44 (t, 2H, J = 6.2 Hz), 1.8−1.7 (m, 4H), 1.6−1.4 (m, 28H), 1.2−1.0 (m, 6H). MS (ES) *m/z* (calcd 561.4): 562.3 (M + 1), 563.3 (M + 2). Anal. ($C_{30}H_{59}NO_8$) C, H, N.

Octyl 2-Amino-2-*N*-benzoyl-2-deoxy-α-D-glucopyranoside (29). A solution of **8** (400 g, 1.2 mmol) in H_2O−methanol (1:2, 6 mL) was heated at 90 °C and $Ba(OH)_2$ (568 mg, 1.80 mmol) was added. The mixture was stirred at 90 °C for 37 h. After this time, it was cooled at room temperature and neutralized by bubbling CO_2 until pH 7. The mixture was filtered off and the filtrate was concentrated to provide a yellow crude product (750 mg), which was dissolved in methanol (9 mL) and treated with triethylamine (166 μL, 1.2 mmol) and benzoic anhydride (299 mg, 1.32 mmol) with stirring at room temperature for 3 h. Removal of the solvent, purification by column chromatography (CH_2Cl_2−methanol, 6:1), and crystallization from methanol gave **29** (211 mg, 45% the two steps). $[\alpha]_D$: +116° (*c* 1.09, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 7.9−7.8 (m, 2H), 7.5−7.4 (m, 3H), 4.95 (d, 1H, J = 3.4 Hz), 4.1−4.0 (m, 1H), 3.9−3.6 (m, 5H), 3.5−3.4 (m, 2H), 1.6−1.5 (m, 2H), 1.4−1.1 (m, 10 H), 0.86 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, CD_3OD): δ 170.12, 133.92, 130.70, 129.49, 129.40, 98.33, 73.78, 72.61, 72.42, 68.93, 62.77, 58.28, 32.92, 30.48, 30.37, 27.34, 27.31, 23.65, 14.42. MS (ES) *m/z* (calcd 395.2): 396.3 (M + 1), 397.2 (M + 2). Anal. ($C_{21}H_{53}NO_6$) C, H, N.

Hexadecanoyl 2-Amino-3,4-di-*O*-benzyl-2-deoxy-2-*N*-(hexadecanoyl)-6-*O*-(2(*R*/*S*),3-dihexadecanoylpropyl)-α-D-glucopyranoside ((*R*/*S*)-31). A solution of **(*R*/*S*)-26** (389 mg, 0.52 mmol) in H_2O−THF (1:1, 3.6 mL) was treated with I_2 (532 mg, 2.10 mmol), with stirring at room temperature for 15 min. After this time, sodium thiosulfate (774 mg, 3.12 mmol) was added and the mixture was concentrated. The residue was purified by column chromatography (hexane−EtOAc−methanol, 1:3:0→0:1:0→0:10:1) (202 mg), dissolved in anhydrous CH_2Cl_2 (3 mL), and treated with anhydrous pyridine (25 μL, 0.30 mmol) and palmitoyl chloride (190 μL, 0.60 mmol). The mixture was stirred under Ar for 1.5 h. Then, the solvent was evaporated and the residue (360 mg) was purified by column chromatography (hexane−EtOAc 2:1) to give **(*R*/*S*)-31** (193 mg, 30%). ^1H NMR (200 MHz, $CDCl_3$): δ 7.4−7.3 (m, 10H), 5.85 (d, 1H, J = 8.8 Hz), 5.30 (s, 4H), 4.77 (d, 1H, J = 4.3 Hz), 4.2−4.0 (m, 3H), 3.8−3.4 (m, 9H), 2.4−2.2 (m, 6H), 1.6−1.2 (m, 106H), 0.9−0.8 (m, 12H). MS (ES) *m/z* (calcd 1372.1): 1372.9 (M), 1373.9 (M + 1), 1374.8 (M + 2).

Hexadecanoyl 2-Amino-2-deoxy-2-*N*-(hexadecanoyl)-6-*O*-(2(*R*/*S*),3-dihydroxypropyl)-α-D-glucopyranoside ((*R*/*S*)-32). **(*R*/*S*)-31** (182 mg, 0.20 mmol) was dissolved in THF (2 mL), and 10% Pd/C (91 mg) was added. The suspension was then stirred under H_2 for 2.5 h. After this time, the mixture was filtered through Celite. Removal of the solvent afforded a residue (240 mg, 0.10 mmol) that was dissolved in 0.1 M NaOMe in methanol (10 mL), with stirring at r room temperature for 1 h. After this time the

mixture was neutralized with Amberlist (IR-120), filtered off, and concentrated. The residue was purified by column chromatography (CH_2Cl_2−methanol, 7:0→7:1) to give **(*R*/*S*)-32** (115 mg, 79%). ^1H NMR (300 MHz, CD_3OD): δ 4.63 (d, 1H, *J* = 3.7 Hz), 3.78 (dd, 1H, *J* = 4.0 Hz, *J* = 10.3 Hz), 3.7−3.6 (m, 4H), 3.5−3.2 (m, 8H), 2.1−2.0 (m, 2H), 1.5−1.4 (m, 4H), 1.2−1.0 (m, 50H), 0.7−0.6 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$−CD_3OD, 10:1): δ 128.65, 97.61, 73.15, 72.89, 72.19, 71.30, 71.13, 70.82, 70.37, 68.45, 63.52, 36.76, 32.17, 29.95, 29.82, 29.74, 29.66, 29.60, 29.50, 29.46, 26.47, 26.05, 22.91, 22.90, 11.22, 11.20. MS (ES) *m*/*z* (calcd 715.6): 716.5 (M + 1). Anal. ($C_{41}H_{81}NO_8$) C, H, N.

Octyl 2-Amino-2-deoxy-6-*O*-[2,2-bis(hydroxymethyl)-3-hydroxypropyl]-2-*N*-oleoyl-α-D-glucopyranoside (35). 1 (210.2 mg, 0.46 mmol) was dissolved in anhydrous pyridine (2 mL), and acetic anhydride (2 mL) was added. The reaction mixture was stirred at room temperature for 12 h, concentrated, and purified by column chromatography (EtOAc−hexane, 2:1) to give a white solid (313 mg), which was dissolved in anhydrous pyridine (5 mL) and treated with 85% oleyl chloride (0.47 mL, 1.40 mmol) and dimethylaminopyridine (4.5 mg, 0.03 mmol). The mixture was refluxed for 2 h, concentrated, and purified by column chromatography (hexane−EtOAc, 2:1→1:1) to give a white solid (241 mg), which was dissolved in methanol (30 mL) and treated with a solution of NaOMe in MeOH (1M, 8 mL), with stirring at room temperature for 2 h. After this time, the solution was neutralized with Amberlist (IR-120), filtered, and concentrated. The residue was purified by column chromatography (CH_2Cl_2−methanol, 10:1) to give **35** (172 mg, 54%). $[\alpha]_D$: +69.7° (*c* 0.96, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 5.4−5.3 (m, 2H), 4.78 (d, 1H, *J* = 4.0 Hz), 3.86 (dd, 1H, *J* = 4.1 Hz, *J* = 10.6 Hz), 3.7−3.3 (m, 15H), 2.23 (t, 2H, *J* = 7.0 Hz), 2.1−1.9 (m, 4H), 1.6−1.5 (m, 4H), 1.3−1.2 (m, 30H), 0.9−0.8 (m, 6H). MS (ES) *m*/*z* (calcd 673.5): 674.5 (M + 1), 675.5 (M + 2). Anal. ($C_{37}H_{71}NO_9$) C, H, N.

Phenylethyl 2-Amino-2-deoxy-2-*N*-(pen-4-enoyl)-3-*O*-(oxosulfonyl)-α-D-glucopyranoside (40). 10 (150 mg, 0.41 mmol) was dissolved in anhydrous DMF (2.5 mL) and treated with 2,2-dimethoxypropane (0.46 mL, 2.05 mmol) and *p*-toluensulphonic acid (10 mg). The mixture was stirred at room temperature for 2 h, neutralized with triethylamine, and concentrated to give a residue (166 mg) that was dissolved in anhydrous pyridine (11 mL) and then treated with the SO_3−pyridine complex (1.3 g, 8.20 mmol), with stirring at room temperature under Ar for 1.5 h. After this time, the mixture was concentrated, and the residue was dissolved in methanol−water (2:1, 5 mL), neutralized with a 0.5 M KOH solution, and concentrated. The residue was extracted with methanol, concentrated, and purified by column chromatography (CH_2Cl_2−methanol, 6:1) to give **40** (178.8 mg, 90%). $[\alpha]_D$: +82.4° (*c* 1.19, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 7.4−7.1 (m, 5H), 5.9−5.7 (m, 1H), 5.05 (dd, 1H, *J* = 2.0 Hz, *J* = 16.9 Hz), 4.97 (dd, 1H, *J* = 2.0 Hz, *J* = 10.0 Hz), 4.87 (d, 1H, *J* = 3.9 Hz), 4.48 (dd, 1H, *J* = 10.7 Hz, *J* = 10.7 Hz), 4.0−3.9 (m, 2H), 3.8−3.4 (m, 4H), 3.20 (dd, 1H, *J* = 7.3 Hz, *J* = 15.1 Hz), 2.91 (t, 2H, *J* = 6.8 Hz), 2.3−2.2 (m, 2H), 1.31 (t, 2H, *J* = 7.3 Hz). ^{13}C NMR (75 MHz, CD_3OD): δ 175.62, 140.43, 138.32, 130.14, 129.46, 127.34, 115.78, 98.32, 79.81, 73.89, 70.79, 69.92, 62.26, 54.05, 36.90, 36.42, 30.67. MS (ES) *m*/*z* (calcd 483.1): 484.1 (M + 1). Anal. ($C_{19}H_{26}KNO_9S$) C, H, N, S.

Hexadecanoyl 2-Amino-2-deoxy-2-*N*-oleoyl-3-*O*-(oxosulfonyl)-α-D-glucopyranoside (41). 11 (60 mg, 0.12 mmol) was reacted under similar conditions as described for **10** to give **41** (47 mg, 63%). $[\alpha]_D$: +62.3° (*c* 1.28, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 5.9−5.8 (m, 1H), 5.08 (dd, 1H, *J* = 1.9 Hz, *J* = 17.0 Hz), 4.98 (dd, 1H, *J* = 1.9 Hz, *J* = 10.2 Hz), 4.90 (d, 1H, *J* = 3.6), 4.50 (dd, 1H, *J* = 8.3 Hz, *J* = 10.9 Hz), 3.95 (dd, 1H, *J* = 3.6 Hz, *J* = 10.7 Hz), 3.8−3.6 (m, 5H), 3.4−3.3 (m, 1H), 2.4−2.3 (m, 4H), 1.7−1.6 (m, 2H), 1.4−1.1 (m, 26H), 0.90 (t, 3H, *J* = 7.0 Hz). ^{13}C NMR (75 MHz, CD_3OD): δ 175.84, 138.23, 115.80, 98.23, 79.85, 73.65, 70.81, 69.10, 62.26, 55.27, 54.07, 36.44, 33.06, 30.77, 30.74, 30.61, 30.51, 30.45, 27.34, 23.72, 14.47. MS (ES) *m*/*z* (calcd 603.0): 604.0 (M + 1). Anal. ($C_{27}H_{50}KNO_9S$) C, H, N, S.

Oleoyl 2-*N*-Acetamide-2-deoxy-3-*O*-(oxosulfonyl)-α-D-glucopyranoside (42). 12 (76 mg, 0.16 mmol) was reacted under similar conditions as described for **10** to give **42** (82.1 mg, 82%). $[\alpha]_D$: +39.4° (*c* 0.89, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 5.4−5.3 (m, 2H), 4.48 (d, 1H, *J* = 3.2 Hz), 4.48 (dd, 1H, *J* = 10.7 Hz, *J* = 11.0 Hz), 3.96 (dd, 1H, *J* = 3.7 Hz, *J* = 10.7 Hz), 3.8−3.5 (m, 4H), 3.4−3.3 (m, 2H), 2.0−1.9 (m, 7H), 1.6−1.5 (m, 2H), 1.3−1.2 (m, 22H), 0.90 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR (75 MHz, CD_3OD): δ 173.69, 130.84, 130.81, 98.32, 80.03, 73.64, 70.85, 69.15, 62.26, 54.10, 33.57, 33.02, 30.86, 30.80, 30.74, 30.65, 30.48, 30.40, 30.35, 30.29, 28.13, 27.28, 23.70, 22.87, 14.46. MS (ES) *m*/*z* (calcd 589.3): 590.2 (M + 1). Anal. ($C_{26}H_{48}KNO_9S$) C, H, N, S.

Octyl 2-*N*-Oleoyl-2-amino-2-deoxy-3-*O*-(oxosulfonyl)-α-D-glucopyranoside (43). 13 (145 mg, 0.26 mmol) was reacted under similar conditions as described for **10** to give **43** (77.2 mg, 42%). $[\alpha]_D$: +43.6° (*c* 2.01, MeOH). ^1H NMR (200 MHz, CD_3OD): δ 5.4−5.3 (m, 2H), 4.87 (d, 1H, *J* = 3.7 Hz), 4.6−4.4 (m, 1H), 3.9−3.3 (m, 7H), 2.3−2.2 (m, 6H), 1.6−1.1 (m, 34H), 1.0−0.8 (m, 6H). ^{13}C NMR (50 MHz, CD_3OD): δ 176.55, 130.88, 130.80, 98.18, 79.78, 73.80, 70.91, 69.15, 62.40, 54.26, 32.29, 33.14, 33.10, 30.96, 30.91, 30.68, 30.60, 30.64, 30.59, 30.51, 30.49, 30.37, 30.30, 28.24, 26.20, 27.46, 26.98, 23.84, 23.80, 14.54, 14.50. MS (ES) *m*/*z* (calcd 673.4): 674.3 (M + 1). Anal. ($C_{32}H_{60}KNO_9S$) C, H, N, S.

Oleoyl 2-*N*-Acetamide-2-deoxy-3,4-*O*-(2,3-diethoxybut-2,3-diyl)-6-*O*-(oxosulfonyl)-α-D-glucopyranoside (48). A solution of **12** (100 mg, 0.21 mmol) in ethanol (1.5 mL) was treated with butane-2,3-dione (41 μL, 0.47 mmol), camphorsulfonic acid (10 mg, 0.04 mmol), and triethylorthoformiate (0.23 mL, 1.4 mmol) under Ar. The mixture was stirred for 3.5 h at 60 °C. After cooling, the mixture was neutralized with triethylamine, concentrated, and purified by column chromatography (hexane−EtOAc, 1:1→0:1) to give a solid (98 mg), which was dissolved in anhydrous pyridine (5 mL) and then treated with SO_3−pyridine complex (509 mg, 3.20 mmol), with stirring at room temperature under Ar for 1 h. After this time, the mixture was concentrated, and the residue was dissolved in methanol−water (2:1, 7 mL), neutralized with a 0.5 M KOH solution, and concentrated. The residue was purified by column chromatography (CH_2Cl_2−methanol, 6:1) to give **48** (95 mg, 61%). ^1H NMR (200 MHz, CD_3OD): δ 5.4−5.3 (m, 2H), 4.83 (d, 1H, *J* = 3.4 Hz), 4.6−4.4 (m, 2H), 4.3−3.4 (m, 8H), 2.2−2.0 (m, 7H), 1.6−1.2 (m, 36H), 1.0−0.9 (m, 3H).

Oleoyl 2-*N*-Acetyl-2-deoxy-6-*O*-(oxosulfonyl)-α-D-glucopyranoside (50). A solution of **10** (150 mg, 0.41 mmol) in ethanol (3 mL) was treated with butane-2,3-dione (82 μL, 0.93 mmol), camphorsulfonic acid (20 mg, 0.09 mmol), and triethylorthoformate (0.46 mL, 2.8 mmol) under Ar. The mixture was stirred for 3 h at 60 °C. After cooling, the mixture was neutralized with triethylamine and concentrated to give a residue (507 mg) that was dissolved in anhydrous pyridine (10 mL) and treated with SO_3−pyridine complex (1.3 g, 8.20 mmol), with stirring at room temperature under Ar for 1 h. After this time, the mixture was concentrated, and the residue was dissolved in methanol−water (2:1, 7 mL), neutralized with a 0.5 M KOH solution, and concentrated. The residue was extracted with methanol, concentrated, and purified by column chromatography (CH_2Cl_2−methanol, 6:1) to give a solid. The solid was dissolved in a mixture of acetic acid−water (2:1, 20 mL) and stirred at 70 °C for 3 h. The mixture was concentrated and the residue was purified by column chromatography (CH_2Cl_2−methanol, 10:1→4:1) to give **50** (80 mg, 41%, three steps). $[\alpha]_D$: +89.5° (*c* 1.10, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 7.3−7.2 (m, 5H), 5.8−5.7 (m, 1H), 5.0−4.9 (m, 2H), 4.67 (d, 1H, *J* = 3.9 Hz), 4.1−4.0 (m, 2H), 3.9−3.8 (m, 1H), 3.8−3.6 (m, 2H), 3.5−3.4 (m, 1H), 3.4−3.3 (m, 2H), 2.83 (t, 2H, *J* = 5.9 Hz) 2.2−2.1 (m, 4H). MS (ES) *m*/*z* (calcd 483.1): 484.0 (M + 1). Anal. ($C_{19}H_{26}KNO_9S$) C, H, N, S.

Oleoyl 2-*N*-Acetyl-2-amino-2-deoxy-6-*O*-(oxosulfonyl)-α-D-glucopyranoside (51). **48** (79 mg, 0.11 mmol) was dissolved in a

mixture of acetic acid−water (2:1, 10 mL) and stirred at 65 °C for 3 h. The mixture was concentrated and the residue was purified by column chromatography (CH_2Cl_2−methanol, 5:1→4:1) to give **51** (42 mg, 66%). $[\alpha]_D$: +69.0° (*c* 1.18, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 5.4−5.3 (m, 2H), 4.76 (d, 1H, *J* = 3.4 Hz), 4.26 (dd, 1H, *J* = 2.4 Hz, *J* = 11.0 Hz), 4.18 (dd, 1H, *J* = 5.6 Hz, *J* = 10.7 Hz), 3.89 (dd, 1H, *J* = 3.7 Hz, *J* = 10.7 Hz), 3.8−3.6 (m, 4H), 3.4−3.3 (m, 2H), 2.0−1.9 (m, 7H), 1.6−1.5 (m, 2H), 1.3−1.2 (m, 22H), 0.90 (t, 3H, *J* = 6.8 Hz). MS (ES) *m/z* (calcd 589.3): 590.3 (M + 1). Anal. ($C_{26}H_{48}KNO_9S$) C, H, N, S.

Octyl 2-Amino-2-deoxy-2-*N*-oleoyl-6-*O*-(oxosulfonyl)-α-D-glucopyranoside (52). **13** (250 mg, 0.45 mmol) in ethanol (3.2 mL) was treated with butane-2,3-dione (87 μL, 0.99 mmol), camphorsulfonic acid (21 mg, 0.09 mmol), and triethylorthoformate (0.49 mL, 3.0 mmol) under Ar. The mixture was stirred for 3 h at 70 °C. After cooling, the mixture was neutralized with triethylamine and concentrated. The crude was purified by column chromatography (hexane−EtOAc, 2:1) to give a residue (121 mg) that was dissolved in anhydrous pyridine (5 mL) and treated with SO_3−pyridine complex (552 mg, 3.46 mmol), with stirring at room temperature under Ar for 1 h. After this time, the mixture was concentrated, and the residue was dissolved in methanol−water (2:1, 7 mL), neutralized with a 0.5 M KOH solution, and concentrated. The residue was purified by column chromatography (CH_2Cl_2−methanol, 8:1) to give a solid (116 mg) that was dissolved in a mixture of acetic acid−water (2:1, 20 mL) and stirred at 70 °C for 3 h. The mixture was concentrated and the residue was purified by column chromatography (CH_2Cl_2−methanol, 10:1→4:1) to give **52** (80 mg, 13%, three steps). $[\alpha]_D$: +70.3° (*c* 0.86, MeOH). ^{1}H NMR (400 MHz, CD_3OD): δ 5.4−5.3 (m, 2H), 4.76 (d, 1H, *J* = 3.9 Hz), 4.26 (dd, 1H, *J* = 2.4 Hz, *J* = 10.8), 4.18 (dd, 1H, *J* = 5.7 Hz, *J* = 10.8 Hz), 3.88 (dd, 1H, *J* = 3.9 Hz, *J* = 10.8 Hz), 3.8−3.7 (m, 3H), 3.4−3.3 (m, 2H), 2.3−2.2 (m, 2H), 2.0−1.9 (m, 4H), 1.6−1.5 (m, 4H), 1.3−1.2 (m, 30H), 0.9−0.8 (m, 6H). ^{13}C NMR (100 MHz, CD_3OD): δ 176.62, 131.43, 130.37, 98.36, 72.43, 72.14, 71.72, 69.05, 68.30, 55.36, 37.04, 33.11, 33.07, 30.90, 30.85, 30.69, 30.62, 30.61, 30.56, 30.49, 30.46, 30.36, 30.34, 28.18, 28.14, 27.41, 27.16, 23.80, 23.75, 14.50, 14.48. MS (ES) *m/z* (calcd 673.3): 673.4 (M + 1), 673.5 (M + 2). Anal. ($C_{32}H_{60}KNO_9S$) C, H, N, S.

Cell Lines. C6 rat glioma cells[21] and U-373 MG human glioma cells[22] were seeded on plastic flasks and maintained in DMEM culture medium, supplemented with 10% fetal calf serum (FCS), 2 mM glutamine, 50 IU/mL penicillin, and 50 mg/mL streptomycin (DM-10S) and maintained in a humidified atmosphere of 5% CO_2, at 37 °C.

Cell Proliferation Assays. For proliferation assays the C6, U373, or A375 cell lines were seeded in DM-10S at 1 × 10^4 cells/well and allowed to attach for 6 h. After the cells were attached to the substrate, the medium was changed to serum-free DMEM, and the cells were incubated for 36 h. Then the medium was replaced by DMEM medium plus 1% FCS, containing the test inhibitors, in triplicate. The cultures were incubated for 24 h and washed with serum-free DMEM medium. For [^{3}H]thymidine (Amersham) incorporation assay, a 6 h-pulse (0.5 μCi/well) was given; nonincorporated radioactivity was washed away, the cells were lysed with 0.5% SDS solution, diluted in scillation fluid, and the plates were measured in a WALLAC liquid scintillation counter (1450 Microbeta Trilux model; Turku, Finland). Inhibition was calculated using the formula:

$$\% \text{ inhibition} = 100 - 100[(X - B)/(A - B)]$$

where *A* is [^{3}H]thymidine dpm incorporated corresponding to cells maintained in DM-10S (high mitosis control); *B* is the dpm incorporated from cells in serum-free medium (low mitosis control), and *X* corresponds to dpm incorporated in cells treated with test inhibitors.[6] Dose−response plots of percent inhibition versus concentration were obtained from triplicate samples and adjusted to sigmoidal curves, from which values of the 50% inhibitory concentration (ID_{50}) were calculated. The ID_{50} values plus standard error of the mean (SEM) are shown in the tables. For data processing, Microsoft Excel for Windows XP and GraphPad Prism 4 programs were used.

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Supporting Information Available: Elemental analysis data of target compounds **5**−**13**, **19**−**22**, **27**−**29**, **32**, **35**, **40**−**43**, and **50**−**52**. This material is available free of charge via the Internet at http://pubs.acs.org.

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