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Carbohydrate Research 337 (2002) 1979–1992

CARBOHYDRATE RESEARCH

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Synthesis of an ether-linked alkyl 5a-carba-β-D-glucoside, a 5a-carba-β-D-galactoside, a 2-acetamido-2-deoxy-5a-carba-β-D-glucoside, and an alkyl 5a′-carba-β-lactoside

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Received 1 April 2002; accepted 24 June 2002

Dedicated to Professor Derek Horton on the occasion of his 70th birthday

Abstract

For the purpose of providing biologically stable building blocks for the biocombinatorial synthesis using a living cell, some ether-linked alkyl 5a-carba-β-D-glycoside primers were prepared. The key step of the synthesis was coupling of 1-bromo-*n*-alkanes with the 1-OH unprotected derivatives of 5a-carba-sugar analogues of D-glucose, D-galactose, and 2-acetamido-2-deoxy-D-glucose (*N*-acetyl-D-glucosamine), in DMF in the presence of sodium hydride. Alternatively, alkyl carba-lactoside was synthesized by incorporation of a 5a-carba-β-D-galactose residue into the 4-position of dodecyl β-D-glucopyranoside. A strong and specific inhibition of β-galactosidase (K_i 0.67 μM, bovine liver) was found for dodecyl 5a-carba-β-D-galactopyranoside.

Keywords: Sugar mimics; Carba-sugars; Alkyl 5a-carba-glycosides, ether-linked; Biocombinatorial synthesis using a living cell; β-Galactosidase inhibitor

1. Introduction

Biocombinatorial synthesis using a living cell has become an important tool for generating libraries of oligosaccharides and glycopolymers with desirable biological activities.[1] The standard procedure successfully carried out so far is to incorporate the building blocks, glycoside-based primers, into cells in which the primers act as substrates with cellular biosynthetic processes, leading to construction of a large number of oligosaccharides. The building blocks used are amphipathic glycosides, which are hydrophilic hexose moieties with hydrophobic aglycons of various alkyl chain lengths. After incubation of these primers, there should be important processes to isolate oligosaccharides formed effectively from the cell medium. Therefore, tagged hydrophobic-aglycon moieties of the primers would be desirable to remain unchanged throughout successive biochemical processes, allowing easy recovery of oligosaccharides formed. Since certain carba-sugars[2] and oligosaccharides[3] have been well demonstrated to act as substrate analogues of some glycosyltransferases, unhydrolyzable glycoside-mimics 5a-carba-glycosides are now expected to be efficient substrates that can be taken up in a variety of cells. Four structures targeted for synthesis and evaluation are **1**–**4**.

Simple ether-linked methyl, ethyl, and isopropyl carba-hexopyranoside derivatives were previously prepared when some reactivity of the unsaturated carba-hexopyranosyl bromides[4] needed to be elucidated. No alkyl 5a-carba-glycosides have so far been synthesized systematically, except for the preparation of an octyl *N*-acetyl-5a-carba-glucosaminide derivative that was used as a building block of octyl *N*-acetyl-5a-carba-β-D-isolactosaminide.[5]

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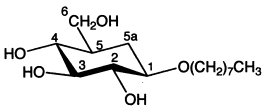
0008-6215/02/$ - see front matter
PII: S0008-6215(02)00294-X



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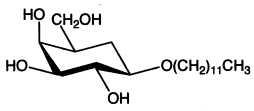

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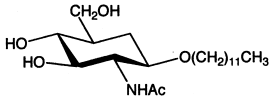

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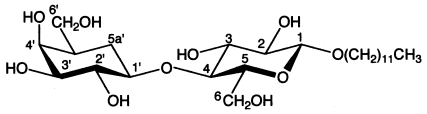

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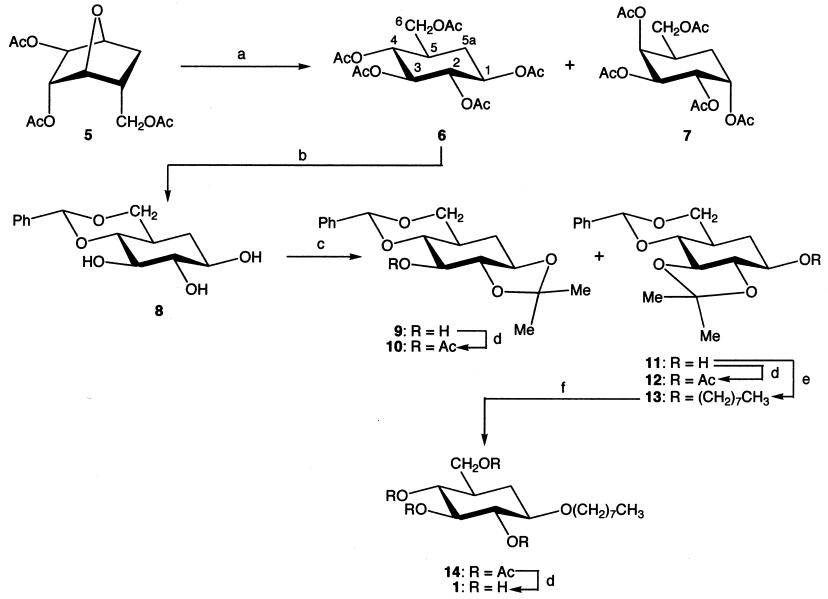
2. Results and discussion

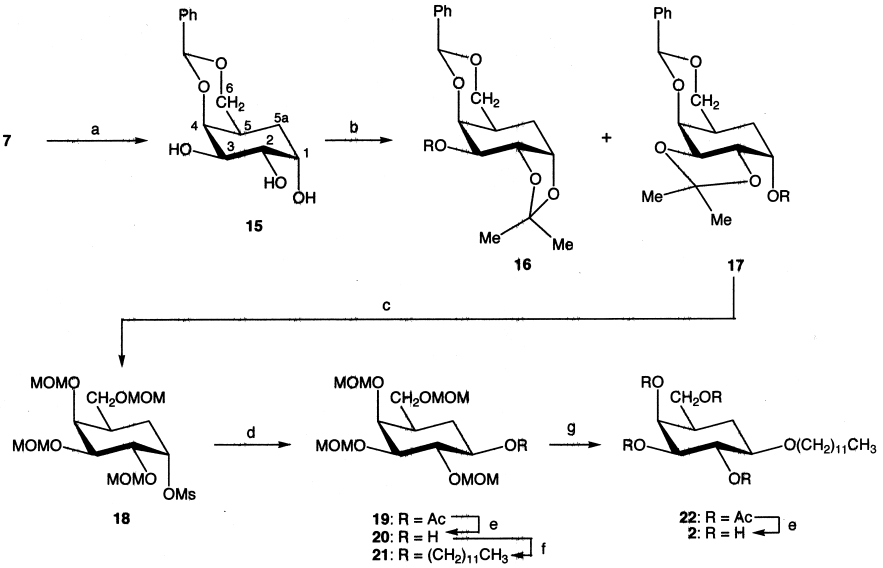
Construction of ether-linked 5a-carba-hexoside derivatives has been conducted by coupling between the 1-OH unprotected derivatives of 5a-carba-D-hexoses and 1-bromo-*n*-alkanes in the presence of sodium hydride in DMF, in order to establish a generally applicable procedure to obtain various 5a-carba-glycosides. All protected carba sugar derivatives used in this study were provided starting from intermediates previously reported by us.

According to the preceding results[1] that dodecyl β-D-glucoside[6] showed high reaction efficiency involving cell uptake, glycosylation, and secretion process, dodecyl ether groups have been chosen for the appropriate aglycons of 5a-carba-β-D-galactoside, 2-acetamido-2-deoxy-5a-carba-β-D-glucoside, and 5a′-carba-β-lactoside. However, since the efficiency of octyl β-D-glucoside as a primer had recently been demonstrated, the octyl ether group was employed for the aglycon of 5a-carba-β-D-glucoside. Certain toxic effects of dodecyl β-glucoside toward cells suggested avoiding the dodecyl group.

*Octyl 5a-carba-β-*D*-glucopyranoside* (**1**).—Acetolysis of (1*S*)-2-*exo*,3-*endo*-diacetoxy-5-*endo*-acetoxymethyl-7-oxabicyclo[2.2.1]heptane[7] (**5**) produced, after chromatography, penta-*O*-acetyl-5a-carba-β-D-glucopyranose (**6**, 42%) and α-D-galactopyranose (**7**, 43%) (Scheme 1). Zemplén O-deacetylation of **6**, followed by treatment with α,α-dimethoxytoluene–TsOH in DMF, gave the 4,6-*O*-benzylidene derivative **8** (59%). Isopropylidenation of **8** with 2,2-methoxypropane[8] in DMF gave, after chromatography, the 1,2- (**9**, 48%) and 2,3-*O*-isopropylidene derivatives (**11**, 52%), which were further characterized as the corresponding acetates **10** and **12**. Treatment of **9** with TsOH in DMF led to a ca. 1:1 equilibrium mixture of positional isomers, from which **11** was obtained in 45% yield, along with **9** (45%). Therefore the desired **11** was practically furnished in ~70% yield through the above process. Treatment of



Scheme 1. *Reagents and conditions*: (a) 15:9:1 HOAc–Ac_2O–concd H_2SO_4, 20 h, 80 °C; (b) 1 M NaOMe, MeOH, rt; α,α-dimethoxytoluene, *p*-TsOH, DMF, 3 h, 50 °C; (c) 2,2-dimethoxypropane, *p*-TsOH, DMF, 1 h, 70 °C; (d) Ac_2O, pyridine, rt; (e) NaH, 1-bromooctane (2 molar equiv), DMF, 5 h, rt; (f) 80% aq HOAc, 50 °C; Ac_2O, pyridine; (g) 1 M NaOMe, MeOH.



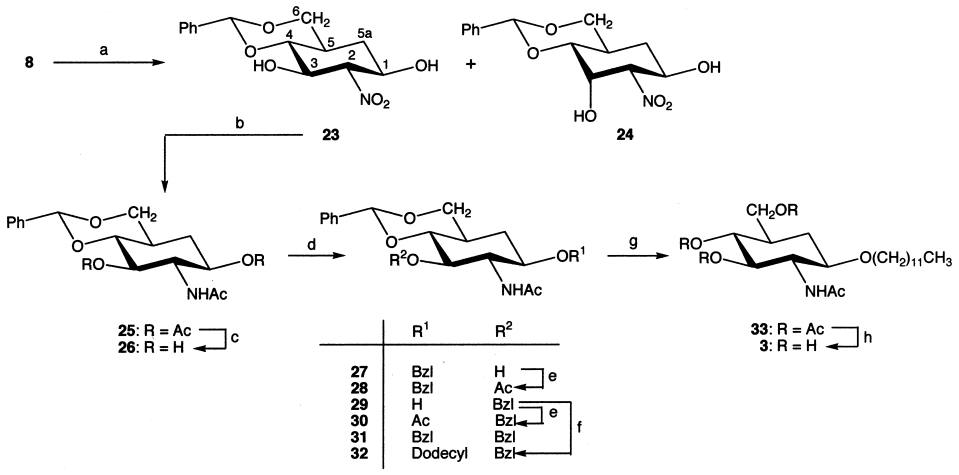
Scheme 2. *Reagents and conditions*: (a) 1 M NaOMe, MeOH, rt; α,α-dimethoxytoluene, *p*-TsOH, DMF, 3 h, 50 °C; (b) 2-methoxypropene, *p*-TsOH, DMF, 0 °C; Ac_2O, pyridine, rt; (c) 1 M NaOMe, rt; MsCl (3 molar equiv), pyridine, rt; 80% aq HOAc, 50 °C; $MeOCH_2Cl$ (8 molar equiv), DMAP, CH_2Cl_2, 40 °C; (d) KOAc (20 molar equiv), DMF, 100 °C; (e) 1 M NaOMe, MeOH; (f) NaH, 1-bromododecane (3 molar equiv), DMF, rt; (g) 4 M HCl, 60 °C; Ac_2O, pyridine, rt; (h) 1 M NaOMe, 1:2 MeOH–CH_2Cl_2.

11 with sodium hydride and 1-bromooctane (2 molar equiv) in DMF at room temperature gave octyl 5a-carba-β-D-glucopyranoside derivative **13** (80%), which was deprotected by treatment with aqueous acetic acid followed by acetylation, giving the tetraacetyl derivative **14** (98%). O-Deacetylation gave the free glucoside **1** (88%).

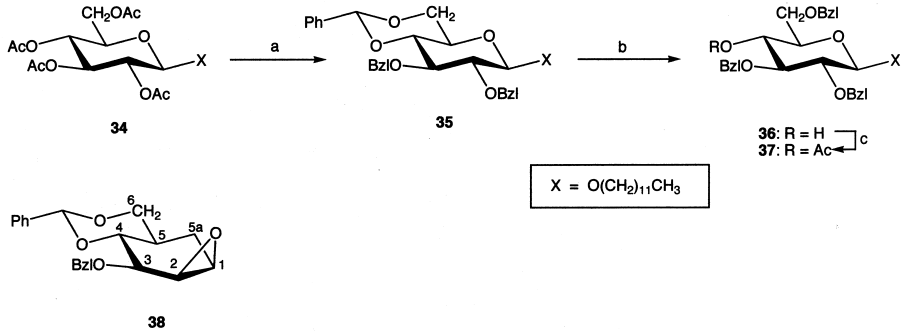
Dodecyl 5a-carba-β-D-galactopyranoside (**2**).—The 4,6-*O*-benzylidene derivative **15** of 5a-carba-α-D-galactose was similarly prepared from **7** in 57% yield (Scheme 2). Acetalation of **15** was effected by using 2-methoxypropene[8] to produce, after acetylation, the 1,2- (**16**, 38%) and 2,3-*O*-isopropylidene derivatives (**17**, 59%). Compound **17** was O-deacetylated, and the resulting alcohol was mesylated conventionally to the mesyl ester, the protecting groups of which were subsequently replaced by methoxymethyl groups (→**18**, 67%). Nucleophilic substitution of **18** with potassium acetate in DMF at 100 °C procceded slowly to give a sole acetate **19** (77%), which was O-deacetylated (→**20**, 88%) and subsequently treated with sodium hydride and 1-bromododecane in DMF to give protected dodecyl 5a-carba-β-D-galactopyranoside **21** (79%). Hydrolysis of **21** with 4 M hydrochloric acid, followed by acetylation, gave the pentaacetyl derivative **22** (72%), which was O-deacetylated to afford the free galactoside **2** (92%).

Dodecyl 2-acetamido-2-deoxy-5a-carba-β-D-glucopyranoside (**3**).—Base-catalyzed nitroaldol condensation of the dialdehyde generated by periodate oxidation of **8** produced two 2-deoxy-2-nitro-5a-carba-D-hexose derivatives **23** (56%) and **24** (18%) (Scheme 3), having the β-*gluco* and β-*gulo* configuration, respectively, following the procedure[9] previously reported for the racemic analogue. Compound **23** was hydrogenated with Raney nickel and acetylated to give the tri-*N*,*O*-acetyl derivative **25** (67%), O-deacetylation of which gave the diol **26** (∼100%). Selective benzylation of **26** was carried out by treatment with a molar equiv of benzyl bromide and sodium hydride in DMF at 0 °C, and the resulting two monobenzyl ethers **27** (3%) and **29** (41%), and dibenzyl ether **31** (32%) were isolated by chromatography. The structures of **27** and **29** were readily established on the basis of the ^1H NMR spectra by converting them into the acetyl derivatives **28** and **30**. The 3-*O*-benzyl ether **29** was treated with 1-bromododecane–NaH in DMF as in the preparation of **21**, giving a 68% yield of **32**. The resulting ether was hydrogenolyzed with 10% Pd/C in ethanol containing small amount of 1 M hydrochloric acid, followed by acetylation, yielding the per-*O*-acetyl derivative **33** (95%), which was O-deacetylated to give the free glycoside **3** (99%).

Dodecyl 5a′-carba-β-lactoside (**4**).—According to the standard procedure[10] to prepare ether-linked 5a′-carbalactose, coupling of 1,2-anhydro-3-*O*-benzyl-4,6-benzylidene-5a-carba-β-D-mannopyranose[11,12] (**38**) and the 4-unprotected derivative of dodecyl β-D-glucopyranoside was conducted to synthesize the target compound. Thus, dodecyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-glucopyranoside (**35**) was prepared conventionally from dodecyl β-D-glucopyranoside[6] (Scheme 4).



Scheme 3. *Reagents and conditions*: (a) $NaIO_4$, $NaHCO_3$, H_2O; $MeNO_2$, NaOMe, MeOH, rt; (b) H_2, Raney Ni, MeOH, Ac_2O; Ac_2O, pyridine; (c) 1 M NaOMe, MeOH, rt; (d) NaH, BzlBr (molar equiv), DMF, 0 °C; (e) Ac_2O, pyridine, rt; (f) NaH, 1-bromododecane (3 molar equiv), DMF, rt; (g) H_2, 10% Pd/C, 1:1 EtOH–EtOAc, HCl; Ac_2O, pyridine, rt; (h) 1 M NaOMe, 1:2 $MeOH–CH_2Cl_2$.

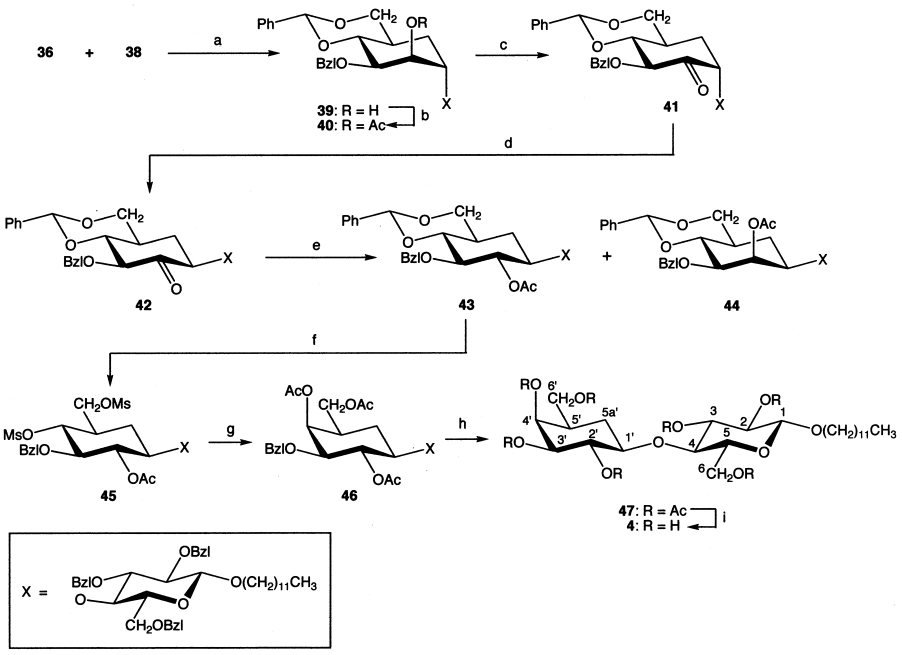


Scheme 4. *Reagents and conditions*: (a) 1 M NaOMe, MeOH; α,α-dimethoxytoluene, *p*-TsOH, DMF, 50 °C; NaH, BzlBr, DMF, rt; (b) $BH_3{\cdot}Et_3N$, $AlCl_3$, THF, 0 °C → rt; (c) Ac_2O, pyridine, rt.

Treatment of **35** with borane·triethylamine and aluminum chloride in THF afforded the 2,3,6-tribenzyl ether **36**. Condensation of **36**, after treatment with 3 molar equiv of sodium hydride, with **38** (2 molar equiv) in DMF was carried out for 5 days at 70 °C, giving the coupled compound **39** (84%), together with **36** (12%) recovered (Scheme 5). The structure was confirmed by converting it into the acetate **40**. Oxidation of **39** with dimethyl sulfoxide in acetic anhydride yielded the ketone (**41**, 98%), which underwent epimerization smoothly by treatment with DBU in toluene at 70 °C, giving a ca. 1:3 mixture of C-1 epimers. Chromatography afforded the major ketone **42** in 67% isolated yield. Selective reduction of **42** was effected by treatment with borane·THF at 0 °C to give, after acetylation, a 52% yield of the desired 5a-carba-β-glucosyl-β-glucoside **43**, together with the β-mannosyl **44** (9%). The structures of **43** and **44** were easily differentiated by the downfield shift ($\sim$0.5 ppm) of the signal for the axial H-5a′, attributable to deshielding effect due to the axial 2′-acetoxyl group of the latter. Removal of the benzylidene group of **43** with aqueous acetic acid, followed by mesylation, led to the dimesylate **45** (59%). Nucleophilic substitution of **45** with excess of sodium acetate in DMF proceeded very slowly at 120 °C to afford the protected 5a′-carbalactoside derivative **46** (91%), which was similarly hydrogenolyzed, followed by acetylation, to give the heptaacetyl derivative **47** of dodecyl 5a′-carba-β-lactoside. Zemplén O-deacetylation afforded the carba-disaccharide **4** (96%).

Biological assay.—Before examining a feasibility[†] of ether-linked carba-hexosides as candidates for the

[†] Very recently, alkyl carba-glycosides **1**–**4** have been shown to be useful as good primers for biocombinatorial glycosylation, involving efficient uptake in mouse melanoma C-13 cells.[13] Interestingly, compounds **1** and **3** produced 2–4 times more glycosphingolipids, containing carba-sugar residues, than the corresponding glycoside primers did.



Scheme 5. *Reagents and conditions*: (a) **38** (2 molar equiv), NaH, 15-crown-5 ether, DMF, 5 days, 70 °C; (b) Ac_2O, pyridine, rt; (c) Ac_2O, Me_2SO, rt; (d) DBU, toluene, 1 h, 70 °C; (e) 1 M BH_3·THF, 0 °C → rt; Ac_2O, pyridine, rt; (f) 80% aq HOAc; MsCl (4 molar equiv), pyridine, rt; (g) NaOAc (40 molar equiv), 80% aq DMF, 3 days, 120 °C; Ac_2O, pyridine, rt; (h) H_2, 10% Pd/C, EtOH, 1 M HCl; Ac_2O, pyridine; (i) 1 M NaOMe, 1:2 MeOH–CH_2Cl_2.

building blocks in biocombinatorial synthesis using a living cell, it was necessary to establish the biological activity of such compounds. In order to test their inhibitory activity, if any, toward several glycosidases, the four compounds were assayed against seven glycosidases: α-glucosidase (baker's yeast and rat intestine), β-glucosidase (almonds), α-galactosidase (green coffee beans and rat liver), β-galactosidase (bovine liver), α-mannosidase (Jack beans), α-fucosidase (bovine kidney), and β-*N*-acetyl-glucosaminidase (bovine liver). Unexpectedly, compound **2** has been demonstrated to be a strong and specific inhibitor of β-galactosidase (IC_{50} 6.4 μM, K_i 0.67 μM, bovine liver), and **3** to be a moderate inhibitor (IC_{50} 52 μM). Compounds **1** and **4** did not show any inhibitory activity at all, while **2** and **3** were only active against β-galactosidase.

Contrary to well-accepted mechanistic rationale concerning hydrolytic transition-state analogue inhibitors,[14] it may be rather surprising that such simple carbohydrate mimics, having neither a basic heteroatom that may be protonated nor biologically active functional groups, seem to play an important role as competitive inhibitors, possibly in binding in the active site of the enzyme as mimics of either the substrate or product in the ground state. In addition to the main subject in hand, the present findings concerning a new-type glycosidase inhibitors are likely to stimulate further interests in carba sugars.

3. Experimental

General methods.—Melting points were determined with micro melting point apparatus (Yanagimoto, Tokyo), and uncorrected. Optical rotations were measured with a Jasco DIP-370 polarimeter. IR spectra were recorded with Jasco FTIR-200 and IR-810 spectrometers. ^1H NMR (300 MHz) spectra were recorded on a Jeol Lambda 300 (300 MHz) spectrometer: solvents: $CDCl_3$ and CD_3OD; internal standard: Me_4Si. Chemical shifts are expressed in ppm. High-resolution (HR) mass spectra were recorded with Jeol GC-Mass GC-Mare, EI (70 eV) or FAB (positive-ion mode) spectrometers. TLC was conducted with Silica Gel 60 GF (E. Merck, Darmstadt), detecting by charring with concd H_2SO_4. Column chromatography was carried out on Silica Gel 60 K070 (Katayama Chemicals, Osaka), Wakogel C-33 (Silica Gel, 300 mesh, Wako Chemical, Osaka), Disogel sp-60 (Silica Gel, 60 mesh, Daiso, Osaka). Organic solutions, after drying with anhydrous Na_2SO_4, were concentrated at < 50 °C at diminished pressure.

*Preparation of pentaacetyl 5a-carba-β-*D*-glucopyranose* (**6**) *and pentaacetyl 5a-carba-α-*D*-galactopyranose* (**7**).—A 3.0-g portion of (1*S*)-2-*exo*,3-*endo*-diacetoxy-5-*endo*-acetoxymethyl-7-oxabicyclo[2.2.1]heptane[7] (10.7 mmol) was treated with a mixture of HOAc (9 mL), Ac_2O (5.5 mL) and concd H_2SO_4 (0.6 mL) in a sealed tube for 20 h at 80 °C. A reaction mixture obtained

from the 14 sealed tubes (totally 42.0 g of the triacetate) was combined and poured into ice-water (300 mL). After neutralization with sodium hydrogen carbonate, the mixture was extracted with EtOAc (1.2 L), and the organic layer was thoroughly washed with brine, dried, and evaporated. Chromatography on silica gel (500 g, 1:8 acetone–hexane) gave **7** (24.5 g, 42.5%) as crystals: R_f 0.21 (1:3 acetone–hexane); $[\alpha]_D^{27}$ +43° (*c* 1.1, $CHCl_3$), and **6** (24 g, 42%) as a syrup: R_f 0.17 (1:3 acetone–hexane); $[\alpha]_D^{27}$ +17° (*c* 1.8, $CHCl_3$). Both compounds were identical with authentic samples[7] in all respects. Data for **6**: ^{1}H NMR ($CDCl_3$) (partial): δ 4.93 [ddd, 1 H, $J_{1,2}$ 10.0, $J_{1,5a(ax)}$ 11.0, $J_{1,5a(eq)}$ 5.7 Hz, H-1], 4.09 (dd, 1 H, $J_{5,6a}$ 5.7, J_{6gem} 11.3 Hz, H-6a), 3.95 (dd, 1 H, $J_{5,6b}$ 5.0 Hz, H-6b), 2.06, 2.05, 2.03, 2.02, and 2.01 (5 s, each 3 H, 5 × Ac), 1.58 [ddd, 1 H, $J_{5,5a(ax)} = J_{5agem} = 12.7$ Hz, H-5a(ax)]. Data for **7**: ^{1}H NMR ($CDCl_3$) (partial): δ 5.51 [ddd, 1 H $J_{1,2} = J_{1,5a(eq)} = 2.7$, $J_{1,5a(ax)}$ 5.6 Hz, H-1], 5.20 (dd, 1 H, $J_{2,3}$ 7.1 Hz, H-2), 5.15 (dd, 1 H, H-3), 3.96 (dd, 1 H, $J_{5,6a}$ 9.4, J_{6gem} 11.0 Hz, H-6a), 3.88 (dd, 1 H, $J_{5,6b}$ 6.1 Hz, H-6b), 2.12, 2.11, 2.04, 2.01, and 1.99 (5 s, each 3 H, 5 × Ac).

*4,6-*O*-Benzylidene-5a-carba-β-*D*-glucopyranose* (**8**).—A solution of **6** (9.68 g, 28 mmol) in MeOH (70 mL) was treated with 1 M methanolic NaOMe (15 mL) for 1 h at room temperature. After neutralization with Amberlite IR-120B (H^+) resin, the mixture was evaporated to dryness. The residue was dissolved in DMF (50 mL), and the solution was treated with α,α-dimethoxytoluene (5.5 mL, 37 mmol) and *p*-TsOH·H_2O (0.85 g, 5.0 mmol) for 3 h at 50 °C. After neutralization with Et_3N, the mixture was concentrated, and the residue was chromatographed on silica gel (300 g, 1:15 MeOH–$CHCl_3$) to give **8** (4.5 g, 59%) as crystals (from EtOH): mp 167–168 °C; $[\alpha]_D^{20}$ −43° (*c* 1.2, MeOH); R_f 0.48 (1:15 MeOH–$CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.52–7.30 (m, 5 H, Ph), 5.55 (s, 1 H, PhC*H*), 4.12 (dd, 1 H, $J_{5,6a}$ 4.4, J_{6gem} 11.0 Hz, H-6a), 3.65 (dd, 1 H, $J_{5,6b}$ 11.0 Hz, H-6b), 3.51 [ddd, 1 H, $J_{1,2}$ 8.8, $J_{1,5a(ax)}$ 11.1, $J_{1,5a(eq)}$ 4.9 Hz, H-1], 3.50–3.36 (m, 2 H, H-3, H-4), 3.23 (dd, 2 H, $J_{2,3}$ 11.0 Hz, H-2), 1.86–1.78 (m, 2 H, H-5, H-5a), 1.10 [ddd, 1 H, $J_{5,5a(ax)} = J_{5agem} = 12.9$ Hz, H-5a(ax)]. HREIMS: Calcd for $C_{11}H_{18}O_5$ [M^+]: 266.1154; Found: 266.1157.

*4,6-*O*-Benzylidene-1,2-*O*-isopropylidene-5a-carba-β-*D*-glucopyranose* (**9**) *and 4,6-*O*-benzylidene-2,3-*O*-isopropylidene-5a-carba-β-*D*-glucopyranose* (**11**).—To a solution of **8** (63 mg, 0.24 mmol) in DMF (1.9 mL) were added 2,2-dimethoxypropane (0.29 mL, 2.2 mmol) and *p*-TsOH·H_2O (9 mg, 0.05 mmol), and the mixture was stirred for 1 h at 70 °C. After neutralization with Et_3N, the mixture was concentrated, and the residue was chromatographed on silica gel (5 g, 1:5 acetone–hexane) to give **9** (38 mg, 52%) and **11** (48 mg, 48%) as a syrup. Compound **9** (54 mg, 0.18 mmol) was isomerized by treatment with DMF (1.6 mL) containing 2,2-dimethoxypropane (0.22 mL) and *p*-TsOH·H_2O (9 mg) for 1 h at 70 °C giving, after chromatography, **11** (24.5 mg, 45%) and **9** (24.5 mg, 45% recovery). Data for **9**: $[\alpha]_D^{21}$ −21° (*c* 1.7, $CHCl_3$); R_f 0.47 (1:2 acetone–toluene); ^{1}H NMR (CD_3OD): δ 7.53–7.35 (m, 5 H, Ph), 5.52 (s, 1 H, PhCH), 4.25 (dd, 1 H, $J_{5,6a}$ 3.7, J_{6gem} 11.0 Hz, H-6a), 3.91 (dd, 1 H, $J_{2,3} = J_{3,4} = 8.8$ Hz, H-3), 3.82–3.36 (m, 5 H, H-1, H-2, H-4, H-6b, OH), 2.04–1.85 [m, 2 H, H-5, H-5a(eq)], 1.47 and 1.45 (2 s, each 3 H, CMe_2), 1.29 [ddd, 1 H, $J_{1,5a(ax)} = J_{5,5a(ax)} = J_{5agem} = 12.5$ Hz, H-5a(ax)]. HREIMS: Calcd for $C_{17}H_{22}O_5$ [M^+]: 306.1467; Found: 306.1466. Data for **11**: mp 150–151 °C; $[\alpha]_D^{20}$ −20° (*c* 1.2, $CHCl_3$); R_f 0.37 (1:2 acetone–toluene); ^{1}H NMR (CD_3OD): δ 7.54–7.30 (m, 5 H, Ph), 5.58 (s, 1 H, PhCH), 4.18 (dd, 1 H, $J_{5,6a}$ 3.9, J_{6gem} 11.7 Hz, H-6a), 3.99 [dd, 1 H, $J_{1,2}$ 9.3, $J_{1,5a(ax)}$ 9.8, $J_{1,5a(eq)}$ 4.9 Hz, H-1], 3.81 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.3$ Hz, H-4), 3.77 (m, 1 H, H-6b), 3.65 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-3), 3.44 (dd, 1 H, H-2), 3.38 (br s, 1 H, OH), 2.02–1.81 [m, 2 H, H-5, H-5a(eq)], 1.49 and 1.46 (2 s, each 3 H, CMe_2), 1.18 [ddd, 1 H, $J_{1,5a(ax)}$ 9.3, $J_{5,5a(ax)}$ 10.3, J_{5agem} 13.2 Hz, H-5a(ax)]. HREIMS: Calcd for $C_{17}H_{22}O_5$ [M^+]: 306.1467; Found: 306.1463.

*3-*O*-Acetyl-4,6-*O*-benzylidene-1,2-*O*-isopropylidene-5a-carba-β-*D*-glucopyranose* (**10**).—Compound **9** (18 mg, 0.057 mmol) was treated with Ac_2O (0.5 mL) in pyridine (1 mL) for 15 h at room temperature. After addition of a small amount of MeOH, the mixture was evaporated, and the residue was chromatographed on silica gel (1:8 acetone–hexane) to give **10** (20 mg, 96%) as a syrup: $[\alpha]_D^{20}$ −26° (*c* 2.0, $CHCl_3$); R_f 0.22 (1:4 acetone–hexane); ^{1}H NMR (CD_3OD): δ 7.50–7.30 (m, 5 H, Ph), 5.48 (s, 1 H, PhC*H*), 5.34 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H-3), 4.23 (dd, 1 H, $J_{5,6a}$ 3.9, J_{6gem} 11.0 Hz, H-6a), 3.72 (dd, 1 H, $J_{5,6b}$ 11.0 Hz, H-6b), 3.72–3.46 (m, 3 H, H-1, H-2, H-4), 2.12 (s, 3 H, Ac), 2.15–1.94 [m, 2 H, H-5, H-5a(eq)], 1.48 and 1.40 (m, 6 H, CMe_2), 1.28 [ddd, 1 H, $J_{1,5a(ax)} = J_{5,5a(ax)} = 11.7$, J_{5agem} 12.0 Hz, H-5a(ax)]. HREIMS: Calcd for $C_{19}H_{24}O_6$ [M^+]: 348.1573; Found: 348.1575.

*1-*O*-Acetyl-4-6-*O*-benzylidene-2,3-*O*-isopropylidene-5a-carba-β-*D*-glucopyranose* (**12**).—Compound **11** (9.5 mg, 0.03 mmol) was acetylated as described in the preparation of **10** to give, after chromatography, **12** (11 mg, 98%) as crystals: mp 167–168 °C; $[\alpha]_D^{20}$ −49° (*c* 1.1, $CHCl_3$); R_f 0.60 (1:4 acetone–hexane); ^{1}H NMR (CD_3OD): δ 7.55–7.20 (m, 5 H, Ph), 5.58 (s, 1 H, PhC*H*), 5.04 [dd, 1 H, $J_{1,2} = J_{1,5a(ax)} = 10.1$, $J_{1,5a(eq)}$ 4.6 Hz, H-1], 4.18 (dd, 1 H, $J_{5,6a}$ 4.2, J_{6gem} 10.9 Hz, H-6a), 3.82 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.3$ Hz, H-4), 3.63 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-2), 2.11 (s, 3 H, Ac), 2.20–1.94 [m, 2 H, H-5, H-5a(eq)], 1.50 and 1.46 (2 s, each 3 H, CMe_2), 1.11 [ddd, 1 H, $J_{5,5a(ax)}$ 12.9, J_{5agem} 13.2 Hz, H-5a(ax)]. HREIMS: Calcd for $C_{19}H_{24}O_6$ [M^+]: 348.1573; Found: 348.1567.

Octyl 4,6-O-benzylidene-1,2-O-isopropylidene-5a-carba-β-D-glucopyranoside (**13**).—To dry DMF (7 mL) were added, in turn, hexane-washed NaH (106 mg, 2.63 mmol) and a solution of **11** (404 mg, 1.32 mmol) in DMF (12 mL) under argon, and the resulting mixture was stirred for 30 min at 0 °C. 1-Bromooctane (0.457 mL, 2.63 mmol) was then added to the mixture, which was stirred for 5 h at room temperature. After addition of a small amount of MeOH, the mixture was diluted with EtOAc (100 mL), and the solution was washed thoroughly with brine, dried, and evaporated. The residue was chromatographed on silica gel (25 g, 1:15 acetone–hexane) to give **13** (439 mg, 79.5%) as crystals: mp 57–58 °C; $[\alpha]_D^{20}$ −27° (*c* 1.5, $CHCl_3$); R_f 0.43 (1:4 acetone–hexane); ^{1}H NMR (CD_3OD): δ 7.60–7.25 (m, 5 H, Ph), 5.58 (s, 1 H, PhC*H*), 4.18 (dd, 1 H, $J_{5,6a}$ 3.7, J_{6gem} 10.7 Hz, H-6a), 3.83–3.40 (m, 7 H, H-1, H-2, H-3, H-4, H-6b, OCH_2), 2.03–1.82 [m, 2 H, H-5, H-5a(eq)], 1.62–1.53 [m, 2 H, OCH_2CH_2], 1.47 and 1.45 (2 s, each 3 H, CMe_2), 1.40–1.15 [m, 10 H, $(CH_2)_5Me$], 1.08 [ddd, 1 H, $J_{1,5a(ax)}$ 10.1, $J_{5,5a(ax)}$ 12.9, J_{5agem} 13.2 Hz, H-5a(ax)], 0.88 (t, 3 H, *J* 6.6 Hz, CH_2CH_3). HREIMS: Calcd for $C_{25}H_{38}O_5$ [M^+]: 418.2719; Found: 418.2746.

Octyl 2,3,4,6-tetra-O-acetyl-5a-carba-β-D-glucopyranoside (**14**).—Compound **13** (387 mg, 0.93 mmol) was treated with 80% aq HOAc (10 mL) for 1 h at 50 °C. A mixture was evaporated to dryness, and the residue was acetylated conventionally to give, after chromatography on silica gel (20 g, 1:4 EtOAc–hexane), **14** (424 mg, 98%) as a syrup: $[\alpha]_D^{20}$ +0.2° (*c* 2.5, $CHCl_3$); R_f 0.38 (1:2 EtOAc–hexane); ^{1}H NMR (CD_3OD): δ 5.04–4.88 (m, 3 H, H-2, H-3, H-4), 4.00 (dd, 1 H, $J_{5,6a}$ 5.6, J_{6gem} 11.6 Hz, H-6a), 3.89 (dd, 1 H, $J_{5,6b}$ 5.6 Hz, H-6b), 3.60–3.58 (m, 2 H, OCH_2), 3.39–3.22 (m, 2 H, OCH_2), 2.08 [ddd, 1 H, $J_{1,5a(eq)} = J_{5,5a(eq)} = 4.2$, J_{5agem} 13.2 Hz, H-5a(eq)], 1.99, 1.97, 1.95, and 1.92 (4 s, each 3 H, 4 × Ac), 1.95–1.80 (m, 1 H, H-5), 1.50–1.30 [m, 3 H, H-5a(ax), OCH_2] 1.30–1.10 [m, 10 H, $(CH_2)_5CH_3$], 0.81 (t, 3 H, *J* 6.1 Hz, CH_2CH_3). HREIMS: Calcd for $C_{23}H_{38}O_9$ [M^+]: 458.2515; Found: 458.2530.

Octyl 5a-carba-β-D-glucopyranoside (**1**).—A solution of **14** (387 mg, 0.84 mmol) in MeOH (2 mL) was treated with 1 M methanolic NaOMe (0.8 mL) at room temperature for 2 h. After neutralization with Amberlite IR-120B (H^+) resin, the mixture was evaporated, and the residue was chromatographed on silica gel (15 g, 1:20 MeOH–$CHCl_3$) to give **1** (215 mg, 88%) as crystals: mp 83–84 °C; $[\alpha]_D^{19}$ −14° (*c* 0.9, 1:1 MeOH–$CHCl_3$); R_f 0.16 (1:10 MeOH–$CHCl_3$), ^{1}H NMR (CD_3OD): δ 3.77–3.70 (m, 2 H, H-6a, OH), 3.54–3.26 (m, 5 H, H-2, H-3, H-4, H-6b, OCH_2), 3.20 (m, 1 H, H-1), 3.06, 2.92, and 2.76 (3 br s, each 1 H, 3 × OH), 1.99 [ddd, 1 H, $J_{1,5a(eq)} = J_{5,5a(eq)} = 4.2$, J_{5agem} 13.4 Hz, H-5a(eq)], 1.80–1.65 (m, 1 H, H-5), 1.65–1.50 (m, 2 H, OCH_2CH_2), 1.40–1.20 [m, 10 H, $(CH_2)_5CH_3$], 1.04 [ddd, $J_{1,5a(ax)}$ 11.7 Hz, H-5a(ax)], 0.81 (t, 3 H, *J* 7.1 Hz, CH_2CH_3). HREIMS: Calcd for $C_{15}H_{30}O_5$ [M^+]: 290.2093; Found: 290.2116.

4,6-O-Benzylidene-5a-carba-α-D-galactopyranose (**15**).—A solution of **7** (12.7 g, 32.8 mmol) in MeOH (50 mL) was treated with methanolic NaOMe (10 mL) for 2 h at room temperature. After neutralization with Amberlite IR-120B (H^+) resin, the mixture as evaporated to dryness. The residue was dissolved in DMF (50 mL), and α,α-dimethoxytoluene (6.8 mL, 46 mmol) and *p*-TsOH·H_2O (1.1 g, 6.4 mmol) were added to it, and the mixture was stirred for 3 h at 50 °C under diminished pressure (water aspirator). After neutralization with Et_3N, the mixture was evaporated, and the residue was chromatographed (silica gel 400 g, 1:20 MeOH–$CHCl_3$) to give **15** (4.95 g, 56.7%) as crystals: mp 155.5–157 °C; $[\alpha]_D^{20}$ +46.5° (*c* 1.0, MeOH); R_f 0.54 (1:10 MeOH–$CHCl_3$); ^{1}H NMR (CD_3OD): δ 7.55–7.25 (m, 5 H, Ph), 5.52 (s, 1 H, C*H*Ph), 4.25 (br s, 1 H, H-4), 4.19–4.06 (m, 2 H, H-1, H-6a), 3.91 (m, 1 H, H-6b), 3.82 (dd, 1 H, $J_{2,3}$ 10.1, $J_{3,4}$ 2.7 Hz, H-3), 3.71 (dd, 1 H, $J_{1,2}$ 2.4 Hz, H-2), 2.34 [ddd, 1 H, $J_{1,5a(eq)}$ 2.0, $J_{5,5a(eq)}$ 12.0, J_{5agem} 13.9 Hz, H-5a(eq)], 1.99–1.88 (m, 1 H, H-5), 1.65 [m, 1 H, H-5a(ax)]. HREIMS: Calcd for $C_{14}H_{18}O_5$ [M^+]: 266.1154; Found: 266.1184.

3-O-Acetyl-4,6-O-benzylidene-1,2-O-isopropylidene-5a-carba-α-D-galactopyranose (**16**) *and 1-O-acetyl-4,6-O-benzylidene-2,3-O-isopropylidene-5a-carba-α-D-galactopyranose acetate* (**17**).—To a solution of **15** (242 mg, 0.91 mmol) in DMF (4.8 mL) were added 2-methoxypropene (0.45 mL, 4.7 mmol) and *p*-TsOH·H_2O (31 mg, 0.18 mmol), and the mixture was stirred for 30 min at 0 °C. After neutralization with Et_3N, the mixture was evaporated, and the residue was chromatographed (silica gel 5 g, 1:2 acetone–hexane) to give an inseparable mixture of the expected alcohols. The mixture was acetylated conventionally, and the products were chromatographed on silica gel (1:10 → 1:5 EtOAc–hexane) to give **16** (111 mg, 38%), as a syrup, and **17** (173 mg, 59%), as crystals. Data for **16**: $[\alpha]_D^{22}$ +131° (*c* 1.1, $CHCl_3$); R_f 0.48 (1:2 EtOAc–hexane); ^{1}H NMR (CD_3OD): δ 7.48–7.35 (m, 5 H, Ph), 5.44 (s, 1 H, CHPh), 4.72 (dd, 1 H, $J_{2,3}$ 8.6, $J_{3,4}$ 2.9 Hz, H-3), 4.47 (m, 1 H, H-1), 4.31–4.27 (m, 2 H, H-2, H-4), 4.10 (dd, 1 H, $J_{5,6a}$ 2.4, J_{6gem} 11.5 Hz, H-6a), 3.97 (dd, 1 H, $J_{5,6b}$ 1.2 Hz, H-6b), 2.63 [dd, 1 H, $J_{1,5a(ax)}$ 4.4, $J_{5,5a(ax)}$ 12.5, J_{5agem} 15.4 Hz, H-5a(ax)], 2.20–2.04 [m, 1 H, H-5a(eq)], 2.14 (s, 3 H, Ac), 2.03–1.94 (m, 1 H, H-5), 1.52 and 1.38 (2 br s, each 3 H, CMe_2). HREIMS: Calcd for $C_{19}H_{24}O_6$ [M^+]: 348.1573; Found: 348.1579. Data for **17**: mp 106–107 °C; $[\alpha]_D^{22}$ +44° (*c* 1.1, $CHCl_3$); R_f 0.38 (1:2 EtOAc–hexane); ^{1}H NMR (CD_3OD): δ 7.49–7.26 (m, 5 H, Ph), 5.55 (s, 1 H, CHPh), 5.60–5.45 (m, 1 H, H-1), 4.58 (m, 1 H, H-4), 4.19 (dd, 1 H, $J_{1,2}$ 2.6, $J_{2,3}$ 9.9 Hz, H-2), 4.17 (dd, 1 H,

$J_{5,6a}$ 2.9, J_{6gem} 11.7 Hz, H-6a), 4.01 (dd, 1 H, $J_{3,4}$ 2.5 Hz, H-3), 4.04–3.95 (m, 1 H, H-6b), 2.37 [ddd, 1 H, $J_{1,5a(ax)}$ 2.9, $J_{5,5a(ax)}$ 12.7, J_{5agem} 17.6 Hz, H-5a(ax)], 2.10 (s, 3 H, Ac), 1.95–1.85 [m, 1 H, H-5a(eq)], 1.85–1.75 (m, 1 H, H-5), 1.45 and 1.44 (2 s, each 3 H, CMe_2). HREIMS: Calcd for $C_{19}H_{24}O_6$ [M^+]: 348.1573; Found: 348.1562.

1-O-*Methanesulfonyl-2,3,4,6-tetra*-O-*methoxymethyl-5a-carba-α*-D-*galactopyranose* (**18**).—Compound **17** (12 mg, 33 μmol) was treated with 1 M methanolic NaOMe (0.2 mL) in MeOH (1.0 mL) for 1 h at room temperature. After careful neutralization with Amberlite IR-120B (H^+) resin, the mixture was evaporated. The residue was dissolved in pyridine (1.0 mL) and treated with methanesulfonyl chloride (7.7 μL, 0.10 μmol) for 22 h at room temperature. The mixture was evaporated after addition of a small amount of MeOH, and the residue was dissolved in EtOAc (15 mL). The solution was washed with brine, dried, and evaporated. The residue was treated with 80% aq HOAc (1 mL) for 1 h at 60 °C, and the mixture was evaporated. The residual product was dissolved in CH_2Cl_2 (1.0 mL) and treated with chloromethylmethyl ether (28 μL, 0.27 μmol) and *N*,*N*-diisopropylethylamine (32 μL, 0.27 μmol) for 12 h at 40 °C. The mixture was extracted with $CHCl_3$ (15 mL), and the solution was thoroughly washed with water. The product was chromatographed (0.5 g, 1:3 acetone–hexane) to give **18** (9.7 mg, 67%) as a syrup: $[\alpha]_D^{22}$ +11° (*c* 2.7, $CHCl_3$); R_f 0.35 (1:2 acetone–hexane); ^{1}H NMR (CD_3OD): δ 5.17–5.10 (s, 1 H, H-1), 4.85–4.60 (m, 8 H, 4 × OCH_2), 4.13 (m, 1 H, H-4), 4.05 (dd, 1 H, $J_{5,6a}$ 2.9, J_{6gem} 10.3 Hz, H-6a), 3.86 (dd, 1 H, $J_{5,6b}$ 2.4 Hz, H-6b), 3.55–3.46 (m, 14 H, H-2, H-3, 4 × OCH_3), 3.12 (s, 3 H, Ms), 2.28–2.15 (m, 1 H, H-5), 1.91 [ddd, 1 H, $J_{1,5a(eq)} = J_{5,5a(eq)}$ 3.7, J_{5agem} 14.4 Hz, H-5a(eq)], 1.11 [m, 1 H, H-5a(ax)]. HREIMS: Calcd for $C_{16}H_{32}O_{11}$ [M^+]: 432.1666; Found: 432.1636.

On a preparative scale, starting from **17** (1.39 g, 3.99 mmol), a syrupy sample of compound **18** (0.894 g, 52%) was obtained.

1-O-*Acetyl-2,3,4,6-tetra*-O-*methoxymethyl-5a-carba-β*-D-*galactopyranose* (**19**).—A mixture of **18** (795 mg, 1.83 mmol), KOAc (3.6 g, 37 mmol), and DMF (16 mL) was stirred for 2 days at 100 °C. The cooled mixture was diluted with EtOAc (150 mL), and the resulting solution washed with brine, dried, and evaporated. The residue was chromatographed on silica gel (40 g, 1:10 acetone–hexane) to give **19** (562 mg, 77%) as a syrup: $[\alpha]_D^{22}$ +52° (*c* 1.0, $CHCl_3$); R_f 0.59 (1:2 acetone–hexane); ^{1}H NMR (CD_3OD): δ 5.17–5.10 (s, 1 H, H-1), 4.88–4.58 (m, 8 H, 4 × OCH_2), 4.08 (m, 1 H, H-4), 3.96 (dd, 1 H, $J_{1,2}$ 9.6, $J_{2,3}$ 8.8 Hz, H-2), 3.53 (dd, 1 H, $J_{5,6a}$ 2.2, J_{6gem} 9.8 Hz, H-6a), 3.49 (dd, $J_{3,4}$ 8.8 Hz, H-3), 3.47–3.30 (m, 13 H, H-6b, 4 × OCH_3), 2.08 (s, 3 H, Ac), 1.90–1.76 [m, 2 H, H-5, H-5a(eq)], 1.52 [m, 1 H, H-5a(ax)]. HREIMS: Calcd for $C_{17}H_{32}O_{10}S$ [M^+]: 396.1996; Found: 396.1985.

2,3,4,6-Tetra-O-*methoxymethyl-5a-carba-β*-D-*galactopyranose* (**20**).—Compound **19** (533 mg, 1.34 mmol) was treated with 1 M NaOMe (0.53 mL) in MeOH (2.7 mL) for 2 h at room temperature. The product was chromatographed (silica gel 20 g, 1:4 acetone–hexane) to give **20** (420 mg, 88%) as a syrup: R_f 0.30 (1:2 acetone–hexane); $[\alpha]_D^{22}$ −51° (*c* 1.1, $CHCl_3$); ^{1}H NMR (CD_3OD): δ 4.80–4.52 (m, 8 H, 4 × OCH_2), 4.10–3.90 (m, 2 H, H-2, H-4), 3.60–3.20 (m, 16 H, H-1, H-3, H-6,6, 4 × OCH_3), 3.12 (s, 3 H, Ms), 1.82–1.65 [m, 2 H, H-5, H-5a(eq)], 1.45 [ddd, 1 H, $J_{1,5a(ax)} = J_{5,5a(ax)}$ 11.2, J_{5agem} 13.4 Hz, H-5a(ax)]. HREIMS: Calcd for $C_{13}H_{25}O_8$ [$M - CH_2OCH_3$]: 309.1549; Found: 309.1543.

Dodecyl 2,3,4,6-tetra-O-*methoxymethyl-5a-carba-β*-D-*galactopyranoside* (**21**).—A solution of **20** (171 mg, 0.48 mmol) in DMF (5.0 mL) was treated with NaH (58 mg, 1.45 mmol) for 30 min at 0 °C as in the preparation of **13**. Then 1-bromododecane (0.35 mL, 1.45 mmol) was added to it, and the resulting mixture was stirred for 27 h at room temperature. After addition of a small amount of MeOH, the mixture was diluted with EtOAc (60 mL), and the solution was washed with brine, dried, and evaporated. The residue was chromatographed (silica gel 15 g, 1:8 EtOAc–toluene) to give **21** (198 mg, 79%) as a syrup: R_f 0.52 (1:2 acetone–hexane); $[\alpha]_D^{22}$ −20° (*c* 1.1, $CHCl_3$); ^{1}H NMR (CD_3OD): δ 4.88–4.56 (m, 8 H, 4 × OCH_2), 4.03 (m, 1 H, H-4), 3.83 (ddd, 1 H, $J_{1,2} = J_{2,3}$ 9.5 Hz, H-2), 3.63–3.48 (m, 4 H, H-6,6, OCH_2CH_2), 3.48–3.15 (m, 14 H, H-1, H-3, 4 × OCH_3), 1.83 [m, 1 H, H-5a(eq)], 1.75–1.48 [m, 4 H, H-5, H-5a(ax), OCH_2CH_2], 1.34–1.18 [m, 18 H, $OCH_2CH_2(CH_2)_9$], 0.88 (t, 3 H, *J* 6.8 Hz, CH_2CH_3). HREIMS: Calcd for $C_{25}H_{49}O_8$ [$M - CH_2OCH_3$]: 477.3427; Found: 477.3428.

Dodecyl 2,3,4,6-tetra-O-*acetyl-5a-carba-β*-D-*galactopyranoside* (**22**).—A solution of **21** (186 mg, 0.35 mmol) in 4 M HCl (5.5 mL) was stirred for 3 h at 60 °C, and then evaporated. The residue was acetylated conventionally, and the product was chromatographed on silica gel (12 g, 1:10 acetone–hexane) to give **22** (132 mg, 72%) as a syrup: $[\alpha]_D^{22}$ −8° (*c* 0.9, $CHCl_3$); R_f 0.46 (1:2 EtOAc–hexane); ^{1}H NMR (CD_3OD): δ 5.45 (m, 1 H, H-4), 5.29 (dd, 1 H, $J_{1,2} = J_{2,3}$ 10.5 Hz, H-2), 4.84 (dd, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 4.10–3.87 (m, 2 H, H-6,6), 4.88–4.56 (m, 8 H, 4 × OCH_2), 4.03 (m, 1 H, H-4), 3.68–3.29 (m, 3 H, H-1, OCH_2CH_2), 2.10, 2.05, 2.04, and 1.98 (4 s, each 3 H, 4 × Ac), 2.10–1.90 [m, 2 H, H-5, H-5a(eq)], 1.65–1.45 [m, 3 H, H-5a(ax), OCH_2CH_2], 1.32–1.24 [m, 18 H, $OCH_2CH_2(CH_2)_9$], 0.88 (t, 3 H, *J* 6.8 Hz, CH_2CH_3). HREIMS: Calcd for $C_{27}H_{46}O_9$ [M^+]: 514.3142; Found: 514.3143.

Dodecyl 5a-carba-β-D-*galactopyranoside* (**2**).—Compound **22** (94 mg, 0.18 mmol) was treated with 1 M methanolic NaOMe (0.4 mL) in 1:2 MeOH–$CHCl_3$ (2

mL) for 2 h at room temperature. The product was chromatographed on silica gel (5 g, 1:20 MeOH–$CHCl_3$) to give **2** (58 mg, 92%) as crystals: mp 78–79 °C; $[\alpha]_D^{22}$ −22° (*c* 0.6, 1:1 MeOH–$CHCl_3$); R_f 0.46 (1:2 MeOH–$CHCl_3$); ^{1}H NMR (CD_3OD): δ 3.95 (m, 1 H, H-4), 3.88–3.65 (m, 5 H, H-2, H-6,6, OCH_2CH_2), 3.26 (m, 1 H, H-3), 3.10 [ddd, 1 H, $J_{1,2}$ 9.4, $J_{1,5a(ax)}$ 10.3, $J_{1,5a(eq)}$ 4.9 Hz, H-1], 1.73 [m, 1 H, H-5a(eq)], 1.60–1.45 (m, 3 H, H-5, OCH_2CH_2), 1.37 [m, 1 H, H-5a(ax)], 1.28–1.17 [m, 18 H, $OCH_2CH_2(CH_2)_9$], 0.80 (t, 3 H, *J* 6.1 Hz, CH_2CH_3). HREIMS: Calcd for $C_{19}H_{38}O_5$ [M^+]: 346.2719; Found: 346.2726.

*4,6-*O*-Benzylidene-2-deoxy-2-nitro-5a-carba-β-*D*-glucopyranose* (**23**) *and 4,6-*O*-benzylidene-2-deoxy-2-nitro-5a-carba-β-*D*-gulopyranose* (**24**).—To a solution of **8** (2.49 g, 9.3 mmol) in water (100 mL) were added, in turn, $NaHCO_3$ (1.49 g, 17 mmol) and $NaIO_4$ (6.97 g, 32.5 mmol), and the resulting mixture was stirred for 5 h at room temperature. Precipitates were removed by filtration, and the filtrate was evaporated. The residue was dissolved in MeOH (75 mL), and the solution was treated with nitromethane (1.66 mL, 31 mmol) and 1 M methanolic NaOMe (6.6 mL) for 12 h at room temperature. After neutralization with Amberlite IR-120B (H^+) resin, the mixture was evaporated. The residual products were chromatographed on a silica gel column (180 g, 1:40 MeOH–$CHCl_3$) to give **23** (1.55 g, 56%) as an amorphous solid and **24** (0.49 g, 18%) as a syrup.

Data for **23**: R_f 0.48 (1:15 MeOH–$CHCl_3$); IR (KBr): *v* 3400, 1560, 1370 cm^{-1}. HREIMS: Calcd for $C_{14}H_{17}NO_6$ [M^+]: 295.1056; Found 295.1055. **24**: R_f 0.55 (1:15 MeOH–$CHCl_3$); IR (neat): *v* 3400, 1550, 1380 cm^{-1}. HREIMS: Calcd for $C_{14}H_{17}NO_6$ [M^+]: 295.1056; Found 295.1061.

*2-Acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-5a-carba-β-*D*-glucopyranose acetate* (**25**).—A solution of **23** (1.47 g, 4.98 mmol) in MeOH (50 mL) containing Ac_2O (2.1 mL, 22.0 mmol) was hydrogenated for 40 h at room temperature in the presence of Raney nickel T-4 (three-microspoonfuls) in a Parr shaker-type apparatus and using an initial hydrogen pressure of ~250 kPa. The catalyst was removed by filtration and the filtrate was evaporated. The residue was acetylated conventionally, and the product was chromatographed on silica gel (130 g, 1:2 acetone–hexane) to give **25** (1.3 g, 67%) as crystals: mp 232–233 °C; $[\alpha]_D^{27}$ −33° (*c* 1.0, $CHCl_3$); R_f 0.34 (1:3 acetone–toluene); IR (KBr): 3305, 1740, 1665, 1540 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.50–7.27 (m, 5 H, Ph), 5.77 (d, 1 H, $J_{2,NH}$ 9.8 Hz, NH), 5.52 (s, 1 H, C*H*Ph), 5.08 (dd, 1 H, $J_{2,3} = J_{3,4} = 10.0$ Hz, H-3), 4.86 (ddd, 1 H, $J_{1,2}$ 10.3, $J_{1,5a(ax)}$ 11.0, $J_{1,5a(eq)}$ 4.9 Hz, H-1), 4.28 (ddd, 1 H, H-2), 4.14 (dd, 1 H, $J_{5,6a}$ 4.4, J_{6gem} 11.0 Hz, H-6a), 3.71–3.58 (m, 2 H, H-4, H-6b), 2.08, 2.04, and 2.02 (3 s, each 3 H, 3 × Ac), 1.71 (m, 1 H, H-5), 1.36–1.20 (m, 2 H, H-5a,5a). HREIMS: Calcd for $C_{20}H_{25}NO_7$ [M^+]: 391.1631; Found 391.1620.

*Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-5a-carba-β-*D*-glucopyranoside* (**26**).—Compound **25** (1.16 g, 2.96 mmol) was O-deacetylated with 1 M NaOMe (2.3 mL) in MeOH (23 mL) as in the preparation of **8** to give **26** (0.91 g, ~100%) as crystals: mp 215–226 °C; $[\alpha]_D^{20}$ +65° (*c* 1.2, MeOH); R_f 0.13 (1:10 MeOH–$CHCl_3$); IR (KBr): *v* 3445, 3275, 1650, 1575 cm^{-1}; ^{1}H NMR (CD_3OD): δ 7.55–7.30 (m, 5 H, Ph), 5.80 (s, 1 H, C*H*Ph), 4.14 (dd, 1 H, $J_{5,6a}$ 3.9, J_{6gem} 10.7 Hz, H-6a), 3.75–3.62 (m, 2 H, H-2, H-3), 3.62–3.45 (m, 3 H, H-1, H-4, H-6b), 2.01 (s, 3 H, Ac), 1.86–1.70 [m, 1 H, H-5, H-5a(eq)], 1.21 [ddd, 1 H, $J_{1,5a(ax)} = J_{5,5a(ax)} =$ 9.8, J_{5agem} 13.3 Hz, H-5a(ax)]. HREIMS: Calcd for $C_{16}H_{21}NO_5$ [M^+]: 307.1420; Found 307.1430.

*Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-5a-carba-β-*D*-glucopyranoside* (**27**), *2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-5a-carba-β-*D*-glucopyranose* (**29**), *and benzyl 2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-5a-carba-β-*D*-glucopyranoside* (**31**).—To a solution of **26** (32 mg, 0.14 mmol) in DMF (1.0 mL) was added NaH (11 mg, 0.27 mmol), and the mixture was stirred for 30 min at 0 °C. After addition of benzyl bromide (18.2 μL, 0.15 mmol), the mixture was stirred for 1 h at 0 °C, and then the reaction was quenched by addition of small amount of MeOH. The mixture was evaporated and the residue was chromatographed on silica gel (5 g, 1:2 acetone–toluene) to give **31** (21 mg, 32%), **27** (2 mg, 3%), **29** (22 mg, 41%), and recovered **26** (10 mg) remained unchanged. Data for **27**: mp 200–201 °C; $[\alpha]_D^{25}$ −50° (*c* 0.8, $CHCl_3$); R_f 0.38 (1:10 MeOH–$CHCl_3$); IR (neat): *v* 3450, 3305, 1650, 1555 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.50–7.20 (m, 10 H, 2 × Ph), 5.49 (s, 1 H, CHPh), 5.42 (d, 1 H, $J_{2,NH}$ 6.6 Hz, NH), 4.64 and 4.34 (ABq, J_{gem} 12.0 Hz, CH_2Ph), 4.12 (dd, 1 H, $J_{5,6a}$ 4.4, J_{6gem} 11.2 Hz, H-6a), 4.04 (br s, 1 H, OH), 3.70 (ddd, 1 H, $J_{1,2} = J_{2,3} = 9.4$ Hz, H-2), 3.67–3.38 (m, 4 H, H-1, H-3, H-4, H-6b), 1.90 (s, 3 H, Ac), 1.93 [m, 1 H, H-5a(eq)], 1.70 (m, 1 H, H-5), 1.17 [m, 1 H, H-5a(ax)]. HREIMS: Calcd for $C_{23}H_{27}NO_5$ [M^+]: 397.1889; Found: 397.1889. Data for **29**: mp 217–218 °C; R_f 0.31 (1:10 MeOH–$CHCl_3$); $[\alpha]_D^{22}$ +30° (*c* 0.8, $CHCl_3$); IR (neat): *v* 3450, 3305, 1650, 1555 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.55–7.34 (m, 10 H, 2 × Ph), 5.61 (s, 1 H, CHPh), 5.35 (d, 1 H, $J_{2,NH}$ 3.4 Hz, NH), 5.00 (br s, 1 H, OH), 4.94 and 4.69 (ABq, J_{gem} 12.2 Hz, CH_2Ph), 4.18 (dd, 1 H, $J_{5,6a}$ 4.2, J_{6gem} 11.0 Hz, H-6a), 3.75–3.50 (m, 4 H, H-1, H-2, H-4, H-6b), 3.44 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.6$ Hz, H-3), 1.84 (s, 3 H, Ac), 1.90–1.72 [m, 2 H, H-5, H-5a(eq)], 1.17 [m, 1 H, H-5a(ax)]. HREIMS: Calcd for $C_{23}H_{27}NO_5$ [M^+]: 397.1889; Found: 397.1887. Data for **31**: mp 210.5–212 °C; $[\alpha]_D^{22}$ −15° (*c* 2.4, $CHCl_3$); R_f 0.48 (1:10 acetone–toluene); IR (neat): *v* 3290, 1650, 1555 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.55–7.20 (m, 10 H, 2 × Ph), 5.57 (s, 1 H, CHPh), 5.27 (d, 1 H, $J_{2,NH}$ 7.8 Hz, NH), 4.91 and 4.43 (ABq, J_{gem} 11.7 Hz, CH_2Ph), 4.17 (dd, 1 H, $J_{5,6a}$

4.4, J_{6gem} 11.0 Hz, H-6a), 3.88 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 3.70–3.50 (m, 3 H, H-2, H-4, H-6b), 1.87 (s, 3 H, Ac), 1.98–1.76 [m, 2 H, H-5, H-5a(eq)], 1.08 [ddd, 1 H, J_{5agem} 12.5 Hz, H-5a(ax)]. HREIMS: Calcd for $C_{30}H_{33}NO_5$ [M^+]: 487.2359; Found: 487.2362.

*Benzyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-5a-carba-β-*D*-glucopyranoside* (**28**).—Compound **27** (1.8 mg, 4.5 mmol) was acetylated conventionally, and the product was chromatographed on silica gel (1.5 g, 1:2 acetone–hexane) to give **28** (2.0 mg, ~100%) as crystals: mp 214–215 °C; $[\alpha]_D^{25}$ −61° (*c* 1.1, $CHCl_3$); R_f 0.53 (1:2 acetone–toluene); IR (neat): *v* 3295, 1635, 1560 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.50–7.20 (m, 10 H, 2 × Ph), 5.51 (s, 1 H, C*H*Ph), 5.35 (d, 1 H, $J_{2,NH}$ 9.5 Hz, NH), 4.97 (dd, 1 H, $J_{2,3} = J_{3,4} = 10.1$ Hz, H-3), 4.66 and 4.38 (ABq, J_{gem} 12.1 Hz, CH_2Ph), 4.23 (m, 1 H, H-2), 4.19 (dd, 1 H, $J_{5,6a}$ 4.4, J_{6gem} 11.0 Hz, H-6a), 3.66 (ddd, 1 H, $J_{5,6b}$ 10.9 Hz, H-6b), 3.64 (dd, 1 H, $J_{4,5}$ 10.1 Hz, H-4), 3.32 [ddd, 1 H, $J_{1,2} = J_{1,5a(ax)} =$ 10.5, $J_{1,5a(eq)}$ 4.4 Hz, H-1], 2.05 and 1.92 (2 s, each 3 H, 2 × Ac), 1.92–1.80 [m, 2 H, H-5, H-5a(eq)], 0.87 [m, 1 H, H-5a(ax)]. HREIMS: Calcd for $C_{25}H_{23}NO_6$ [M^+]: 439.1995; Found: 439.1997.

*2-Acetamido-1-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-5a-carba-β-*D*-glucopyranose* (**30**).—Compound **29** (17 mg, 0.043 mmol) was acetylated conventionally, and the product was chromatographed on silica gel (1.5 g, 1:2 acetone–hexane) to give **30** (19 mg, ~100%) as crystals: mp 208–209 °C; $[\alpha]_D^{20}$ +15° (*c* 0.8, $CHCl_3$); R_f 0.47 (1:2 acetone–toluene); ^1H NMR ($CDCl_3$): δ 7.55–7.25 (m, 10 H, 2 × Ph), 5.59 (s, 1 H, C*H*Ph), 5.14 (d, 1 H, $J_{2,NH}$ 9.5 Hz, NH), 4.91 and 4.67 (ABq, J_{gem} 12.0 Hz, CH_2Ph), 4.81 [ddd, 1 H, $J_{1,2}$ 9.3, $J_{1,5a(ax)}$ 11.0, $J_{1,5a(eq)}$ 4.6 Hz, H-1], 4.18 (dd, 1 H, $J_{5,6a}$ 4.4, J_{6gem} 11.2 Hz, H-6a), 4.08 (ddd, 1 H, $J_{1,2} = J_{2,3} =$ 9.3 Hz, H-2), 3.72 (dd, 1 H, $J_{3,4}$ 9.6, $J_{4,5}$ 11.0 Hz, H-4), 3.64 (ddd, 1 H, $J_{5,6b}$ 11.0 Hz, H-6b), 3.47 (dd, 1 H, H-3), 2.02 and 1.84 (2 s, each 3 H, 2 × Ac), 1.98–1.70 [m, 2 H, H-5, H-5a(eq)], 1.27 [ddd, 1 H, $J_{5,5a(ax)}$ 11.2, J_{5agem} 12.5 Hz, H-5a(ax)]. HREIMS: Calcd for $C_{25}H_{23}NO_6$ [M^+]: 439.1995; Found: 439.1990.

*Dodecyl 2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-5a-carba-β-*D*-glucopyranoside* (**32**).—Compound **29** (36.0 mg, 0.091 mmol) was treated with 1-bromododecane (43.4 μL, 0.18 mmol) in the presence of NaH (7.2 mg, 0.18 mmol) in DMF (1.0 mL) as in the preparation of **13**. The product was chromatographed on silica gel (4 g, 1:3 EtOAc–hexane) to give **32** (35.0 mg, 68%) as crystals: mp 97–98 °C; $[\alpha]_D^{25}$ −5° (*c* 1.0, $CHCl_3$); R_f 0.47 (1:2 acetone–toluene); IR (neat): *v* 3280, 2915, 2855, 1650, 1555 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.50–7.10 (m, 10 H, 2 × Ph), 5.50 (s, 1 H, C*H*Ph), 5.40 (d, 1 H, $J_{2,NH}$ 7.8 Hz, NH), 4.84 and 4.56 (ABq, J_{gem} 12.0 Hz, CH_2Ph), 4.10 (dd, 1 H, $J_{5,6a}$ 3.9, J_{6gem} 11.2 Hz, H-6a), 3.87 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H-3), 3.64–3.18 (m, 6 H, H-1, H-2, H-4, H-6b, OCH_2), 1.83 (s, 3 H, Ac), 1.85–1.60 [m, 2 H, H-5, H-5a(eq)], 1.48–1.30 (m, 2 H, OCH_2CH_2), 1.28–1.00 [m, 18 H, $(CH_2)_9CH_3$], 0.92 [m, 1 H, $J_{5,5a(ax)}$ 11.0, J_{5agem} 13.2 Hz, H-5a(ax)]. 0.81 (t, 3 H, *J* 6.8 Hz, CH_2CH_3). HREIMS: Calcd for $C_{28}H_{44}NO_5$ [M − Bzl]: 474.3279; Found: 474.3217.

*Dodecyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-5a-carba-β-*D*-glucopyranoside* (**33**).—A solution of **32** (217 mg, 0.38 mmol) in a mixture (22 mL) in 1:1 EtOH–EtOAc containing 1 M aq HCl (0.2 mL) was hydrogenolyzed in the presence of 10% Pd/C (two-microspoonfuls) in an atmospheric pressure of hydrogen. After removal of the catalyst, the solution was evaporated, and the residue was acetylated conventionally. The product was chromatographed on silica gel (15 g, 1:3 acetone–hexane) to give **33** (187 mg, 95%) as a colorless syrup: $[\alpha]_D^{25}$ −5° (*c* 1.3, $CHCl_3$); R_f 0.60 (1:2 acetone–toluene); IR (neat): *v* 3275, 2925, 2855, 1745, 1655, 1560 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.43 (d, 1 H, $J_{2,NH}$ 9.3 Hz, NH), 5.00 (dd, 1 H, $J_{2,3}$ 9.8, $J_{3,4}$ 10.3 Hz, H-3), 4.90 (dd, 1 H, $J_{4,5}$ 10.5 Hz, H-4), 4.03 (dd, 1 H, $J_{5,6a}$ 5.1, J_{6gem} 11.2 Hz, H-6a), 3.93 (dd, 1 H, $J_{5,6b}$ 3.9, H-6b), 4.30–3.93 (m, 1 H, H-2), 3.60–3.25 (m, 3 H, H-1, OCH_2), 2.03, 1.98, and 1.91 (3 s, 3, 6, 3 H, 4 × Ac), 2.00–1.80 (m, 1 H, H-5), 1.55–1.45 [m, 3 H, H-5a(ax), OCH_2CH_2], 1.30–1.19 [m, 18 H, $(CH_2)_9CH_3$], 0.84 (t, 3 H, *J* 6.6 Hz, CH_2CH_3). HREIMS: Calcd for $C_{27}H_{47}NO_8$ [M^+]: 513.3301; Found: 513.3305.

*Dodecyl 2-acetamido-2-deoxy-5a-carba-β-*D*-glucopyranoside* (**3**).—Compound **35** (162 mg, 0.32 mmol) was O-deacetylated in a mixture (2 mL) of 1:2 MeOH–CH_2Cl_2 with 1 M methanolic NaOMe (0.4 mL). The product was chromatographed on silica gel (6 g, gradient 1:20 → 1:10 MeOH–$CHCl_3$) to give **3** (120 mg, 99%) as crystals: mp 72–73 °C; $[\alpha]_D^{25}$ −9° (*c* 1.2, 1:1 MeOH–$CHCl_3$); R_f 0.60 (1:2 acetone–toluene); IR (neat): *v* 3380, 3280, 2915, 2850, 1650, 1560 cm^{-1}; ^1H NMR (1:1 CD_3OD–$CDCl_3$): δ 3.78–3.15 (m, 8 H, H-1, H-2, H-3, H-4, H-6,6, OCH_2), 4.90 (dd, 1 H, $J_{3,4}$ 9.8, $J_{4,5}$ 10.5 Hz, H-4), 2.40–2.00 [m, 1 H, H-5a(eq)], 1.55–1.45 [m, 3 H, H-5a(ax), OCH_2CH_2], 1.40–1.16 [m, 18 H, $(CH_2)_9CH_3$], 0.84 (t, 3 H, *J* 6.1 Hz, CH_2CH_3). HREIMS: Calcd for $C_{21}H_{41}NO_5$ [M^+]: 387.2985; Found: 387.2989.

*Preparation of dodecyl 2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranoside* (**34**).—This compound was prepared conventionally by coupling of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with dodecanol in CH_2Cl_2 in the presence of silver perchlorate, silver carbonate, and 4 Å molecular sieves. The product was purified by chromatography on silica gel (1:4 EtOAc–hexane) to give colorless crystals: mp 53–54.5 °C; $[\alpha]_D^{20}$ −14° (*c* 1.1, $CHCl_3$); R_f 0.63 (1:3 acetone–toluene); ^1H NMR (CD_3OD) (inter alia): δ 5.21 (dd, 1 H, $J_{2,3}$ 8.8, $J_{3,4}$ 9.5 Hz, H-3), 5.09 (dd, 1 H, $J_{4,5}$ 9.8 Hz, H-4), 4.99 (1 H, $J_{1,2}$ 8.8 Hz, H-2), 4.49 (d, 1 H, H-1), 4.27 (dd, 1 H, $J_{5,6a}$ 4.6, J_{6gem} 12.5 Hz, H-6a), 4.13 (d, 1 H, $J_{5,6b}$ ~0 Hz,

H-6b), 2.09, 2.04, 2.03, and 2.01 (4 s, each 3 H, 4 × Ac), 0.88 (t, 3 H, *J* 6.8 CH_2CH_3). HREIMS: Calcd for $C_{24}H_{40}O_8$ [M − HOAc]: 456.2723; Found: 456.2726.

*Dodecyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-*D*-glucopyranoside* (**35**).—Compound **34** (11.0 g, 21.3 mmol) was O-deacetylated as in the preparation of **8**. The product was dissolved in DMF (100 mL) and treated with α,α-dimethoxytoluene (4.7 mL, 32 mmol) and *p*-TsOH·H_2O (0.73 g, 4.3 mmol) for 4.5 h at 50 °C under diminished pressure (water aspirator). The mixture was evaporated after treatment with Et_3N, and the residue was chromatographed on silica gel (300 g, 1:2 EtOAc–hexane) to give the 4,6-*O*-benzylidene derivative as a syrup. This compound was directly benzylated with benzyl bromide and NaH in DMF as in the preparation of **13**, and the product was chromatographed on silica gel (500 g, 1:30 EtOAc–hexane) to give **35** (10.1 g, 77%) as crystals: mp 78–79 °C; $[\alpha]_D^{21}$ −23° (*c* 1.4, $CHCl_3$); R_f 0.74 (1:3 EtOAc–hexane); ^{1}H NMR (CD_3OD): δ 7.51–7.20 (m, 15 H, 3 × Ph), 5.57 (s, 1 H, C*H*Ph), 4.91 (ABq, 2 H, J_{gem} 11.0 Hz, CH_2Ph), 4.80 (ABq, J_{gem} 11.5 Hz, CH_2Ph), 4.50 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.35 (dd, 1 H, $J_{5,6a}$ 4.9, J_{6gem} 10.5 Hz, H-6a), 3.88 and 3.56 (2 m, each 1 H, OCH_2), 3.79 (dd, 1 H, $J_{5,6b}$ 10.3 Hz, H-6b), 3.80–3.60 (m, 2 H, H-3, H-4), 3.46 (dd, 1 H, $J_{2,3}$ 7.6 Hz, H-2), 3.40 (m, 1 H, H-5), 1.71–1.58 (m, 2 H, OCH_2CH_2), 1.36–1.20 [m, 18 H, $(CH_2)_9CH_3$], 0.88 (t, 3 H, *J* 7.1 Hz, CH_2CH_3). HREIMS: Calcd for $C_{24}H_{40}O_8$ [M − Bzl]: 456.2723; Found: 456.2726.

*Dodecyl 2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**36**).—To a stirred suspension of **35** (3.99 g, 6.47 mmol) and 4 Å molecular sieves (16 g) in THF (240 mL) were added borane·Et_3N (2.92 g, 38.8 mmol) and $AlCl_3$ (5.18 g, 38.8 mmol) at 0 °C, and the mixture was stirred for 21 h at room temperature. An insoluble material was removed by filtration, and the filtrate was evaporated. The product was chromatographed on silica gel (300 g, 1:8 EtOAc–hexane) to give **36** (3.81 g, 95%) as crystals: mp 42–43 °C; $[\alpha]_D^{22}$ −12° (*c* 1.3, $CHCl_3$); R_f 0.38 (1:3 EtOAc–hexane); ^{1}H NMR (CD_3OD): δ 7.35–7.20 (m, 15 H, 3 × Ph), 4.95 and 4.71 (ABq, *J* 11.0 Hz), 4.93 and 4.73 (ABq, *J* 11.4 Hz), and 4.58 (m, 2 H) (3 × CH_2Ph), 4.40 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1), 3.98–3.88 (m, 1 H, OCH_2), 3.77 (dd, 1 H, $J_{5,6a}$ 2.4, J_{6gem} 10.4 Hz, H-6a), 3.69 (dd, 1 H, $J_{5,6b}$ 5.4 Hz, H-6b), 3.62–3.49 (m, 2 H, H-4, OCH_2), 3.49–3.36 (m, 3 H, H-2, H-3, H-5), 2.55 (m, 1 H, OH), 1.70–1.55 (m, 2 H, OCH_2CH_2), 1.42–1.20 [m, 18 H, $(CH_2)_9CH_3$], 0.86 (t, 3 H, *J* 5.6 Hz, CH_2CH_3). HREIMS: Calcd for $C_{32}H_{47}O_6$ [M − Bzl]: 527.3373; Found: 527.3373.

*Dodecyl 4-*O*-acetyl-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**37**).—Compound **36** (50 mg, 8.3 mmol) was acetylated conventionally, and the product was chromatographed on silica gel (5 g, EtOAc–hexane) to give **37** (47 mg, 88%) as a syrup: $[\alpha]_D^{22}$ −11° (*c* 1.3, $CHCl_3$); R_f 0.54 (1:3 EtOAc–hexane); ^{1}H NMR (CD_3OD): δ 7.35–7.20 (m, 15 H, 3 × Ph), 4.94 and 4.70 (ABq, *J* 11.0 Hz), and 4.82 and 4.70 (ABq, *J* 11.4 Hz), 4.53 (m, 2 H) (3 × CH_2Ph), 4.42 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 4.01–3.91 (m, 1 H, OCH_2), 3.75–3.40 (m, 7 H, H-2, H-3, H-4, H-5, H-6,6, OCH_2), 1.82 (s, 3 H, Ac), 1.75–1.55 (m, 2 H, OCH_2CH_2), 1.45–1.20 [m, 18 H, $(CH_2)_9CH_3$], 0.88 (t, 3 H, *J* 6.6 Hz, CH_2CH_3). HREIMS: Calcd for $C_{34}H_{49}O_7$ [M − Bzl]: 569.3478; Found: 569.3473.

*Preparation of 1,2-*O*-anhydro-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-β-*D*-mannopyranose* (**38**).—Epoxidation of (1*R*,3*R*,6*R*,10*S*)-10-hydroxy-3-phenyl-2,4-dioxabicylo[4.4.0]dec-8-ene,[11] prepared in four steps through 3,4-di-*O*-acetyl-2-bromo-5a-carba-β-D-glucuropyranuronic acid bromide,[12] with MCPBA in CH_2Cl_2 in the presence of phosphate buffer solution and subsequent benzylation with BzlBr–NaH in DMF gave, after chromatography (silica gel, 1:6 → 1:5 EtOAc–hexane gradient), **38** [∼20% overall yield based on the (−)-*endo*-adduct[7] of furan and acrylic acid], identical with an authentic sample in all respects.[11]

*Dodecyl 3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-α-*D*-mannopyranosyl-(1 → 4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**39**).—To a solution of **36** (6.55 g, 10.6 mmol) in DMF (50 mL) were added NaH (1.27 g, 31.8 mmol, washed thoroughly with hexane) and 15-crown-5 ether (6.31 mL, 31.8 mmol) under argon, and the mixture was stirred for 1.5 h at room temperature. A solution of **38** (7.16 g, 21.2 mmol) in DMF (50 mL) was added to it, and the mixture was stirred for 5 days at 70 °C. After addition of MeOH (1 mL), the mixture was diluted with EtOAc (1.2 L), and the solution was thoroughly washed with water, dried, and evaporated. The product was chromatographed on silica gel (500 g, 1:40 acetone–toluene) to give **39** (8.53 g, 96% based on **36** consumed) as a syrup, together with **36** (0.77 g, 12%) recovered: $[\alpha]_D^{23}$ −10° (*c* 1.8, $CHCl_3$); R_f 0.38 (1:10 EtOAc–toluene); ^{1}H NMR (CD_3OD): δ 7.55–7.20 (m, 25 H, 5 × Ph), 5.59 (s, 1 H, C*H*Ph), 5.09 (ABq, 1 H, J_{gem} 11.2 Hz) and 4.96 (ABq, J_{gem} 10.7 Hz), 4.39 (ABq, J_{gem} 11.7 Hz) (3 × CH_2Ph), 4.38 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.20–3.87 (m, 3 H, H-4′, H-6′, OCH_2), 4.16–4.09 (m, 2 H, H-1′, H-2′), 3.75–3.67 (m, 3 H, H-3, H-6a, H-3′), 3.62–3.41 (m, 5 H, H-2, H-4, H-6b, H-6′b, OCH_2), 3.37–3.29 (m, 1 H, H-5), 2.39 (m, 1 H, OH), 2.18–2.02 (m, 1 H, H-5′), 1.70–1.55 (m, 2 H, OCH_2CH_2), 1.50–1.20 [m, 20 H, H-5a,5a, $(CH_2)_9CH_3$], 0.88 (t, 3 H, *J* 7.1 Hz, CH_2CH_3). HRFABMS: Calcd for $C_{60}H_{76}O_{10}Na$ [M + Na]: 979.5337; Found: 979.5339.

*Dodecyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-α-*D*-mannopyranosyl-(1 → 4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**40**).—Compound **39** (20.4 mg, 21 μmol) was acetylated conventionally, and the product was chromatographed on silica gel (1 g, 1:10

H-6b), 2.09, 2.04, 2.03, and 2.01 (4 s, each 3 H, 4 × Ac), 0.88 (t, 3 H, *J* 6.8 CH_2CH_3). HREIMS: Calcd for $C_{24}H_{40}O_8$ [M − HOAc]: 456.2723; Found: 456.2726.

*Dodecyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-*D*-glucopyranoside* (**35**).—Compound **34** (11.0 g, 21.3 mmol) was O-deacetylated as in the preparation of **8**. The product was dissolved in DMF (100 mL) and treated with α,α-dimethoxytoluene (4.7 mL, 32 mmol) and *p*-TsOH·H_2O (0.73 g, 4.3 mmol) for 4.5 h at 50 °C under diminished pressure (water aspirator). The mixture was evaporated after treatment with Et_3N, and the residue was chromatographed on silica gel (300 g, 1:2 EtOAc–hexane) to give the 4,6-*O*-benzylidene derivative as a syrup. This compound was directly benzylated EtOAc–hexane) to give **40** (21.6 mg, ∼100%) as a syrup: $[\alpha]_D^{22}$ +0.4° (*c* 1.1, $CHCl_3$); R_f 0.35 (1:5 EtOAc–toluene); ^{1}H NMR (CD_3OD) (inter alia): δ 7.55–7.20 (m, 25 H, 5 × Ph), 5.60 (s, 1 H, C*H*Ph), 5.57 (m, 1 H, H-2′), 4.38 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.20–3.87 (m, 3 H, H-4′, H-6′, OCH_2), 4.20–4.10 (m, 2 H, H-1′, H-2′), 3.98 (dd, 1 H, $J_{5',6'a}$ 4.4, $J_{6'gem}$ 11.0 Hz, H-6′a), 4.00–3.78 (m, 4 H, H-1′, H-3′, H-6′b, OCH_2), 3.76–3.43 (m, 6 H, H-2, H-3, H-4, H-6,6, OCH_2), 3.37–3.28 (m, 1 H, H-5), 2.20–2.00 (m, 1 H, H-5′), 1.75–1.55 [m, 3 H, H-5a′(eq), OCH_2CH_2], 1.50–1.12 [m, 19 H, H-5a′(ax), $(CH_2)_9CH_3$], 0.88 (t, 3 H, *J* 7.1 Hz, CH_2CH_3). Anal. Calcd for $C_{62}H_{78}O_{11}$ (999.3): C, 74.52; H, 7.87. Found: C, 74.40; H, 7.57.

*Dodecyl 3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-α-*D*-arabino-hex-2-ulopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**41**).—A solution of **40** (7.39 g, 77.2 mmol) in DMSO (120 mL) was treated with Ac_2O (22 mL, 0.23 mol) for 11 h at room temperature. After careful addition of MeOH (10 mL), the mixture was diluted with EtOAc (1.2 L), and the solution was thoroughly washed with water, dried, and evaporated. The residue was chromatographed on silica gel (500 g, 1:8 EtOAc–hexane) to give **41** (7.2 g, 98%) as a syrup: $[\alpha]_D^{22}$ −8° (*c* 1.1, $CHCl_3$); R_f 0.41 (1:5 EtOAc–toluene); ^{1}H NMR (CD_3OD) (inter alia): δ 8.10–7.20 (m, 25 H, 5 × Ph), 5.53 (s, 1 H, C*H*Ph), 4.37 (d, 1 H, $J_{3',4'}$ 7.6 Hz, H-3′), 4.31 (m, 1 H, H-1′), 3.32 (ddd, 1 H, $J_{4,5}$ 9.0, $J_{5,6a} = J_{5,6b} = 2.7$ Hz, H-5), 2.52 (m, 1 H, H-5′), 1.81 [ddd, 1 H, $J_{1',5a'(eq)} = J_{5',5a'(eq)} = 2.9$, $J_{5a'gem}$ 14.7 Hz, H-5a′(eq)], 1.03 [ddd, 1 H, $J_{1',5a'(ax)}$ 6.3, $J_{5',5a'(ax)}$ 6.8 Hz, H-5a′(ax)], 0.88 (t, 3 H, *J* 6.4 Hz, CH_2CH_3). HRFABMS: Calcd for $C_{60}H_{74}NaO_{10}$ [M + Na]: 977.5180; Found: 977.5171.

*Dodecyl 3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-β-*D*-arabino-hex-2-ulopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**42**).—A solution of **41** (6.98 g, 7.31 mmol) in toluene (140 mL) was treated with DBU (2.2 mL, 14.6 mmol) for 1 h at 70 °C. The mixture was diluted with EtOAc (1.2 L), and the solution was washed with water, dried, and evaporated. The product was chromatographed on silica gel (500 g, 1:40 EtOAc–toluene) to give **42** (4.66 g, 67%), together with **41** (1.63 g, 23%) unchanged: $[\alpha]_D^{22}$ −8° (*c* 0.5, $CHCl_3$); R_f 0.40 (1:10 EtOAc–toluene); ^{1}H NMR (CD_3OD) (inter alia): δ 7.50–7.20 (m, 25 H, 5 × Ph), 5.46 (s, 1 H, C*H*Ph), 4.40 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.28 [dd, 1 H, $J_{1',5a'(ax)}$ 12.5, $J_{1',5a'(eq)}$ 6.8 Hz, H-1′], 1.03 [m, 1 H, H-5a′(ax)], 0.88 (t, 3 H, *J* 6.8 Hz, CH_2CH_3). HRFABMS: Calcd for $C_{60}H_{74}NaO_{10}$ [M + Na]: 977.5180; Found: 977.5178.

*Dodecyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-β-*D*-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**43**) *and dodecyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-β-*D*-mannopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**44**).—To a solution of **42** (304 mg, 0.32 mmol) in THF (6.0 mL) was added 1 M BH_3·THF complex (1.27 mL, 1.27 mmol) under argon, and the mixture was stirred for 16 h at 0 °C to room temperature. The mixture was diluted with EtOAc (60 mL), and a solution was washed with water, dried, and evaporated. A mixture of the products was chromatographed on silica gel (30 g, 1:10 acetone–hexane) to give a crude mixture of the 5a-carba-β-D-glucosyl (∼220 mg) and α-D-mannosyl compounds (∼27 mg), the structures of which were roughly assigned on the basis of their ^{1}H NMR spectral data. The former was acetylated conventionally, and the product was chromatographed on silica gel (18 g, 1:10 EtOAc–hexane) to give **43** (136 mg, 52% based on **42**) as a syrup. The latter was acetylated, and the product was chromatographed on silica gel (18 g, 1:7 EtOAc–hexane) to give **44** (16 mg, 9% based on **42**) as a syrup. Data for **43**: $[\alpha]_D^{22}$ +9° (*c* 0.9, $CHCl_3$); R_f 0.52 (1:3 EtOAc–hexane); ^{1}H NMR (CD_3OD) (inter alia): δ 7.50–7.20 (m, 25 H, 5 × Ph), 5.44 (s, 1 H, CHPh), 4.34 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1), 3.94 (m, 1 H, OCH_2), 3.82 (dd, 1 H, $J_{5',6'a}$ 4.6, $J_{6'gem}$ 11.0 Hz, H-6′a), 3.72 (m, 2 H, H-6,6), 3.18 (dd, 1 H, $J_{5',6'b}$ 10.7 Hz, H-6′b), 1.91 (s, 3 H, Ac), 1.85 [m, 1 H, H-5a′(eq)], 1.72–1.53 (m, 2 H, OCH_2CH_2), 1.50–1.20 [m, 19 H, H-5′, $(CH_2)_9CH_3$], 0.88 (t, 3 H, CH_2CH_3), 0.67 [ddd, 1 H, $J_{1,5a'(ax)} = J_{5',5a'(ax)} = 12.0$, $J_{5a'gem}$ 13.7 Hz, H-5a′(ax)]. HRFABMS: Calcd for $C_{62}H_{79}O_{11}$ [M + H]: 999.5623; Found: 999.5632. Data for **44**: $[\alpha]_D^{23}$ −1.4° (*c* 0.7, $CHCl_3$); R_f 0.45 (1:3 EtOAc–hexane); ^{1}H NMR (CD_3OD) (inter alia): δ 7.55–7.15 (m, 25 H, 5 × Ph), 5.64 (m, 1 H, H-2′), 5.50 (s, 1 H, CHPh), 4.36 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 3.95 (m, 1 H, OCH_2), 3.24 (dd, 1 H, $J_{2,3}$ 2.7, $J_{3,4}$ 9.8 Hz, H-3), 2.11 (s, 3 H, Ac), 1.80–1.50 (m, 3 H, H-5′, OCH_2CH_2), 1.50–1.20 [m, 20 H, H-5a′,5a′, $(CH_2)_9CH_3$], 0.88 (t, 3 H, *J* 6.8 Hz, CH_2CH_3).

*Dodecyl 2-*O*-acetyl-3-*O*-benzyl-4,6-di-*O*-methanesulfonyl-5a-carba-β-*D*-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**45**).—A solution of **43** (1.42 g, 1.42 mmol) in 80% aq HOAc (60 mL) was heated for 10 h at 70 °C and then evaporated. The residue was chromatographed on silica gel (100 g, 1:2 EtOAc–hexane) to give crude diol (805 mg). This com-

pound was treated with MsCl (0.41 mL, 5.3 mmol) in pyridine (16 mL) for 14 h at 0 °C to room temperature. After addition of MeOH (0.1 mL), the mixture was evaporated. The residue was diluted with EtOAc (180 mL), and the solution was washed successively with 1 M HCl, satd aq $NaHCO_3$, and water, dried, and evaporated. The product was chromatographed on a silica gel (60 g, 1:5 EtOAc–hexane) to give **45** (888 mg, 59%) as a syrup: R_f 0.25 (1:2 EtOAc–hexane); $[\alpha]_D^{23}$ +10° (*c* 1.2, $CHCl_3$); ^{1}H NMR (CD_3OD): δ 7.30–7.20 (m, 20 H, 4 × Ph), 4.95–4.82 (m, 3 H, H-2′, CH_2Ph), 4.62–4.41 (m, 6 H, 3 × CH_2Ph), 4.31–4.20 (m, 2 H, H-1, H-4′), 3.95–3.80 (m, 4 H, H-6′,6′, OCH_2), 3.71–3.57 (m, 2 H, H-6,6), 3.27–3.10 (m, 2 H, H-5, H-3′), 3.08 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 2.7 Hz, H-3), 2.85 and 2.70 (2 s, each 3 H, 2 × Ms), 2.06 [m, 1 H, H-5a′(eq)], 1.82 (s, 3 H, Ac), 1.65–1.40 (m, 3 H, H-5′, OCH_2CH_2), 1.50–1.20 [m, 19 H, H-5a′(ax), $(CH_2)_9CH_3$], 0.81 (t, 3 H, *J* 6.8 Hz, CH_2CH_3). Anal. Calcd for $C_{57}H_{78}O_{15}S$ (1067.4): C, 64.14; H, 7.37. Found: C, 64.14; H, 6.99.

Dodecyl 2,4,6-tri-O-*acetyl-3*-O-*benzyl-5a-carba-β*-D-*galactopyranosyl-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**46**).—A mixture of **45** (723 mg, 0.72 mmol) and NaOAc (2.38 g, 29 mmol) in aqueous 80% DMF (15 mL) was stirred for 3 days at 120 °C. The mixture was diluted with EtOAc (150 mL), and the solution was washed with water, dried, and evaporated. The residue was acetylated conventionally, and the product was chromatographed on silica gel (60 g, 1:10 acetone–hexane) to give **46** (653 mg, 91%) as a syrup: $[\alpha]_D^{23}$ +17° (*c* 1.2, $CHCl_3$); R_f 0.39 (1:2 acetone–hexane); ^{1}H NMR (CD_3OD): δ 7.45–7.20 (m, 20 H, 4 × Ph), 5.44 (m, 1 H, H-4′), 5.05–4.90 (m, 2 H, CH_2Ph), 4.70–4.60 (m, 6 H, H-6′,6′, 2 × CH_2Ph), 4.46 and 4.30 (ABq, J_{gem} 12.2 Hz, CH_2Ph), 4.35 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1), 3.98–3.89 (m, 1 H, OCH_2), 3.79–3.34 (m, 7 H, H-2, H-3, H-4, H-6,6, H-1′, OCH_2), 3.35–3.25 (m, 1 H, H-5), 3.08 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 2.7 Hz, H-3), 2.06, 2.01, and 1.94 (3 s, each 3 H, 3 × Ac), 2.05–1.95 [m, 2 H, H-5′, H-5a′(eq)], 1.70–1.50 (m, 2 H, H-2, OCH_2CH_2), 1.45–1.20 [m, 19 H, H-5a′(eq), $(CH_2)_9CH_3$], 0.88 (t, 3 H, *J* 6.8 Hz, CH_2CH_3). Anal. Calcd for $C_{59}H_{78}O_{13}$ (995.2): C, 71.20; H, 7.90. Found: C, 71.02; H, 7.48.

Dodecyl 2,3,4,6-tetra-O-*acetyl-5a-carba-β*-D-*galactopyranosyl-(1→4)-2,3,6-tri*-O-*acetyl-β*-D-*glucopyranoside (dodecyl 5a′-carba-β-lactoside heptaacetate)* (**47**).—A solution of **46** (551 mg, 0.553 mmol) in EtOH (16 mL) containing 1 M HCl (0.5 mL) was hydrogenolyzed in the presence of 10% Pd/C (five-microspoonfuls) in an atmospheric pressure of hydrogen for 7 h at room temperature. The product was acetylated conventionally, and chromatographed (silica gel 30 g, 1:5 acetone–hexane) to give **47** (407 mg, 92%) as a syrup: $[\alpha]_D^{22}$ −7° (*c* 0.9, $CHCl_3$); R_f 0.37 (1:2 acetone–hexane); ^{1}H NMR (CD_3OD): δ 5.35 (m, 1 H, H-4′), 5.15 (dd, 1 H, $J_{1',2'} = J_{2',3'} = 9.9$ Hz, H-2′), 5.04 (dd, 1 H, $J_{2,3} = J_{3,4} = 8.8$ Hz, H-3), 4.76 (dd, 1 H, $J_{1,2}$ 7.8 Hz, H-2), 4.68 (dd, 1 H, $J_{3',4'}$ 2.7 Hz, H-3′), 4.45 (m, 1 H, H-6a), 4.38 (d, 1 H, H-1), 4.10 (dd, 1 H, $J_{5,6b}$ 4.8, J_{6gem} 12.0 Hz, H-6b), 3.95–3.70 (m, 3 H, H-6′,6′, OCH_2), 3.52–3.33 (m, 4 H, H-4, H-5, H-1′, OCH_2), 2.07, 2.04, 1.98, 1.96, and 1.89 (5 s, 3, 3, 9, 3, 3 H, 7 × Ac), 2.00–1.90 [m, 2 H, H-5′, H-5a′(eq)], 1.55–1.40 (m, 2 H, OCH_2CH_2), 1.50–1.00 [m, 19 H, H-5a′(ax), $(CH_2)_9CH_3$], 0.80 (t, 3 H, *J* 7.3 Hz, CH_2CH_3). HR-FABMS: Calcd for $C_{39}H_{63}O_{17}$ [M + H]: 803.4065; Found: 803.4056. Anal. Calcd for $C_{39}H_{62}O_{17}$ (802.90): C, 58.34; H, 7.78. Found: C, 58.18; H, 7.32.

Dodecyl 5a′-carba-β-lactoside (**4**).—Compound **47** (336 mg, 0.42 mmol) was O-deacetylated as in the preparation of **1**, and the product was chromatographed on silica gel (20 g, 1:5 MeOH–$CHCl_3$) to give **4** (204 mg, 96%) as crystals: mp 76–78 °C; $[\alpha]_D^{19}$ −21° (*c* 1.0, 1:1 MeOH–$CHCl_3$); R_f 0.13 (1:5 MeOH–$CHCl_3$); ^{1}H NMR (CD_3OD) (inter alia): δ 4.24 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 2.00–1.90 [m, 1 H, H-5a′(eq)], 1.40–1.20 [m, 18 H, $(CH_2)_9CH_3$], 0.89 (t, 3 H, *J* 6.8 Hz, CH_2CH_3). HRFABMS: Calcd for $C_{25}H_{48}NaO_{10}$ [M + Na]: 531.3146; Found: 531.3144. Anal. Calcd for $C_{25}H_{48}O_{10}\cdot H_2O$ (508.3): C, 58.01; H, 9.54. Found: C, 57.92; H, 9.30.

Biological Assay.—Evaluation of inhibitory activity of compounds **1**–**4** for seven glycosidases were carried out in the standard manner[15] by Dr Akihiro Tomoda (Hokko Chemical Industry Co. Ltd.). α-Glucosidases (baker's yeast) was purchased from Wako Chemical Co., β-glucosidase (almonds), β-galactosidase (bovine liver), α-mannosidase (Jack beans), α-fucosidase (bovine kidney) and *N*-acetyl-β-glucosaminidase (bovine liver) from Sigma Chemical Co., and α-galactosidase (green coffee beans) from Boellinger–Mannheim. α-Glucosidase (rat intestine) and α-galactosidase (rat liver) were provided with by Hokko Chemical Industry.

Acknowledgements

The authors sincerely thank Drs A. Takahashi and A. Tomoda (Hokko Chemical Industry Co. Ltd., Atsugi, Tokyo) for biological assays, Miss L. Zhao for elemental analyses, and Yamakawa Chemical Industry Co. Ltd. (Tokyo) for providing optical resolution reagents.

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