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Chemical Modification of β-Glucocerebrosidase Inhibitor *N*-Octyl-β-valienamine: Synthesis and Biological Evaluation of *N*-Alkanoyl and *N*-Alkyl Derivatives

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Abstract—Several *N*-alkanoyl **4a–d** and *N*-alkyl derivatives **5a–g** of the potent β-glucocerebrosidase inhibitor *N*-octyl β-valienamine (**3**) were synthesized in order to elucidate a role of hydrophobic portion in the inhibitory action. Although the former lacked inhibitory potency, the latter were strong β-glucocerebrosidase inhibitors (cf. *N*-decyl-*N*-octyl-β-valienamine **5d**: K_i 6.6×10^{-8} M). Furthermore, when being prescribed into mouse-derived B16 melanoma cells, *N*-butyl-*N*-octyl-β-valienamine **5a** and **5d** were shown to change the amount of GlcCer and GM3, which suggests that they are possibly introduced into cells and influence glycolipids biosynthesis.

Introduction

Very potent and specific glucosylceramide synthase inhibitor, PDMP (D-*threo*-1-phenyl-2-decanoylamino-3-morpholino-1-propanol) **1** and homologues have so far been extensively studied[1–3] in order both to elucidate biosynthesis of glycosylceramides and glycolipids, and practically to extend these potential to therapeutic agents (Scheme 1). We have so far developed several specific glycocerebrosidase inhibitors, carbaglucosylceramide[4] **2** and some analogues[5–7] composed of unsaturated 5a-carba-amino sugar β-valienamine.[8] They however completely lack inhibition potential against glucosylceramide synthase. Therefore, we have been interested in elucidation of the structure–inhibitory activity relationship, controlling a mode of the inhibitory action depending on the two enzymes involved in biosynthesis of glycosylceramides. In this paper, chemical modification of *N*-octyl β-valienamine[6] (**3**), the most potent inhibitor in vitro of this kind, has been carried out mainly to demonstrate its structure–inhibitory activity relationship of the hydrophobic moiety, as well as, to provide appropriate inhibitors active in vivo.

The hydrophobic portion of **3** was modified by introducing a double-chain structure by converting it into *N*-alkanoyl and *N*-alkyl derivatives (Scheme 2). Thus, the *N*-alkanoyl **4a–d** and *N*-alkyl derivatives **5a–g** were prepared conventionally by treatment of *N*-octyl 2,3:4,6-di-*O*-isopropylidene-β-valienamine[6] (**6**) with the corresponding acid chloride in pyridine (**6**→**7a–g**) and subsequent reduction with LAH in THF (**7a–g**→**8a–g**). Removal of the protecting groups of **7a–d** and **8a–g** afforded **4a–d** and **5a–g**, respectively. These compounds were subjected to assay for β-glucocerebrosidase (mouse liver) in vitro and, especially, four compounds **4a, 4d, 5a**, and **5d** were prescribed into mouse-derived B16 melanoma cells and evaluated the amount of glucosylceramide and GM3 in cells after treatment.

Key words: Carbohydrate mimics; 5a-carba-sugar derivatives; 5a-carba-amino sugar derivatives; glucosidase inhibitors; glucocerebrosidase inhibitors.
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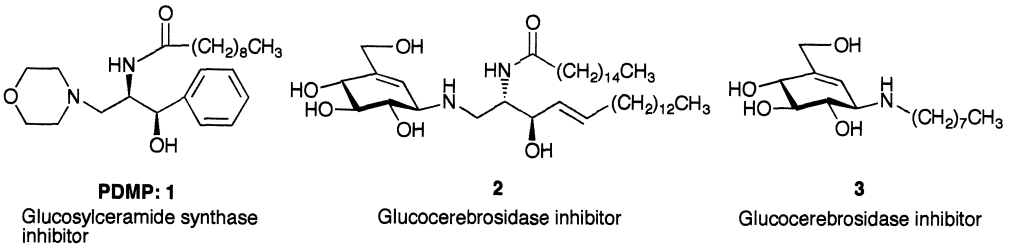
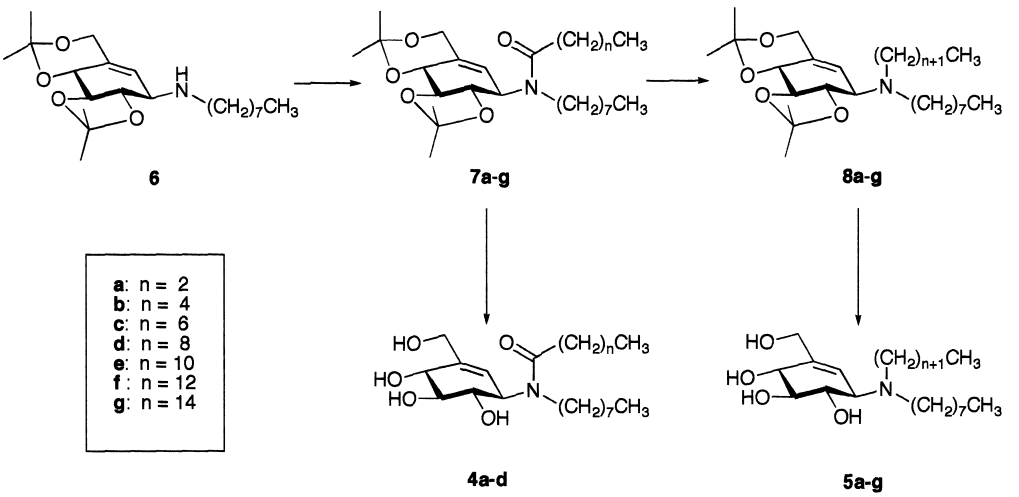


Scheme 1.



Scheme 2.

Chemistry

Treatment of **6** with 1.4 molar equiv of alkanoyl chlorides in pyridine for 1 h at room temperature produced, after purification by silica gel chromatography with ethyl acetate and toluene as an eluent, the corresponding *N*-alkanoyl derivatives **7a–g** as a syrup in >90% yield. Their ^{1}H NMR spectra (300 MHz in hexadeuteriodimethylsufoxide) were shown to be complex due to a restricted rotation of the tertiary amido linkages at room temperature. However the spectra became simple and interpretable when the solution temperature raised to 110 °C.

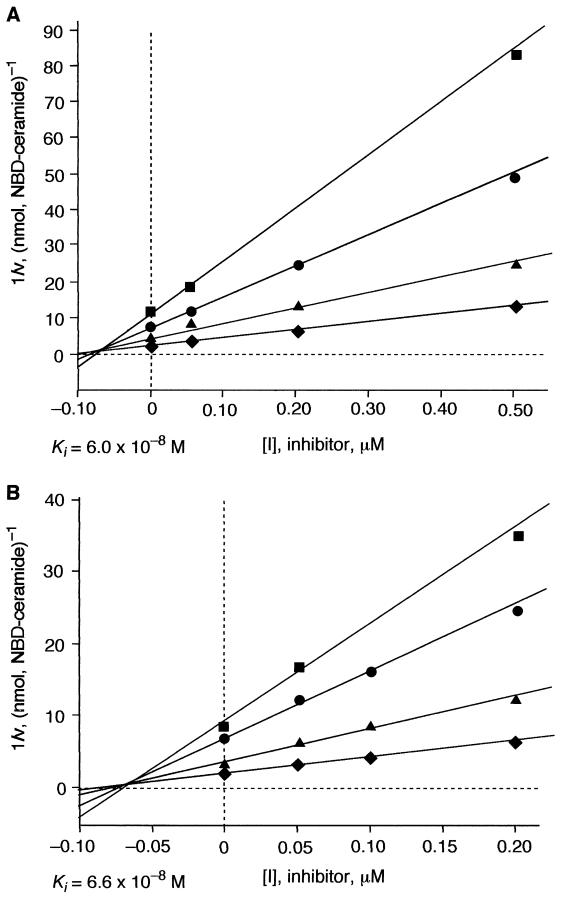
O-Deisopropylidenation of **7a–d** was carried out in 80% acetic acid for 30 min at 80 °C and the products were purified by a silica gel column with 1:6 ethanol/toluene to give the *N*-alkanoyl-*N*-octyl-β-valienamines **4a–d** in ~90% yield. Their ^{1}H NMR spectra also became recognizable at 110 °C. On the other hand, reduction of the amido to amino functions in **7a–g** was conducted by use of excess lithium aluminium hydride in THF for 1 h at reflux temperature. The products were purified by a silica gel column with ethyl acetate and hexane to give the *N*-alkyl-*N*-octyl-di-*O*-isopropylidene derivatives **8a–g** in 60–80% yields. Similar treatment of **8a–g** with 80% aqueous acetic acid and subsequent purification by silica gel column with a gradient elution of a mixture of ethanol and toluene afforded the *N,N*-dialkyl derivatives **5a–g** as a syrup in ~90% yields.

Inhibitory activity of **4a–d** and **5a–g** against β-glucocerebrosidase (mouse liver) were listed in Table 1. All *N*-alkanoyl derivatives **4a–d** completely lack the activity, whereas *N*-alkyl derivatives **5a–g** were shown to possess the strong potential comparable to the parent **3**. These results demonstrated that the basic cationic property of the alkyl amino functions should be very important, and the structures of the hydrophobic portions seem to be not so strictly recognized at its binding to the enzyme, although the appropriate combination of chain lengths of the *N*-alkyl functions, e.g. C_8 and C_{10}, should be preferred for exhibiting optimum activity. Furthermore, inhibition constants (K_i) of **3** and the most potent **5d** against mouse liver β-glucocerebrosidase were determined by means of Dixon plot (Scheme 3). The assay

Table 1. Inhibitory activity (IC_{50}, M) of *N*-alkanoyl-*N*-octyl **4a–d** and *N*-alkyl-*N*-octyl-β-valienamines **5a–g** against β-glucocerebrosidase mouse liver

Compd	Inhibitory activity against β-glucocerebrosidase (IC_{50}, M)
4a	—*
4b	—
4c	—
4d	—
5a	1.4×10^{-6}
5b	3.5×10^{-7}
5c	3.5×10^{-7}
5d	1.4×10^{-7}
5e	3.2×10^{-7}
5f	3.5×10^{-7}
5g	4.2×10^{-7}

*Activity less than IC_{50} 1.0×10^{-4} M.



Scheme 3. Inhibition analysis of compounds **3** and **5d**. Graph A: **3**; B: **5d**. Concentration of the NBD-glucosylceramide: ◆ 30 μM, ▲ 15 μM, ● 7.5 μM, ■ 5 μM.

was carried out following the standard conditions[9] except that varying amount of substrate were incubated with the quantities of inhibitor indicated on the abscissa. The reactions were stopped after 2 h incubation at 37 °C and the quantity of NBD-glucosylceramide cleaved was determined by spectrofluorometer. As shown in the plot, the compounds **3** and **5d** were found to be competitive inhibitor with K_i 6.0×10^{-8} and 6.6×10^{-8} M, respectively. The structural feature of the hydrophobic portions of this kind of inhibitors seems not to influence strongly the activity potential in vitro.

Next, in order to evaluate in culture cells activity, five compounds **3, 4a, 4d, 5a**, and **5d** were prescribed into mouse-derived B16 melanoma cells, and measured changes in the amount of glycosphingolipids in the cells. B16 melanoma cells were plated at 5.0×10^6 cell per 150 cm^2 flask and 3 days later, were exposed for 24 h to 10 μM *N*-octyl β-valienamine derivatives in the culture medium. The method of glucolipid analysis was as in reference[2,10]. Changes in the amount of glycosphingolipids in B16 melanoma cells after treatment with five compounds were listed in Table 2. The B16 melanoma cells treated with **5d** for one day apparently increased the amount of GlcCer and GM3, whereas, no changes were observed in the case of **3**. These results demonstrate that **5d** is likely to influence the biosyntheis of glycosphingolipids in the cell, which may be understood by assuming its permeability to cell membrane and/or retention time in the cell, possibly improved by introduction of the second hydrophobic alkyl chain into **3**. Cell toxicity of **3** and **5d** were measured by MTT method, demonstrating that the latter showed toxicity at >40 μM.

Of note, **4d** which has no inhibitory activity against β-glucocerebrosidase (Table 1) could reduce the cellular glycolipid content in B16 cells. This result suggests that the *N*-alkanoyl derivatives interfere with the biosynthetic pathway of glycolipids. We are currently investigating the effect of **4d** on several glycolipid synthesizing enzymes. Thus some glucosylceramide mimics prepared in this

Table 2. Changes in the amount of GlcCer and GM_3 in B16 melanoma cells after treatment with **3, 4a, 4d, 5a**, or **5d***

Compd	Glucolipid content (μg in 10^7 cells)	
	GlcCer	GM_3
Controls	5.8	8.0
3	5.9	8.5
4a	5.0	8.2
4d	4.5	5.6
5a	6.3	8.7
5d	7.7	9.7

*The cells were incubated for 24 h in the presence of the standard medium (controls), **3, 4a, 4d, 5a**, or **5d** at 10 μM.

study may have other biological potentials, possibly attracting the attention of researchers in biochemistry of glycolipids.

Experimental

General methods

Optical rotations were measured with a JASCO DIP-370 polarimeter, and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H NMR spectra were recorded for solutions in deuteriochloroform with internal tetramethylsilane (TMS) as a reference, hexadeuteriodimethylsulfoxide with internal acetone (δ 2.08) as a reference with a JEOL JNM-GX 270 FT (270 MHz) or JEOL JNM Lambda-300 (300 MHz) instrument. IR spectra were measured with a JASCO IR-810 (neat) or Hitachi Bio-Rad Digital Lab FTS-65 (KBr disk) spectrometer. TLC was performed on silica gel 60 F-254 (E. Merck, Darmstadt). The silica gel used for column chromatography was Wakogel C-300 (Wako Junyaku Kogyo Co., Osaka, Japan; 200–300 mesh) or silica gel 60 KO (Katayama Kagaku Kogyo Co., Osaka, Japan; 70–230 mesh). Organic solutions were dried over anhydrous Na_2SO_4 and concentrated at <45 °C under diminished pressure. Typical synthetic procedures for **4a, 5a, 7a**, and **8a** were described in detail, and each respective homologues were similarly prepared, the yields being only noted.

***N*-Butanoyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (7a).** To a solution of 2,3:4,6-di-*O*-isopropylidene-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine[6] **6** (127 mg, 0.346 mmol) in pyridine (3 mL) was added *n*-butynyl chloride (50 μL, 0.481 mmol), and the mixture was stirred for 1 h at room temperature. The mixture was diluted with EtOAc (60 mL) and the solution was washed with brine (3×20 mL), dried over Na_2SO_4, and evaporated. The crude product was purified by silica gel column chromatography (13 g, 1:6 EtOAc/toluene) to yield **7a** (140 mg, 93%) as a colorless syrup, TLC: R_f 0.20 (1:5 EtOAc/toluene), $[\alpha]^{25}_D$ −67° (*c* 1.15, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2), 1650 (amide) cm^{-1}, ^{1}H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.21 (1 H, br s, 5a-H), 4.85 (1 H, br s, 1-H), 4.65 (1 H, m, 4-H), 4.42 and 4.12 (each 1 H, 2 d, J_{gem} = 13.3 Hz, 2 6-H), 3.78–3.60 (2 H, m, 2-H, 3-H), 3.19 (1 H, m, 2″a-H), 3.04–2.82 (1 H, m, 2″b-H), 2.35–2.23 (2 H, m, 2 1′-H), 1.60–1.19 (14 H, m, 7 CH_2), 1.48, 1.37, 1.36 and 1.29 (each 3 H, 4 s, 2 CMe_2), 0.86 (6 H, 2 t, $J_{7',8'}$ = 7.1 Hz, $J_{3'',4''}$ = 7.1 Hz, 2 CH_3). Anal. calcd for $C_{25}H_{43}O_5N$: C, 68.61; H, 9.90; N, 3.20%. Found: C, 68.34; H, 10.13; N, 3.48%.

***N*-Hexanoyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (7b).** A colorless syrup (yield 91%), TLC: R_f 0.29 (1:5 EtOAc/toluene), $[\alpha]^{26}_D$ −67° (*c* 1.10, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2930 and 2855 (CH_2), 1650 (amide) cm^{-1}, ^{1}H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.22 (1 H, br s, 5a-H), 4.85 (1 H, br s, 1-H), 4.66 (1 H, br d, $J_{3,4}$ = 5.9 Hz, 4-H), 4.42 and 4.13 (each 1 H, 2 d, J_{gem} = 13.8 Hz, 2 6-H), 3.80–3.60 (2 H, m, 2-H, 3-H), 3.20 (1 H, m, 2″a-H), 3.04–2.83 (1 H, m, 2″b-H), 2.41–2.21 (2 H, m, 2 1′-H), 1.61–1.18 (18 H, m, 9 CH_2), 1.48, 1.37, 1.36 and 1.30 (each 3 H, 4 s, 2 CMe_2), 0.86 (6 H, 2 t, $J_{7',8'}$ = 6.7 Hz, $J_{5'',6''}$ = 6.7 Hz, 2 CH_3). Anal. calcd for $C_{27}H_{47}O_5N$: C, 69.64; H, 10.17; N, 3.01%. Found: C, 69.54; H, 10.24; N, 3.04%.

***N*-Octanoyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (7c).** A colorless syrup (yield 97%), $[\alpha]^{25}_D$ −58° (*c* 1.08, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2), 1655 (amide) cm^{-1}, ^{1}H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.21 (1 H, br s, 5a-H), 4.85 (1 H, br s, 1-H), 4.66 (1 H, br d, $J_{4,3}$ = 6.3 Hz, 4-H), 4.42 and 4.12 (each 1 H, 2 d, J_{gem} = 13.9 Hz, 2 6-H), 3.78–3.60 (2 H, m, 2-H, 3-H), 3.20 (1 H, m, 2″a-H), 3.04–2.83 (1 H, m, 2″b-H), 2.40–2.20 (2 H, m, 2 1′-H), 1.60–1.18 (22 H, m, 11 CH_2), 1.48, 1.37, 1.36 and 1.30 (each 3 H, 4 s, 2 CMe_2), 0.86 (6 H, 2 t, $J_{7',8'}$ = 6.2 Hz, $J_{7'',8''}$ = 6.2 Hz, 2 CH_3). Anal. calcd for $C_{29}H_{51}O_5N$: C, 70.55; H, 10.41; N, 2.83%. Found: C, 70.53; H, 10.74; N, 3.00%.

***N*-Decanoyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (7d).** A colorless syrup (yield 99%), TLC: R_f 0.39 (1:5 EtOAc/toluene), $[\alpha]^{23}_D$ −47° (*c* 0.98, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2), 1650 (amide) cm^{-1}. ^{1}H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.21 (1 H, br s, H-5a), 4.84 (1 H, br s, H-1), 4.65 (1 H, br d, $J_{4,3}$ = 6.3 Hz, 4-H), 4.43 and 4.12 (each 1 H, 2 d, J_{gem} = 14.3 Hz, 2 6-H), 3.78–3.59 (2 H, m, 2-H, 3-H), 3.20 (1 H, m, 2″a-H), 3.08–2.77 (1 H, m, 2″b-H), 2.41–2.21 (2 H, m, 2 1′-H), 1.60–1.20 (26 H, m, 13 CH_2), 1.48, 1.37, 1.36 and 1.30 (each 3 H, 4 s, 2 CMe_2), 0.86 (6 H, 2 t, $J_{7',8'}$ = 6.7 Hz, $J_{9'',10''}$ = 6.7 Hz, 2 CH_3). Anal. calcd for $C_{31}H_{55}O_5N$: C, 71.36; H, 10.63; N, 2.68%. Found: C, 71.11; H, 10.90; N, 2.68%.

***N*-Dodecanoyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (7e).** A colorless syrup (yield ∼100%), TLC: R_f 0.43 (1:5 EtOAc/toluene), $[\alpha]^{23}_D$ −44° (*c* 1.03, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2), 1650 (amide) cm^{-1}, ^{1}H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.21 (1 H, br s, 5a-H), 4.85 (1 H, br s, 1-H), 4.66 (1 H, br d, $J_{4,3}$ = 5.9 Hz, 4-H), 4.42 and 4.12 (each 1 H, 2 d, J_{gem} = 14.2 Hz, 2 6-H), 3.82–3.61 (2 H, m, 2-H, 3-H), 3.20 (m, 1 H, 2″a-H), 3.04–2.83 (m, 1 H, 2″b-H), 2.40–2.20 (2 H, m, 2 1′-H), 1.60–1.18 (30 H, m, 15 CH_2), 1.48,

1.37, 1.36 and 1.30 (each 3 H, 4 s, 2 CMe_2), 0.86 (6 H, 2 t, $J_{7',8'} = 6.6$ Hz, $J_{11'',12''} = 6.6$ Hz, 2 CH_3). Anal. calcd for $C_{33}H_{59}O_5N$: C, 72.09; H, 10.82; N, 2.55%. Found: C, 72.00; H, 11.12; N, 2.73%.

***N*-Octyl-*N*-tetradecanoyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (7f).** A colorless syrup (yield ~100%), TLC: R_f 0.45 (1:5 EtOAc/toluene), $[\alpha]^{23}_D$ −50° (*c* 1.19, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2), 1650 (amide) cm^{-1}, ^1H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.21 (1 H, br s, 5a-H), 4.86 (1 H, br s, 1-H), 4.66 (1 H, br d, $J_{3,4} = 6.3$ Hz, 4-H), 4.42 and 4.12 (each 1 H, 2 d, $J_{gem} = 13.8$ Hz, 2 6-H), 3.79–3.61 (2 H, m, 2-H, 3-H), 3.20 (1 H, m, 2″a-H), 3.04–2.83 (1 H, m, 2″b-H), 2.41–2.21 (2 H, m, 2 1′-H), 1.60–1.19 (34 H, m, 17 CH_2), 1.48, 1.37, 1.36 and 1.30 (each 3 H, 4 s, 2 CMe_2), 0.86 (6 H, 2 t, $J_{7',8'} = 6.8$ Hz, $J_{13'',14''} = 6.8$ Hz, 2 CH_3). Anal. calcd for $C_{35}H_{63}O_5N$: C, 72.74; H, 10.99; N, 2.42%. Found: C, 72.58; H, 11.29; N, 2.64%.

***N*-Hexadecanoyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (7g).** A colorless syrup (yield ~100%), TLC: R_f 0.46 (1:5 EtOAc/toluene), $[\alpha]^{23}_D$ −48° (*c* 1.10, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2), 1650 (amide) cm^{-1}, ^1H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.20 (1 H, br s, 5a-H), 4.83 (1 H, br s, 1-H), 4.65 (1 H, br d, $J_{3,4} = 6.8$ Hz, 4-H), 4.42 and 4.12 (each 1 H, 2 d, $J_{gem} = 14.1$ Hz, 2 6-H), 3.78–3.60 (2 H, m, 2-H, 3-H), 3.20 (1 H, m, 2″a-H), 3.04–2.83 (1 H, m, 2″b-H), 2.40–2.20 (2 H, m, 2 1′-H), 1.60–1.19 (38 H, m, 19 CH_2), 1.48, 1.37, 1.36 and 1.30 (each 3 H, 4 s, 2 CMe_2), 0.86 (6 H, 2 t, $J_{7',8'} = 6.8$ Hz, $J_{15'',16''} = 6.8$ Hz, 2 CH_3). Anal. calcd for $C_{37}H_{67}O_5N$: C, 73.34; H, 11.15; N, 2.31%. Found: C, 73.22; H, 11.44; N, 2.54%.

***N*-Butanoyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (4a).** A solution of **7a** (48 mg, 0.110 mmol) and aqueous 80% acetic acid (2 mL) was stirred for 30 min at 80 °C and evaporated. The residue was co-evaporated three times with ethanol and then three times with toluene. The crude product was purified by column chromatography on silica gel (4 g, 1:6 EtOH/toluene) to give **4a** (36 mg, 92%) as a colorless syrup, TLC: R_f 0.48 (1:5 MeOH/$CHCl_3$), $[\alpha]^{24}_D$ −89° (*c* 1.00, MeOH), ν_{max} (KBr) 3420 (OH), 2960 (CH_3), 2930 and 2855 (CH_2), 1620 (amide) cm^{-1}, ^1H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.25 (1 H, br s, 5a-H), 4.58–4.07 (4 H, m, H-1, 3 OH), 4.07–3.89 (3 H, m, 4-H, 2 6-H), 3.43 (1 H, br s, 2-H), 3.35 (1 H, dd, $J_{2,3} = 9.5$ Hz, $J_{3,4} = 7.2$ Hz, 3-H), 3.16–2.83 (2 H, m, 2 2″-H), 2.36–2.20 (2 H, m, 2 1′-H), 1.62–1.16 (14 H, m, 7 CH_2), 0.89 and 0.86 (2 t, 6 H, $J_{7',8'} = 7.0$ Hz, $J_{3'',4''} = 7.0$ Hz, 2 CH_3). Anal. calcd for $C_{19}H_{35}O_5N$: C, 63.84; H, 9.87; N, 3.92%. Found: C, 63.88; H, 10.17; N, 4.15%.

***N*-Hexanoyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (4b).** A colorless syrup (yield 92%), TLC: R_f 0.52 (1:5 MeOH/$CHCl_3$), $[\alpha]^{24}_D$ −83° (*c* 0.88, MeOH), ν_{max} (KBr) 3430 (OH), 2960 (CH_3), 2930 and 2855 (CH_2), 1625 (amide) cm^{-1}, ^1H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.26 (br s, 1 H, 5a-H), 4.62–4.07 (4 H, m, 1-H, 3 OH), 4.07–3.85 (3 H, m, 4-H, 2 6-H), 3.44 (1 H, br s, 2-H), 3.35 (1 H, dd, $J_{2,3} = 8.1$ Hz, $J_{3,4} = 7.8$ Hz, 3-H), 3.20–2.82 (2 H, m, 2 2″-H), 2.37–2.22 (2 H, m, 2 1′-H), 1.60–1.16 (18 H, m, 9 CH_2), 0.86 (6 H, 2 t, $J_{7',8'} = 6.1$ Hz, $J_{5'',6''} = 6.1$ Hz, 2 CH_3). Anal. calcd for $C_{21}H_{39}O_5N$: C, 65.42; H, 10.20; N, 3.63%. Found: C, 65.14; H, 10.14; N, 3.54%.

***N*-Octanoyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (4c).** A colorless syrup (yield 89%), TLC: R_f 0.55 (1:5 MeOH/$CHCl_3$), $[\alpha]^{24}_D$ −76° (*c* 0.80, MeOH), ν_{max} (neat) 3430 (OH), 2955 (CH_3), 2925 and 2855 (CH_2), 1625 (amide) cm^{-1}, ^1H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.26 (1 H, br s, 5a-H), 4.63–4.08 (4 H, m, 1-H, 3 OH), 4.05–3.92 (3 H, m, 4-H, 2 6-H), 3.45 (1 H, br s, 2-H), 3.35 (1 H, dd, $J_{2,3} = 9.3$ Hz, $J_{3,4} = 7.3$ Hz, 3-H), 3.17–2.82 (2 H, m, 2 2″-H), 2.37–2.24 (2 H, m, 2 1′-H), 1.61–1.17 (22 H, m, 11 CH_2), 0.86 (6 H, 2 t, $J_{7',8'} = 6.3$ Hz, $J_{7'',8''} = 6.3$ Hz, 2 CH_3). Anal. calcd for $C_{23}H_{43}O_5N$: C, 66.79; H, 10.48; N, 3.39%. Found: C, 66.60; H, 10.77; N, 3.41%.

***N*-Decanoyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (4d).** A colorless syrup (yield 91%), TLC: R_f 0.56 (1:5 MeOH/$CHCl_3$), $[\alpha]^{21}_D$ −67° (*c* 1.04, MeOH), ν_{max} (neat) 3430 (OH), 2955 (CH_3), 2925 and 2855 (CH_2), 1625 (amide) cm^{-1}, ^1H NMR [300 MHz, $(CD_3)_2SO$, 110 °C] δ_H 5.26 (1 H, br s, 5a-H), 4.58–4.08 (4 H, m, H-1, 3 OH), 4.04–3.92 (3 H, m, 4-H, 2 6-H), 3.45 (1 H, br s, 2-H), 3.35 (1 H, dd, $J_{2,3} = 9.0$ Hz, $J_{3,4} = 7.6$ Hz, 3-H), 3.20–2.82 (2 H, m, 2 2″-H), 2.36–2.22 (2 H, m, 2 1′-H), 1.60–1.16 (26 H, m, 13 CH_2), 0.86 (6 H, 2 t, $J_{7',8'} = 6.3$ Hz, $J_{9'',10''} = 6.3$ Hz, 2 CH_3). Anal. calcd for $C_{25}H_{47}O_5N$: C, 67.99; H, 10.73; N, 3.17%. Found: C, 68.15; H, 10.65; N, 3.18%.

***N*-Butyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (8a).** Lithium aluminum hydride (105 mg, 2.77 mmol) was suspended in THF (5 mL) at 0 °C. A solution of **7a** (92 mg, 0.210 mmol) in THF (3 mL) was added dropwise and the suspension was heated to reflux for 1 h. The reaction mixture was allowed to cool to 0 °C and the reaction was quenched with water (15 mL). The mixture was extracted with $CHCl_3$ (4×60 mL) and the organic extracts were dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel chromatography (11 g, gradient elution, 1:19 to 1:18 EtOAc/hexane) to give **8a** (68 mg, 76%) as a colorless syrup, TLC: R_f 0.47 (1:5 EtOAc/hexane), $[\alpha]^{25}_D$ −44° (*c*

1.15, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, $CDCl_3$) δ_H 5.42 (1 H, br s, 5a-H), 4.61 (1 H, br d, $J_{2,1}=8.4$ Hz, 4-H), 4.50 and 4.17 (each 1 H, 2 d, $J_{gem}=13.7$ Hz, 2 6-H), 3.73–3.56 (3 H, m, 1-H, 2-H, 3-H), 2.60–2.37 (4 H, m, 2 CH_2), 1.68–1.18 (16 H, m, 8 CH_2), 1.57, 1.45, 1.44 and 1.43 (each 3 H, 4 s, 2 CMe_2), 0.90 and 0.88 (6 H, 2 t, $J_{7',8'}=7.0$ Hz, $J_{3'',4''}=7.0$ Hz, 2 CH_3). Anal. calcd for $C_{25}H_{45}O_4N$: C, 70.88; H, 10.71; N, 3.31%. Found: C, 70.67; H, 10.98; N, 3.51%.

***N*-Hexyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (8b).** A colorless syrup (yield 76%), TLC: R_f 0.50 (1:5 EtOAc/hexane), $[\alpha]^{25}_D$ −44° (*c* 0.99, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2930 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, $CDCl_3$) δ_H 5.42 (1 H, br s, 5a-H), 4.61 (1 H, br d, $J_{4,3}=8.4$ Hz, 4-H), 4.50 and 4.17 (each 1 H, 2 d, $J_{gem}=13.7$ Hz, 2 6-H), 3.73–3.56 (3 H, m, 1-H, 2-H, 3-H), 2.59–2.37 (4 H, m, 2 CH_2), 1.70–1.20 (20 H, m, 10 CH_2), 1.57, 1.45, 1.44 and 1.43 (each 3 H, 4 s, 2 CMe_2), 0.89 and 0.88 (6 H, 2 t, $J_{7',8'}=6.6$ Hz, $J_{5'',6''}=6.6$ Hz, 2 CH_3). Anal. calcd for $C_{27}H_{49}O_4N$: C, 71.80; H, 10.93; N, 3.10%. Found: C, 71.51; H, 11.32; N, 3.11%.

***N*,*N*-Dioctyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (8c).** A colorless syrup (yield 60%), TLC: R_f 0.52 (1:5 EtOAc/hexane), $[\alpha]^{24}_D$ −41° (*c* 1.09, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, $CDCl_3$) δ_H 5.42 (1 H, br s, 5a-H), 4.61 (1 H, br d, $J_{3,4}=8.6$ Hz, 4-H), 4.50 and 4.16 (each 1 H, 2 d, $J_{gem}=13.7$ Hz, 2 6-H), 3.73–3.56 (3 H, m, 1-H, 2-H, 3-H), 2.58–2.37 (4 H, m, 2 CH_2), 1.73–1.20 (24 H, m, 12 CH_2), 1.57, 1.45, 1.44 and 1.43 (each 3 H, 4 s, 2 CMe_2), 0.88 (6 H, 2 t, $J_{7',8'}=6.6$ Hz, $J_{7'',8''}=6.6$ Hz, 2 CH_3). Anal. calcd for $C_{29}H_{53}O_4N$: C, 72.60; H, 11.14; N, 2.92%. Found: C, 72.57; H, 11.43; N, 2.95%.

***N*-Decyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (8d).** A colorless syrup (yield 82%), TLC: R_f 0.53 (1:5 EtOAc/hexane), $[\alpha]^{25}_D$ −36° (*c* 0.81, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2930 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, $CDCl_3$) δ_H 5.42 (1 H, br s, 5a-H), 4.61 (1 H, br d, $J_{3,4}=8.4$ Hz, 4-H), 4.50 and 4.17 (each 1 H, 2 d, $J_{gem}=13.6$ Hz, 2 6-H), 3.73–3.56 (3 H, m, 1-H, 2-H, 3-H), 2.58–2.35 (4 H, m, 2 CH_2), 1.70–1.20 (28 H, m, 14 CH_2), 1.57, 1.45, 1.44 and 1.43 (each 3 H, 4 s, 2 CMe_2), 0.88 (6 H, 2 t, $J_{7',8'}=6.8$ Hz, $J_{9'',10''}=6.8$ Hz, 2 CH_3). Anal. calcd for $C_{31}H_{57}O_4N$: C, 73.32; H, 11.31; N, 2.76%. Found: C, 73.21; H, 11.54; N, 3.02%.

***N*-Dodecyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (8e).** A colorless syrup (yield 55%), TLC: R_f 0.54 (1:5 EtOAc/hexane), $[\alpha]^{25}_D$ −30° (*c* 0.94, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, $CDCl_3$) δ_H 5.41 (1 H, br s, 5a-H), 4.61 (1 H, br d, $J_{2,1}=8.8$ Hz, 4-H), 4.50 and 4.16 (each 1 H, 2 d, $J_{gem}=13.9$ Hz, 2 6-H), 3.73–3.56 (3 H, m, 1-H, 2-H, 3-H), 2.58–2.35 (m, 4 H, m, 2 CH_2), 1.73–1.20 (32 H, m, 16 CH_2), 1.57, 1.45, 1.44 and 1.43 (each 3 H, 4 s, 2 CMe_2), 0.88 (6 H, 2 t, $J_{7',8'}=6.6$ Hz, $J_{11'',12''}=6.6$ Hz, 2 CH_3). Anal. calcd for $C_{33}H_{61}O_4N$: C, 73.97; H, 11.47; N, 2.61%. Found: C, 73.85; H, 11.40; N, 2.87%.

***N*-Octyl-*N*-tetradecyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (8f).** A colorless syrup (yield 67%), TLC: R_f 0.55 (1:5 EtOAc/hexane), $[\alpha]^{22}_D$ −31° (*c* 1.03, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, $CDCl_3$) δ_H 5.41 (1 H, br s, H-5a), 4.61 (1 H, br d, $J_{2,1}=8.8$ Hz, H-4), 4.50 and 4.16 (each 1 H, 2 d, $J_{gem}=13.9$ Hz, 2 6-H), 3.73–3.56 (m, 3 H, 1-H, 2-H, 3-H), 2.58–2.35 (4 H, m, 2 CH_2), 1.72–1.20 (36 H, m, 18 CH_2), 1.57, 1.45, 1.44 and 1.43 (each 3 H, 4 s, 2 CMe_2), 0.88 (6 H, 2 t, $J_{7',8'}=6.6$ Hz, $J_{13'',14''}=6.6$ Hz, 2 CH_3). Anal. calcd for $C_{35}H_{65}O_4N$: C, 74.55; H, 11.62; N, 2.48%. Found: C, 74.73; H, 11.33; N, 2.48%.

***N*-Hexadecyl-*N*-octyl-2,3:4,6-di-*O*-isopropylidene-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (8g).** A colorless syrup (yield 87%), TLC: R_f 0.56 (1:5 EtOAc/hexane), $[\alpha]^{21}_D$ −33° (*c* 1.18, $CHCl_3$), ν_{max} (neat) 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, $CDCl_3$) δ_H 5.41 (1 H, br s, 5a-H), 4.61 (1 H, br d, $J_{2,1}=8.8$ Hz, 4-H), 4.50 and 4.17 (each 1 H, 2 d, $J_{gem}=13.9$ Hz, 2 6-H), 3.73–3.56 (3 H, m, 3 H, 1-H, 2-H, 3-H), 2.58–2.35 (4 H, m, 2 CH_2), 1.72–1.20 (40 H, m, 20 CH_2), 1.57, 1.45, 1.44 and 1.43 (each 3 H, 2 CMe_2), 0.88 (6 H, 2 t, $J_{7',8'}=6.6$ Hz, $J_{15'',16''}=6.6$ Hz, 2 CH_3). Anal. calcd for $C_{37}H_{69}O_4N$: C, 75.07; H, 11.75; N, 2.37%. Found: C, 75.06; H, 12.05; N, 2.58%.

***N*-Butyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (5a).** A solution of **8a** (61 mg, 0.144 mmol) and aqueous 80% acetic acid (2 mL) was stirred for 30 min at 80 °C and then concentrated. The residue was co-evaporated three times with ethanol, and then three times with toluene. The residue was dissolved in MeOH (2 ml) and stirred with Dowex 1×8 200–400 mesh OH^- ion exchange resin (0.5 g dry resin). After 30 min, the mixture was filtered and the filtrate was concentrated. The crude product was purified by column chromatography on silica gel (6 g, gradient elution, 1:9 to 1:6 EtOH/toluene) to yield **5a** (48 mg, 98%) as a colorless syrup, TLC: R_f 0.16 (1:5 MeOH/$CHCl_3$), $[\alpha]^{24}_D$ −110° (*c* 1.00, MeOH), ν_{max} (KBr) 3420 (OH), 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, 1:2 $CD_3OD/CDCl_3$) δ_H 5.69 (1 H, br s, 5a-H), 4.20 (1 H, br d, $J_{3,4}=7.3$ Hz, 4-H), 4.20 and 4.12 (each 1 H, 2 d,

J_{gem} = 13.6 Hz, 2 6-H), 3.60 (1 H, dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 7.3 Hz, 3-H), 3.48 (1 H, dd, $J_{1,2}$ = 8.8 Hz, $J_{2,3}$ = 9.9 Hz, 2-H), 3.30 (1 H, br d, $J_{1,2}$ = 8.8 Hz, 1-H), 2.61–2.40 (4 H, m, 2 CH_2) 1.56–1.25 (16 H, m, 8 CH_2), 0.92 and 0.89 (6 H, 2 t, $J_{7',8'}$ = 7.0 Hz, $J_{3'',4''}$ = 7.0 Hz, 2 CH_3). Anal. calcd for $C_{19}H_{37}O_4N$: C, 66.43; H, 10.86; N, 4.08%. Found: C, 66.18; H, 11.23; N, 4.21%.

***N*-Hexyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (5b).** A colorless syrup (yield 85%), TLC: R_f 0.26 (1:5 MeOH/$CHCl_3$), $[\alpha]^{23}_D$ −102° (*c* 0.87, MeOH), ν_{max} (KBr) 3430 (OH), 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, 1:2 CD_3OD/$CDCl_3$) δ_H 5.69 (1 H, br s, 5a-H), 4.20 (1 H, br d, $J_{3,4}$ = 7.7 Hz, 4-H), 4.20 and 4.12 (each 1 H, 2 d, J_{gem} = 13.6 Hz, 2 6-H), 3.60 (1 H, dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 7.7 Hz, 3-H), 3.48 (1 H, dd, $J_{1,2}$ = 8.8 Hz, $J_{2,3}$ = 9.9 Hz, 2-H), 3.31 (1 H, br d, $J_{1,2}$ = 8.8 Hz, 1-H), 2.62–2.40 (4 H, m, 2 CH_2), 1.56–1.21 (20 H, m, 10 CH_2), 0.90 and 0.89 (6 H, 2 t, $J_{7',8'}$ = 7.0 Hz, $J_{5'',6''}$ = 7.0 Hz, 2 CH_3). Anal. calcd for $C_{21}H_{41}O_4N$: C, 67.88; H, 11.12; N, 3.77%. Found: C, 67.95; H, 10.97; N, 3.80%.

***N*,*N*-Dioctyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (5c).** A colorless syrup (yield 90%), TLC: R_f 0.32 (1:5 MeOH/$CHCl_3$), $[\alpha]^{23}_D$ −77° (*c* 0.37, MeOH), ν_{max} (KBr) 3430 (OH), 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, 1:2 CD_3OD/$CDCl_3$) δ_H 5.69 (1 H, br s, 5a-H), 4.20 (1 H, br d, $J_{3,4}$ = 7.3 Hz, 4-H), 4.20 and 4.13 (each 1 H, 2 d, J_{gem} = 13.9 Hz, 2 6-H), 3.61 (1 H, dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 7.3 Hz, 3-H), 3.49 (1 H, dd, $J_{1,2}$ = 8.8 Hz, $J_{2,3}$ = 9.9 Hz, 2-H), 3.34 (1 H, br d, $J_{1,2}$ = 8.8 Hz, 1-H), 2.64–2.42 (4 H, m, 2 CH_2) 1.57–1.18 (24 H, m, 12 CH_2), 0.88 (6 H, 2 t, $J_{7',8'}$ = 6.6 Hz, $J_{7'',8''}$ = 6.6 Hz, 2 CH_3). Anal. calcd for $C_{23}H_{45}O_4N$: C, 69.13; H, 11.35; N, 3.51%. Found: C, 68.84; H, 11.65; N, 3.57%.

***N*-Decyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (5d).** A colorless syrup (yield 90%), TLC: R_f 0.36 (1:5 MeOH/$CHCl_3$), $[\alpha]^{23}_D$ −86° (*c* 0.90, MeOH), ν_{max} (KBr) 3430 (OH), 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, 1:2 CD_3OD/$CDCl_3$) δ_H 5.69 (1 H, br s, 5a-H), 4.20 (br d, 1 H, $J_{3,4}$ = 7.7 Hz, 4-H), 4.20 and 4.12 (each 1 H, 2 d, J_{gem} = 13.6 Hz, 2 6-H), 3.61 (1 H, dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 7.7 Hz, 3-H), 3.48 (1 H, dd, $J_{1,2}$ = 8.8 Hz, $J_{2,3}$ = 9.9 Hz, 2-H), 3.31 (1 H, br d, $J_{1,2}$ = 8.8 Hz, 1-H), 2.62–2.40 (4 H, m, 2 CH_2), 1.57–1.20 (28 H, m, 14 CH_2), 0.89 (6 H, 2 t, $J_{7',8'}$ = 6.5 Hz, $J_{9'',10''}$ = 6.5 Hz, 2 CH_3). Anal. calcd for $C_{25}H_{49}O_4N$: C, 70.21; H, 11.55; N, 3.28%. Found: C, 70.41; H, 11.54; N, 3.20%.

***N*-Dodecyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (5e).** A colorless syrup (yield 89%), TLC: R_f 0.38 (1:5 MeOH/$CHCl_3$), $[\alpha]^{19}_D$ −82° (*c* 0.93, MeOH), ν_{max} (KBr) 3440 (OH), 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, 1:2 CD_3OD/$CDCl_3$) δ_H 5.69 (1 H, br s, 5a-H), 4.20 (1 H, br d, $J_{3,4}$ = 7.3 Hz, 4-H), 4.20 and 4.13 (each 1 H, 2 d, J_{gem} = 13.6 Hz, 2 6-H), 3.60 (1 H, dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 7.3 Hz, 3-H), 3.49 (1 H, dd, $J_{1,2}$ = 8.8 Hz, $J_{2,3}$ = 9.9 Hz, 2-H), 3.32 (1 H, br d, $J_{1,2}$ = 8.8 Hz, 1-H), 2.63–2.42 (4 H, m, 2 CH_2), 1.57–1.17 (32 H, m, 16 CH_2), 0.89 (6 H, 2 t, $J_{7',8'}$ = 6.6 Hz, $J_{11'',12''}$ = 6.6 Hz, 2 CH_3). Anal. calcd for $C_{27}H_{53}O_4N$: C, 71.16; H, 11.72; N, 3.07%. Found: C, 71.16; H, 11.72; N, 3.06%.

***N*-Octyl-*N*-tetradeyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (5f).** A colorless syrup (yield 91%), TLC: R_f 0.40 (1:5 MeOH/$CHCl_3$), $[\alpha]^{22}_D$ −73° (*c* 0.83, MeOH), ν_{max} (KBr) 3440 (OH), 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, 1:2 CD_3OD/$CDCl_3$) δ_H 5.69 (1 H, br s, 5a-H), 4.20 (1 H, br d, $J_{3,4}$ = 7.7 Hz, 4-H), 4.20 and 4.13 (each 1 H, 2 d, J_{gem} = 13.6 Hz, 2 6-H), 3.61 (1 H, dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 7.7 Hz, 3-H), 3.48 (1 H, dd, $J_{1,2}$ = 8.8 Hz, $J_{2,3}$ = 9.9 Hz, 2-H), 3.31 (1 H, br d, $J_{1,2}$ = 8.8 Hz, 1-H), 2.62–2.41 (4 H, m, 2 CH_2), 1.56–1.18 (36 H, m, 18 CH_2), 0.89 (6 H, 2 t, $J_{7',8'}$ = 6.6 Hz, $J_{13'',14''}$ = 6.6 Hz, 2 CH_3). Anal. calcd for $C_{29}H_{57}O_4N$: C, 72.01; H, 11.88; N, 2.90%. Found: C, 71.85; H, 12.01; N, 2.93%.

***N*-Hexadecyl-*N*-octyl-5a-carba-β-D-*xylo*-hex-5(5a)-enopyranosylamine (5g).** A colorless syrup (yield 87%), TLC: R_f 0.42 (1:5 MeOH/$CHCl_3$), $[\alpha]^{21}_D$ −76° (*c* 1.00, MeOH), ν_{max} (KBr) 3450 (OH), 2955 (CH_3), 2925 and 2855 (CH_2) cm^{-1}, ^1H NMR (270 MHz, 1:2 CD_3OD/$CDCl_3$) δ_H 5.69 (1 H, br s, 5a-H), 4.20 (1 H, br d, $J_{3,4}$ = 7.7 Hz, 4-H), 4.20 and 4.13 (each 1 H, 2 d, J_{gem} = 13.6 Hz, 2 6-H), 3.61 (1 H, dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 7.7 Hz, 3-H), 3.48 (1 H, dd, $J_{1,2}$ = 8.8 Hz, $J_{2,3}$ = 9.9 Hz, 2-H), 3.32 (1 H, br d, $J_{1,2}$ = 8.8 Hz, 1-H), 2.62–2.41 (4 H, m, 2 CH_2) 1.57–1.20 (40 H, m, 20 CH_2), 0.89 (6 H, 2 t, $J_{7',8'}$ = 6.6 Hz, $J_{15'',16''}$ = 6.6 Hz, 2 CH_3). Anal. calcd for $C_{31}H_{61}O_4N$: C, 72.75; H, 12.01; N, 2.74%. Found: C, 72.73; H, 12.14; N, 2.65%.

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References and Notes

1. Radin, N. S.; Shayman, J. A.; Inokuchi, J. *Adv. Lipid Res.* **1993**, *26*, 183.

2. Inokuchi, J.; Jimbo, M.; Momosaki, K.; Shimeno, H.; Nagamatsu, A.; Radin, N. S. *Cancer Res.* **1990**, *50*, 6731.

3. Kyogashima, M.; Inoue, M.; Seto, A.; Inokuchi, J. *Cancer Lett.* **1996**, *101*, 25, and references cited therein.

4. Tsunoda, H.; Ogawa, S. *Liebigs Ann. Chem.* **1995**, 267.

5. Tsunoda, H.; Inokuchi, J.; Yamagishi, K.; Ogawa, S. *Liebigs Ann. Chem.* **1995**, 279.

6. Ogawa, S.; Ashiura, M.; Uchida, C.; Watanabe, S.; Yamazaki, C.; Yamagishi, K.; Inokuchi, J. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 929.

7. Ogawa, S; Mito, T; Taiji, E; Jimbo, M; Yamagishi, K; Inokuchi, J. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1915.

8. Ogawa, S.; Uchida, C.; Shibata, Y. *Carbo. Res.* **1992**, *223*, 279.

9. Inhibitory activities (IC_{50}) listed in Table 1 were measured by the following procedures. β-Glucocerebrosidase: The assay was performed with the fluorogenic substrate, NBD-glucosylceramide, with microsomal fraction of mouse liver in a total volume 0.2 mL containing glucocerebroside from Gaucher spleen, Trinton X-100, sodium taurocholate and phosphate-citrate (pH 5.5) as reported: Grabowski, G. A.; Dinur, T.; Gatt, S.; Desnick, R. J. *Clin. Chim. Acta.* **1982**, *124*, 123.

10. Inokuchi, J.; Momosaki, K.; Shimeno, H.; Nagamatsu, A.; Radin, N. S. *J. Cell. Phys.* **1989**, *141*, 573.