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STEREOSELECTIVE β-D-PSICOFURANOSYLATION AND SYNTHESIS OF β-D-PSICOFURANOSYLCERAMIDE

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Abstract — Psicofuranosylations of alcohols and phenol **3a-e** with benzyl D-psicosyl phthalate **2** occurred on the β-face to give β-D-psicoside **4a-e** in excellent yields. The reaction of ceramide **5** with **2** and deprotections of acetonide and three benzoates of the resulting glycoside afforded β-D-psicosylceramide **1**.

INTRODUCTION

Cerebrosides are glycoshingolipids and important components of a wide variety of issues and organs in biological system.[1] They serve as structural part of cellular membranes and metabolic precursors for sphigosines and ceramides, which play important physiological and pathophysiological roles.[2] Cerebrosides consist of a hexose unit and a ceramide unit linked with a glycosidic bond. Ceramide is a C-18 carbon chain aminoalcohol with *N*-alkanoyl moiety. Although cerebroside composes a hexose commonly galactose or glucose,[3] and rarely mannose or oligosaccharide,[4] only a few hexofuranosylceramides has been studied.[5] D-Psicofuranose is a diastereomer of D-fructofuranose at C-3 carbon center. We are interested in hexofuranosylceramide having a D-psicosyl unit. In this paper, we describe i) β-D-psicosylation of primary and secondary alcohols and phenol and ii) synthesis of β-D-psicofuranosylceramide **1** of which structure is shown in Figure 1.

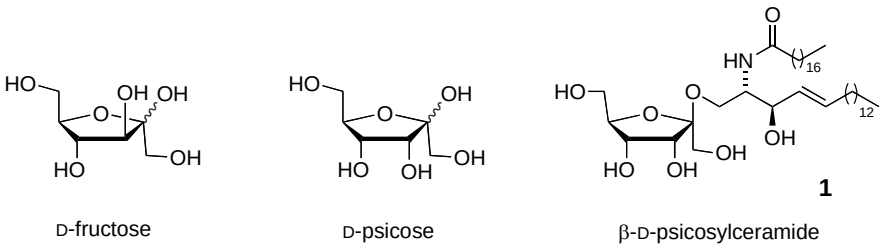
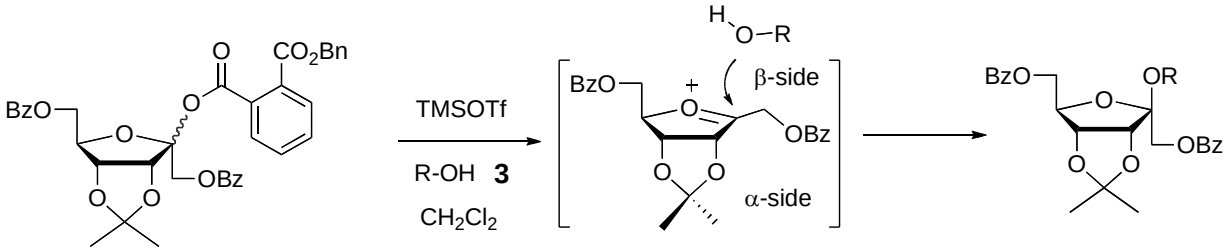


Figure 1

This paper is dedicated to Professor Emeritus Keiichiro Fukumoto on the occasion of his 75th birthday.

RESULTS AND DISCUSSION

D-Psicose is an expensive rare sugar.[6] The chemistry of psicose has not been investigated well. D-Psicose has been provided by fermentation being converted from D-fructose by D-tagatose-3-epimerase.[7] Recently, we have prepared it chemically from D-ribose in the synthetic process of (+)-sucrose.[8] The synthesis of (+)-sucrose involved the psicosylation of α-D-glucose with benzyl D-psicosyl phthalate **2**. This glycosylation was promoted by TMSOTf generating cyclic oxonium intermediate, as shown in Scheme 1. Glycosidation of D-glucose (R = α-D-glucosyl in **3**) with **2** occurred from β-side of the furanose ring. The stereoselectivity can be explained that one of the methyl group of the acetonide covers the α-side of the cyclic oxonium ion, and glycosyl acceptor **3** is unable to attack from the α-face of the ring.[9]



2 **4**

Scheme 1. Glycosidation of 3 with D-psicofuranosyl donor 2

The result encouraged us to examine glycosidations of other substrates. The reaction of 2-propanol with a 94:6 ratio of β:α diastereomeric mixtures **2** was conducted in CH_2Cl_2 at –40 °C in the presence of TMSOTf.[10] Isopropyl β-D-psicoside **4a** was obtained in 79% yield. The nmr spectrum of the crude product indicated no existence of the α–isomer. Other common Lewis acid promoters such as BF_3 etherate or $SnCl_4$ were less reactive and gave poor results. The structure was determined by NOE experiments, and the result is shown in Figure 2. Three NOE relations were observed clearly between one CH_3 protons of the isopropyl group and one of C-6 protons, one of C-1 protons and the inside CH_3 protons of the acetonide, and C-5 proton and the inside CH_3 protons of the acetonide. The relations are clearly supported that psicoside **4a** possesses β-glycosidic linkage.

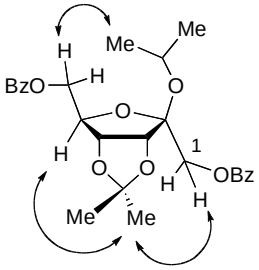
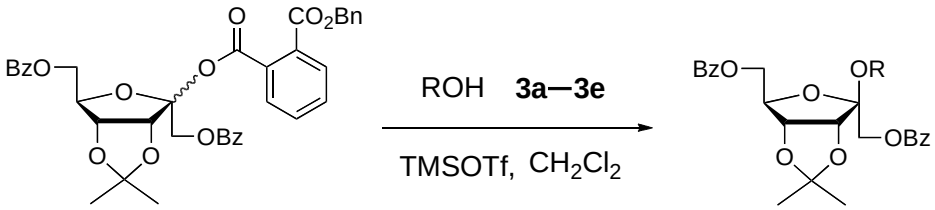


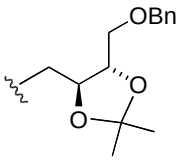
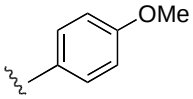
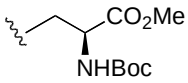
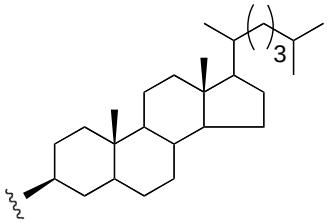
Figure 2. NOE relations in compound 4a

The result of other glycosidation reactions with alcohols and phenol are listed in Table 1. The reaction with D-threitol 2,3-acetonide **3b** gave the corresponding psicoside **4b** in 91% yield. The reaction of primary alcohol proceeded faster then that of secondary alcohol. The reaction with *p*-methoxyphenol gave **4c** in 83% yield. *N*-Boc protected serine methyl ester **3d** and ®-cholestanol **3e** reacted with **2** to afford **4d** and **4e** in 94 and 55% yields, respectively. All the psicosylation reactions gave β-glycoside products exclusively.

Table 1. Glycosidation of 3a–3e with benzyl D-psicofuranosyl phthalate 2

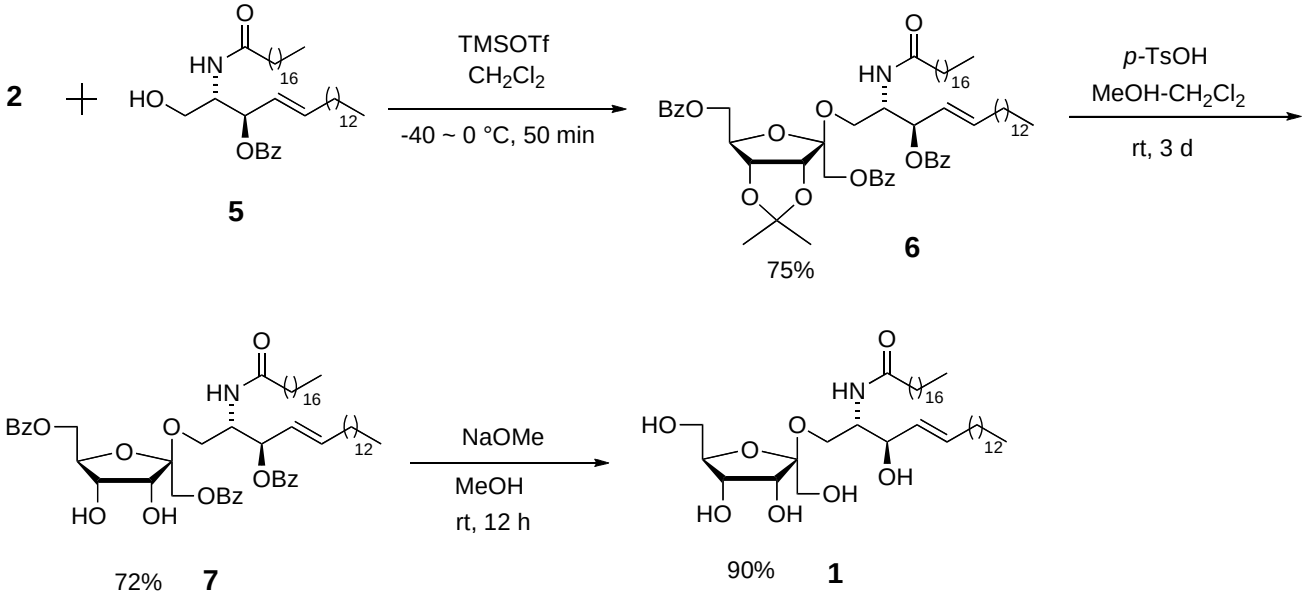


2 **4a-4e**

Entry	R-OH	R	Product	Temp. (°C)	Time (min)	Yield (%)
1	**3a**		**4a**	—40 to 0	80	79
2	**3b**		**4b**	—40	20	91
3	**3c**		**4c**	—40	20	83
4	**3d**		**4d**	—40 to -30	120	94
5	**3e**		**4e**	—40 to 0	60	55

Since psicosylation reactions took place quite selectively to give β–D-psicofuranosides with excellent yields, we have examined psicofuranosylation of ceramide. The reaction of *O*-benzoyl-*N*-stearoylceramide **5**[11] with **2** occurred well under the same conditions described for **4** to give β-D-psicofuranosylceramide **6** in 75% yield as a single stereoisomer. The compound **6** was converted to

1 in two steps. Mild deprotection of acetonide with *p*-TsOH in a mixture of MeOH and CH_2Cl_2 for 3 days gave diol **7** in 72% yield based on the recovery of the starting material. Methanolysis of three benzoates accomplished full deprotections of **7** to give the desired β-D-psicofuranosylceramide **1** in 90% yield.



Scheme 3. Synthesis of β-D-psicofuranosylceramide 1

In conclusion, glycosidation of **3** with **2** took place on the β-side and gave β-D-psicoside **4** in good yield. Psicosylceramide **1** was first synthesized by this method.

EXPERIMENTAL

General. Melting points were taken on a Yanako micromelting apparatus and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on JEOL JMN-AL-300 (300 MHz and 75 MHz) or Varian Inova Unity XL-400 (400 MHz and 100 MHz) spectrometers in C_6D_6, CD_3OD, or $CDCl_3$ with tetramethylsilane or $CDCl_3$ as an internal standard. IR spectra were recorded on JASCO FT/IR-410 instrument. Specific rotation was measured on a JASCO DIP-360 instrument. Low and high resolution mass spectra (LRMS and HRMS) were obtained on a JEOL JMS 303HF spectrometer. Column chromatography was carried out using Merck silica gel 60 (230-400 mesh).

General procedure for the glycosylation reaction.

A mixture of **2** (1 mmol) and **3** or **5** (1.2–1.5 mmol) was taken in a 50 mL flask and pre-dried azeotropically by evaporation with dry toluene. The residual oily material was further dried under reduced pressure over the presence of P_4O_{10}. Dry CH_2Cl_2 (20 mL) was added to the flask and in the case

of **3a** was added at this stage. The mixture was cooled to –40 °C and TMSOTf (1.5 mmol) was added. The reaction was continued during the time indicated at Table 1. To the reaction mixture, aqueous sat. $NaHCO_3$ (10 mL) and CH_2Cl_2 (20 mL) were added. Organic layer was washed with water and brine and dried over $MgSO_4$. Solvent was removed and residue was purified by flash chromatography on silica gel. A mixtureof EtOAc in hexane was used as an eluent for the chromatography; 10% for **4a**, 15% for **4b**, **4c**, **4d** and **6**, and 5% for **4e**. Chemical yields are indicated in Table and physical and spectroscopic data are following.

2-Propyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-psicofuranoside (4a): Viscous liquid. R_f = 0.73 (30% EtOAc in hexane). $[\alpha]^{25}_D$ –25.6 (*c* 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, C_6D_6) δ: 8.27–8.24 (2H, m), 8.20–8.17 (2H, m), 7.13–6.99 (6H, m), 4.96 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1a), 4.77 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1b), 4.73 (1H, d, $J_{3,4}$ = 6.0 Hz, H-3), 4.59 (1H, ddd, $J_{5,6b}$ = 7.3, $J_{5,6a}$ = 6.6, $J_{4,5}$ = 1.6 Hz, H-5), 4.51 (1H, dd, $J_{3.4}$ = 6.0, $J_{4,5}$ = 1.6 Hz, H-4), 4.35 (1H, dd, $J_{6a,6b}$ = 11.2, $J_{5,6a}$ = 6.6 Hz, H-6a), 4.31 (1H, dd, $J_{6a,6b}$ = 11.2, $J_{5,6b}$ = 7.3 Hz, H-6b), 4.05 (1H, qq, *J* = 6.0, 6.0 Hz, OC*H*$(CH_3)_2$), 1.38 (3H, s, $(CH_3)_2C$), 1.12 (3H, d, *J* = 6.0 Hz, OCH$(CH_3)_2$), 1.05 (3H, s, $(CH_3)_2C$), 1.05 (3H, d, *J* = 6.0 Hz, OCH$(CH_3)_2$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.2, 165.9, 133.2, 133.0, 130.0, 129.7, 128.4, 113.2, 109.6, 86.3, 84.1, 82.4, 65.7, 65.6, 61.2, 26.6, 25.1, 24.3, 24.1. IR (film) cm^{-1}: 2977, 1725, 1602, 1453, 1381, 1272, 1111, 989, 871, 710, 681. MS (FAB) *m*/*z*: 493 $(M+Na)^+$. HR-MS (FAB) *m*/*z*: Calcd for $C_{26}H_{30}O_8Na$: 493.1838. Found: 493.1842.

(4-*O*-Benzyl-2,3-*O*-isopropylidene-L-threityl)-1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-psicofuranoside (4b): Syrup. R_f = 0.51 (30% EtOAc in hexane). $[\alpha]^{22}_D$ –12.9 (*c* 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.09–8.05 (4H, m), 7.61–7.53 (2H, m), 7.47–7.40 (4H, m), 7.28–7.23 (5H, m), 4.81 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 1.3 Hz, H-4), 4.74 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1a), 4.66 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.58–4.46 (5H, m, H-1a, 5, 6a, CH_2Ph), 4.38 (1H, dd, $J_{6a,6b}$ = 10.4, $J_{5,6b}$ = 6.7 Hz, H-6b), 3.97–3.87 (2H, m), 3.78 (1H, dd, *J* = 9.5, 6.2 Hz), 3.71 (1H, dd, *J* = 9.5, 3.7 Hz), 3.54 (1H, dd, *J* = 10.1, 4.8 Hz), 3.50 (1H, dd, *J* = 10.1, 4.2 Hz), 1.53 (3H, s), 1.36 (3H, s), 1.34 (3H, s), 1.32 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.8, 165.7, 137.7, 133.1, 133.0, 129.7, 129.7, 129.6, 128.3, 128.3, 128.2, 127.6, 127.5, 113.2, 109.8, 109.1, 85.3, 84.5, 82.2, 77.5, 77.0, 73.3, 70.3, 65.0, 63.1, 59.4, 26.8, 26.7, 26.5, 25.1. IR (film) cm^{-1}: 2986, 1729, 1602, 1453, 1373, 1273, 1087, 871, 710. MS (FAB) *m*/*z*: 685 $(M+Na)^+$. HR-MS (FAB) *m*/*z*: Calcd for $C_{37}H_{42}O_{11}Na$: 685.2625. Found: 685.2619.

4-Methoxyphenyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-psicofuranoside (4c): Colorless crystals, mp 150–151 °C (EtOAc:hexane = 1:7). R_f = 0.47 (30% EtOAc in hexane). $[\alpha]^{24}_D$ +57.2 (*c* 1.02,

$CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 8.10–8.03 (4H, m), 7.61–7.55 (2H, m), 7.49–7.43 (4H, m), 7.18–7.12 (2H, m), 6.68–6.62 (2H, m), 5.02 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.97 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 1.5 Hz, H-4), 4.72 (1H, ddd, $J_{5,6b}$ = 7.5, $J_{5,6a}$ = 6.2, $J_{4,5}$ = 1.5 Hz, H-5), 4.60 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6a}$ = 6.2 Hz, H-6a), 4.56 (2H, s, H-1), 4.54 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6b}$ = 7.5 Hz, H-6b), 3.68 (3H, s), 1.54 (3H, s), 1.38 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.0, 165.4, 155.6, 146.9, 133.1, 132.9, 129.8, 129.6, 129.6, 129.5, 128.3, 128.3, 121.7, 114.2, 113.4, 111.2, 86.0, 85.2, 81.9, 65.0, 60.4, 55.3, 26.5, 25.2. IR (KBr) cm^{-1}: 2990, 1721, 1601, 1507, 1454, 1375, 1270, 1073, 1038, 844, 709. MS (FAB) *m*/*z*: 557 $(M+Na)^+$. HR-MS (FAB) *m*/*z*: Calcd for $C_{30}H_{30}O_9Na$: 557.1787. Found: 557.1780. *Anal.* Calcd for $C_{30}H_{30}O_9$: C, 67.41; H, 5.66. Found: C, 67.53; H, 5.64.

***O*-(1,6-Di-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-psicofuranosyl)-*N*-(*tert*-butoxycarbonyl)-L-serine methyl ester (4d):** Syrup. R_f = 0.16 (20% EtOAc in hexane). $[\alpha]^{23}_D$ +3.2 (*c* 0.99, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 8.09–8.06 (4H, m), 7.62–7.56 (2H, m), 7.50–7.44 (4H, m), 5.36 (1H, d, *J* = 9.0 Hz, N*H*), 4.75 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 1.4 Hz, H-4), 4.71 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.64 (1H, d, $J_{1a,1b}$ = 12.3 Hz, H-1a), 4.55 (1H, ddd, $J_{5,6b}$ = 7.6, $J_{5,6a}$ = 7.3, $J_{4,5}$ = 1.4 Hz, H-5), 4.49 (1H, d, $J_{1a,1b}$ = 12.3 Hz, H-1b), 4.46 (1H, ddd, *J* = 9.0, 3.2, 2.7 Hz, N-C*H*), 4.37 (1H, dd, $J_{6a,6b}$ = 11.2, $J_{5,6a}$ = 7.3 Hz, H-6a), 4.21 (1H, dd, $J_{6a,6b}$ = 11.2, $J_{5,6b}$ = 7.6 Hz, H-6b), 4.05 (1H, dd, *J* = 9.6, 2.7 Hz, one of CH_2CHN), 3.85 (1H, dd, *J* = 9.6, 3.2 Hz, one of CH_2CHN), 3.77 (3H, s, COOCH_3), 1.50 (3H, s), 1.32 (3H, s), 1.26 (9H, s, *t*-Bu). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.8, 165.8, 165.5, 155.3, 133.2, 133.1, 129.7, 129.6, 129.4, 128.4, 113.3, 109.5, 85.3, 84.5, 82.2, 79.7, 64.6, 62.3, 59.2, 53.2, 52.6, 28.0, 26.4, 24.9. IR (KBr) cm^{-1}: 3396, 2983, 1703, 1509, 1452, 1271, 1105, 974, 876, 719. MS (FAB) *m*/*z*: 652 $(M+Na)^+$. HR-MS (FAB) *m*/*z*: Calcd for $C_{32}H_{39}NO_{12}Na$: 652.2370. Found: 652.2361.

β-Cholestanyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-psicofuranoside (4e): Oil. R_f = 0.28 (10% EtOAc in hexane). $[\alpha]^{22}_D$ +8.1 (*c* 1.00, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 8.10–8.06 (4H, m), 7.60–7.56 (2H, m), 7.48–7.43 (4H, m), 4.83 (1H, dd, $J_{3,4}$ = 6.0, $J_{4,5}$ = 1.3 Hz, H-4), 4.70 (1H, d, $J_{3,4}$ = 6.0 Hz, H-3), 4.60 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1a), 4.54 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1b), 4.53 (1H, ddd, $J_{5,6a}$ = 6.8, $J_{5,6b}$ = 6.1, $J_{4,5}$ = 1.3 Hz, H-5), 4.48 (1H, dd, $J_{6a,6b}$ = 10.2, $J_{5,6a}$ = 6.8 Hz, H-6a), 4.40 (1H, dd, $J_{6a,6b}$ = 10.2, $J_{5,6b}$ = 6.1 Hz, H-6b), 3.81 (1H, tt, *J* = 10.8, 5.0 Hz, H-3'), 1.94–0.48 (52H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.1, 165.9, 133.1, 132.9, 130.0, 129.7, 129.7, 128.3, 128.3, 113.1, 109.6, 86.3, 83.9, 82.4, 72.7, 65.6, 61.5, 56.3, 56.1, 54.2, 44.8, 42.5, 39.9, 39.4, 37.1, 36.6, 36.1, 35.7, 35.3, 35.1, 31.9, 30.1, 28.6, 28.1, 27.9, 26.5, 25.1, 24.1, 23.7, 22.8, 22.5, 21.0, 18.6, 12.1, 12.0. IR (KBr) cm^{-1}: 2935, 1725, 1602, 1451, 1381, 1270, 1088, 871, 710. MS (FAB) *m*/*z*: 821 $(M+Na)^+$. HR-MS (FAB) *m*/*z*: Calcd for $C_{50}H_{70}O_8Na$: 821.4968. Found: 821.4974.

3-*O*-Benzoyl-1-*O*-(1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-psicofuranosyl)-*N*-stearoyl-D-*erythro*-sphingosine (6): Colorless crystals, mp 105–107 °C (EtOAc:hexane, 1:8). R_f = 0.55 (30% EtOAc in hexane). $[\alpha]^{22}_D$ –0.5 (*c* 1.18, $CHCl_3$). ^{1}H NMR (300 MHz, C_6D_6) δ: 8.27–8.23 (2H, m), 8.19–8.16 (2H, m), 8.05–8.00 (2H, m), 7.12–6.94 (9H, m), 6.34 (1H, d, *J* = 9.2 Hz, N*H*), 6.03 (1H, dd, $J_{3',4'}$ = 7.1, $J_{2',3'}$ = 5.9 Hz, H-3'), 5.93 (1H, dt, $J_{4',5'}$ = 15.2, $J_{5',6'}$ = 6.6 Hz, H=5'), 5.67 (1H, dd, $J_{4',5'}$ = 15.2, $J_{3',4'}$ = 7.1 Hz, H-4'), 5.04–4.96 (1H, m, H-2'), 4.89 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1a), 4.79 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1b), 4.71 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.66–4.57 (2H, m, H-6), 4.42 (1H, d, $J_{3,4}$ = 5.9 Hz, H-4), 4.08 (1H, dd, $J_{5,6a}$ = 15.8, $J_{5,6b}$ = 9.9 Hz, H-5), 3.95–3.86 (2H, m, H-1'), 2.22–2.05 (2H, m), 1.86–1.73 (4H, m), 1.35–1.17 (53H, m), 1.07 (3H, s), 0.92 (6H, t, *J* = 6.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 173.0, 166.2, 165.6, 165.4, 136.8, 133.2, 132.8, 129.9, 129.7, 129.7, 129.5, 129.5, 129.2, 128.5, 128.3, 128.2, 124.2, 113.4, 109.4, 85.2, 84.9, 81.7, 75.0, 65.3, 60.2, 59.5, 51.2, 36.5, 32.1, 31.9, 29.6, 29.6, 29.5, 29.5, 29.4, 29.3, 29.2, 29.2, 28.7, 26.5, 25.7, 25.1, 22.6, 14.1. IR (KBr) cm^{-1}: 3369, 2920, 2851, 1717, 1655, 1516, 1452, 1269, 1097, 864, 705. MS (FAB) *m*/*z*: 1102 $(M+Na)^+$. HR-MS (FAB) *m*/*z*: Calcd for $C_{66}H_{97}NO_{11}Na$: 1102.6959. Found: 1102.6964). *Anal.* Calcd for $C_{66}H_{97}NO_{11}$: C, 73.37; H, 9.05; N, 1.30. Found: C, 73.25; H, 8.93; N, 1.35.

3-*O*-Benzoyl-1-*O*-(1,6-di-*O*-benzoyl-β-D-psicofuranosyl)-*N*-stearoyl-D-*erythro*-sphingosine (7): A mixture of **6** (58.2 mg, 54 μmol) and *p*-TsOH·H_2O (31 mg, 162 μmol) in a 1:1 mixture of MeOH and CH_2Cl_2 (1 mL) was stirred at rt for 3 days. Aq. $NaHCO_3$ (2 mL) was added to the mixture and the mixture was extracted with EtOAc (10 mL). The organic extract was washed with water and brine, dried over $MgSO_4$ and evaporated. The residual oil was purified by flash column chromatography on silica gel eluted with 30% EtOAc in hexane to give **7** (29 mg) as a solid in 72% yield based on the 29% recovery of starting material (17 mg). Colorless crystals, mp 93–94 °C (EtOAc:hexane, 1:10). R_f = 0.37 (40% EtOAc in hexane). $[\alpha]^{24}_D$ +19.5 (*c* 0.94, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 8.04–8.02 (2H, m), 7.99–7.96 (2H, m), 7.90–7.88 (2H, m), 7.61–7.51 (3H, m), 7.44–7.35 (6H, m), 6.56 (1H, d, *J* = 9.2 Hz), 5.82 (1H, dt, $J_{4',5'}$ = 14.9, $J_{5',6'}$ = 6.8 Hz, H-5'), 5.57 (1H, dd, $J_{3',4'}$ = 7.1, $J_{2',3'}$ = 5.5 Hz, H-3'), 5.51 (1H, dd, $J_{4',5'}$ = 14.9, $J_{3',4'}$ = 7.1 Hz, H-4'), 4.79 (1H, d, $J_{1a,1b}$ = 12.8 Hz, H-1a), 4.70 (1H, dd, *J* = 11.2, 8.4 Hz), 4.54–4.48 (1H, m, H-2'), 4.45 (1H, d, *J* = 2.7 Hz, OH), 4.29–4.21 (4H, m), 3.93–3.91 (1H, m), 3.85 (1H, dd, $J_{1a',1b'}$ = 9.2, $J_{1a',2}$ = 7.2 Hz, H-1'a), 3.79 (1H, dd, $J_{1a',1b'}$ = 9.2, $J_{1b',2}$ = 3.2 Hz, H-1'b), 2.85 (1H, br s), 2.10–1.96 (4H, m), 1.27–1.17 (50H, m), 1.59–1.50 (2H, m), 0.88–0.85 (6H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 173.4, 167.1, 166.7, 165.5, 136.8, 133.7, 133.2, 133.1, 133.0, 130.1, 129.9, 129.8, 129.8, 129.7, 129.6, 129.0, 128.6, 128.4, 128.4, 128.3, 124.5, 107.7, 81.8, 81.8, 75.1, 74.3, 74.1, 72.8, 71.9, 66.5, 64.7, 60.1, 59.8, 59.2, 51.5, 48.8, 36.6, 32.4, 29.7, 29.6, 29.5, 29.4, 29.3, 29.3, 28.9, 25.8. IR (KBr) cm^{-1}: 3396,

2918, 2850, 1725, 1654, 1262, 1105, 800, 710. MS (FAB) *m/z*: 1062 $(M+Na)^+$. HR-MS (FAB) *m/z*: Calcd for $C_{63}H_{93}NO_{11}Na$: 1062.6646. Found: 1062.6643. *Anal.* Calcd for $C_{63}H_{93}NO_{11}$: C, 72.73; H, 9.01; N, 1.35. Found: C, 72.46; H, 9.18; N, 1.60.

1-*O*-(β-D-Psicofuranosyl)-*N*-stearoyl-D-*erythro*-sphingosine (1): To a stirred solution of **7** (29.9 mg, 28.7 μmol) in MeOH (2 mL) was added sodium methoxide (2 mg, 37 μmol) and the mixture was stirred at rt for 12 h. Amberlite IRC-50 (50 mg) was added and the mixture was stirred for 30 min. The resin was removed by filtration and the organic phase was condensed. The residue was chromatographed on silica gel eluted with 5% MeOH in $CHCl_3$ to give **1** (18.9 mg) in 90% yield. Colorless solid, mp 89–91 °C (EtOAc:hexane, 1:4). R_f = 0.33 (10% MeOH in $CHCl_3$). $[\alpha]^{24}_D$ –20.5 (*c* 0.80, $CHCl_3$). ^{1}H-NMR (400 MHz, CD_3OD-$CDCl_3$ = 1:1) δ: 5.69 (1H, dt, $J_{4',5'}$ = 15.0, $J_{5',6'}$ = 7.3 Hz, H-5'), 5.47 (1H, dd, $J_{4',5'}$ = 15.0, $J_{3'4'}$ = 7.5 Hz, H-4'), 4.32–4.27 (1H, m), 4.08–4.04 (1H, m), 4.00–3.61 (8H, m), 3.58 (1H, dd, *J* = 9.8, 3.6 Hz), 2.20–2.16 (2H, m), 2.05–2.00 (2H, m), 1.62–1.55 (2H, m), 1.37–1.22 (50H, m), 0.89 (6H, t, *J* = 6.9 Hz). ^{13}C NMR (100 MHz, CD_3OD-$CDCl_3$ = 1:1) δ: 174.3, 133.4, 128.9, 107.9, 83.3, 74.3, 71.8, 69.8, 61.3, 59.1, 57.7, 53.1, 35.7, 31.8, 31.3, 31.3, 29.1, 29.1, 29.1, 29.0, 29.0, 29.0, 29.0, 29.0, 28.9, 28.8, 28.7, 28.7, 28.7, 25.4, 22.0, 13.1. IR (KBr) cm^{-1}: 3319, 2917, 2849, 1646, 1533, 1465, 1027, 720. MS (FAB) *m/z*: 750 $(M+Na)^+$. HR-MS (FAB) *m/z*: Calcd for $C_{42}H_{81}NO_8Na$: 750.5860. Found: 750.5855. *Anal.* Calcd for $C_{42}H_{81}NO_8$: C, 69.28; H, 11.21; N, 1.92. Found: C, 68.99; H, 11.27; N, 1.94.

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REFERENCES AND NOTES

1. E. Bapreto-Bergter, M. R. Pinto, and M. L. Rodrigues, *An. Acad. Bras. Cienc.*, 2004, **76**, 67; R. X. Tan and J. H. Chen, *Nat. Prod. Rep.*, 2003, **20**, 509.
2. E. Bieberich, *Neurosignals*, 2008, **16**, 124; S. Pandey, R. F. Murphy, and D. K. Agrawal, *Exp. Mol. Pathol.*, 2007, **82**, 298; E. Gulbins and P. L. Li, *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 2006, **290**, R11; R. Bittman, *Chem. Phys. Lipids*, 2004, **129**, 111; S. Brodesser, P. Sawatzki, and T. Kolter, *Eur. J. Org. Chem.* 2003, 2021.
3. J. M. Boggs, W. Gao, and Y. Hirahara, *Biochim. Biophys. Acta,* 2008, **1780**, 445; M. Shimamura, *Mini-rev. in Med. Chem.*, 2008. **8**, 285; F. M. Platt, M. Jeyakumar, U. Andersson, R. A. Dwek, and T. D. Butters, *Adv. in Exp. Med. Biol.*, 2005, **564**, 117; H. Iijima, K. Kimura, T. Sakai, A. Uchimura,

T. Shimizu, H. Ueno, T. Natori, and Y. Koezuka, *Bioorg. Med. Chem.*, 1998, **6**, 1905.

4. T. Hori, M. Sugita, and H. Shimizu, *Biochim. Biophys. Acta, Lipid and Lipid Metabolism,* 1981, **665**, 170; K. Yamada, *Yakugaku Zasshi*, 2002, **122**, 1133.
5. K. Motoki, M. Morita, E. Kobayashi, T. Uchida, K. Akimoto, H. Fukushima, and Y. Koezuka, *Bio. Pharm. Bull.,* 1995, **18**, 1487; V. Costantino, E. Fattorusso, C. Imperatore, and A. Mangoni, *Eur. J. Org. Chem.,* 2003, 1433.
6. Commercially available from Sigma-Aldrich Co. Ltd. at the price of US $836.00/g.
7. Enzymatic synthesis of D-psicose; H. Itoh, T. Sato, and K. Izumori, *J. Ferment. Bioeng.*, 1995, **80**, 101.
8. J. Uenishi and A. Ueda, *Tetrahedron:Asymmetry,* 2008, **19**, 2210.
9. Similar synthetic design for the β-selectivity was reported in the nucleoside synthesis; S. Hirano, S. Ichikawa, and A. Matsuda, *J. Org. Chem.,* 2007, **72**, 9936.
10. The use of monobenzyl phthaloyl group for glycosidation was reported by Kim *et al*.: K. S. Kim, Y. J. Lee, H. Y. Kim, S. S. Kang, and S. Y. Kwon, *Org. Biomol. Chem.,* 2004, **2**, 2408.
11. G. R. Duffin, G. J. Ellames, S. Hartmann, J. M. Herbert, and D. I. Smith, *J. Chem. Soc., Perkin Trans. 1,* 2000, 2237.