Chemoenzymatic Synthesis of Sacranosides A and B

Eiji KAWAHARA,[a,b] Mikio FUJII,[c] Yoshiteru IDA,[c] and Hiroyuki AKITA*,[a]

[a] *School of Pharmaceutical Sciences, Toho University; 2–2–1 Miyama, Funabashi, Chiba 274–8510, Japan:* [b] *Tsukuba Research Institute, Novartis Pharma K.K.; 8 Ohkubo, Tsukuba, Ibaraki 300–2611, Japan: and* [c] *School of Pharmaceutical Sciences, Showa University; 1–5–8 Hatanodai, Shinagawa-ku, Tokyo 142–8555, Japan.*

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Direct β-glucosidation between (−)-myrtenol and nerol and D-glucose (3) using the immobilized β-glucosidase from almonds with the synthetic prepolymer ENTP-4000 gave myrtenyl *O*-β-D-glucoside (4) and neryl *O*-β-D-glucoside (10), respectively. The coupling of the myrtenyl or neryl *O*-β-D-glucopyranoside congeners (7 or 13) and 2,3,4-tri-*O*-benzoyl-β-L-arabinopyranosyl bromide (8) afforded the coupled products (9 or 14), respectively. Deprotection of the coupled products (9 or 14) afforded the synthetic myrtenyl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside (Sacranoside A, 1) or neryl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside (Sacranoside B, 2), respectively.

Key words β-glucosidase; β-glucosidation; natural product synthesis; Sacranoside

Monoterpene glycosides are a group of water soluble natural products widely distributed in the plant kingdom.[1)] The biological activity of some compounds has been determined and has been reported to indicate antibacterial activity, cytotoxic and antioxidant properties, enzyme inhibition, and immunomodulatory properties.[2—5)] Among them, two kinds of naturally occurring monoterpene alcohol 6-*O*-glycosy-β-D-glucopyranoside congeners, myrtenyl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside (Sacranoside A, **1**) and neryl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside (Sacranoside B, **2**) were isolated from a methanol extract of *Rhodiola sacra* (PRAIN ex HAMET) S. H. FU (Crassulaceae).[2)] Synthesis of these β-D-glucopyranoside congeners aroused our interest for the purpose of investigating their pharmacological activity. In this paper, we describe the total synthesis of naturally occurring **1** and **2** based on the selective β-glycosidation catalyzed by the immobilized β-glucosidase (EC 3.2.1.21) from almonds between D-glucose (**3**) and monoterpene alcohol.

Enzymatic β-Glycosidation In direct β-glycosidation between D-glucose (**3**) and primary alcohols using β-glucosidase (EC 3.2.1.21) from almonds under thermodynamic conditions, a high concentration of alcohol or a medium with low water activity is reported to be effective.[6)] On the other hand, we reported the effectiveness of immobilization of β-glucosidase (EC 3.2.1.21) from almonds with a photocrosslinkable resin prepolymer (ENTP-4000) in the direct β-glucosidation between D-glucose (**3**) and 1,8-octanediol.[7)] We then examined the direct β-glucosidation between D-glucose (**3**) and monoterpene alcohols using the reported immobilized β-glucosidase (EC 3.2.1.21)[7)] from almonds. When a large amount of (−)-myrtenol and nerol (19.2 eq) was used as an acceptor for D-glucose (**3**) in the presence of the immobilized β-glucosidase, 4.2% yield of myrtenyl *O*-β-D-glucopyranoside (**4**) and 7.2% yield of neryl *O*-β-D-glucopyranoside (**10**) were obtained, respectively.

Synthesis of Myrtenyl 6-*O*-α-L-Arabinopyranosyl-β-D-glucopyranoside (Sacranoside A, 1) *tert*-Butyldimethylsilylation of **4** gave a silyl ether (**5**; 57% yield), which was subjected to benzoylation to give a benzoate (**6**) in 98% yield. Desilylation of **6** using 1 N HCl provided the desired **7** in 79% yield. By applying the reported procedure,[8)] coupling reaction of myrtenyl β-D-glucopyranoside congener (**7**) and 2,3,4-tri-*O*-benzoyl-β-L-arabinopyranosyl bromide (**8**)[9)] in the presence of silver triflate (AgOTf) and tetramethylurea (TMU) gave the corresponding coupling product (**9**) in 74% yield. Finally, treatment of **9** with NaOMe in MeOH provided the synthetic myrtenyl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside (**1**) in 44% yield. The spectral data (^{13}C- and ^{1}H-NMR) and optical rotation {$[\alpha]_D^{28}$ −52.2° (c=1.55, MeOH)} of the synthetic (**1**) were identical to those of natural product **1**{$[\alpha]_D^{25}$ −33.9° (c=0.1, MeOH)}.[2)]

Synthesis of Neryl 6-*O*-α-L-Arabinopyranosyl-β-D-glucopyranoside (Sacranoside B, 2) *tert*-Butyldimethylsilylation of **10** gave a silyl ether (**11**; 80% yield), which was subjected to benzoylation to give a benzoate (**12**) in 98% yield. Desilylation of **12** using 1 N HCl provided the desired **13** in 93% yield. The coupling reaction of neryl β-D-glucopyranoside congener (**13**) and **8** in the presence of AgOTf and TMU gave the coupled product (**14**) in 96% yield. Finally, treatment of **14** with NaOMe in MeOH provided the synthetic neryl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside (**2**) in 48% yield. The spectral data (^{13}C- and ^{1}H-NMR) of the synthetic **2** were consistent with those of natural product **2**, while optical rotation of synthetic **2** {$[\alpha]_D^{26}$ −34.9° (c=1.85, MeOH)} were found to be different from the reported data {$[\alpha]_D^{25}$ +11.6° (c=0.3, MeOH)}.[2,10)]

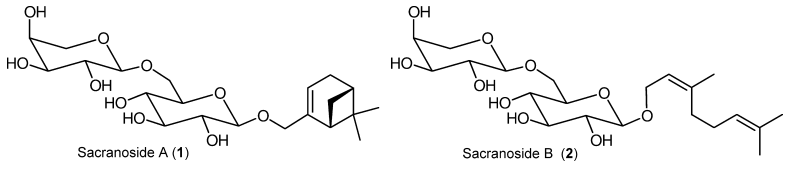

Chart 1

* To whom correspondence should be addressed. e-mail: akita@toho-u.ac.jp

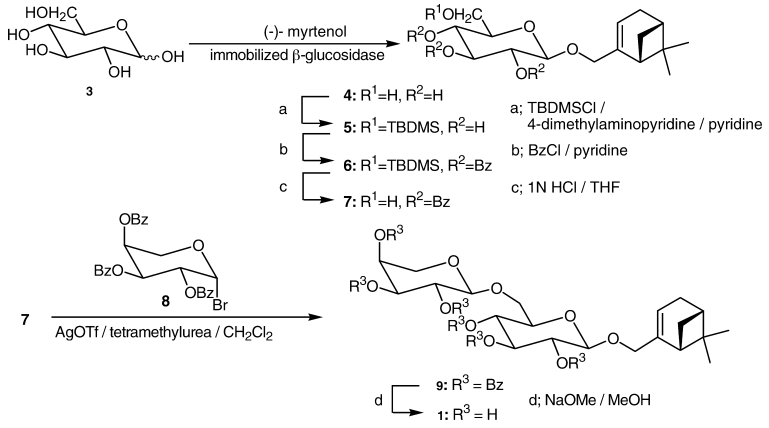

Chart 2

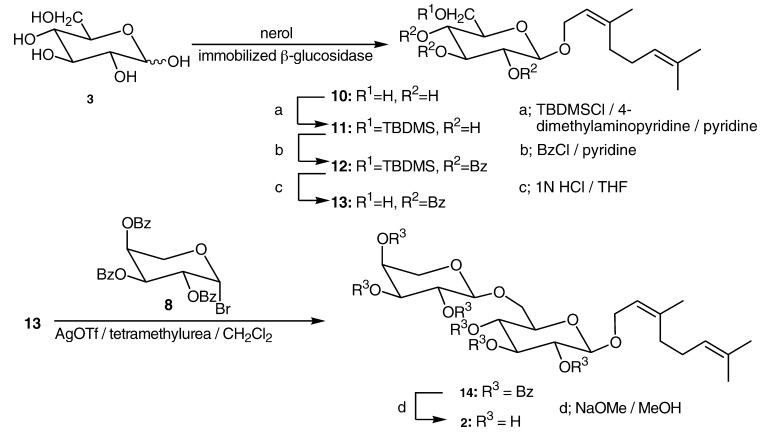

Chart 3

Conclusion

In conclusion, direct β-glucosidation between (−)-myrtenol and nerol and D-glucose (**3**) using the immobilized β-glucosidase from almonds with the synthetic prepolymer ENTP-4000 gave myrtenyl *O*-β-D-glucoside (**4**) in 4.2% yield and neryl *O*-β-D-glucoside (**10**) in 7.2% yield, respectively. The coupling of the myrtenyl or neryl *O*-β-D-glucopyranoside congeners (**7**, **13**) and 2,3,4-tri-*O*-benzoyl-β-L-arabinopyranosyl bromide (**8**) afforded the coupled products (**9** or **14**), respectively. Deprotection of the coupled products (**9** or **14**) afforded the synthetic myrtenyl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside (Sacranoside A, **1**) or neryl 6-*O*-α-L-arabinopyranosyl-β-D-glucopyranoside (Sacranoside B, **2**), respectively.

Experimental

^{1}H- and ^{13}C-NMR spectra were recorded on a BRUKER AV400M spectrometer or JEOL AL 400 spectrometer. Spectra were recorded with 5—10% (w/v) solution in $CDCl_3$ or CD_3OD with Me_4Si as an internal reference. High-resolution mass spectra (HR-MS) and the fast atom bombardment mass spectra (FAB-MS) were obtained with a JEOL JMS 600H spectrometer. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. IR spectra were recorded on a JASCO FT/IR-300 spectrophotometer. All reagents were purchased from commercial sources and used without purification. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed for flash column chromatography and silica gel (silica gel 60N, spherical, neutral, 40—50 mm) was employed.

Immobilization of β-D-Glucosidase Using a Prepolymer β-D-Glucosidase (EC 3.2.1.21) from almonds was purchased from Sigma Chemical Co. (G-0395, 2.5—3.6 U/mg). Immobilization of this β-D-glucosidase on the photocross-linkable resin prepolymer (ENTP-4000) was carried out using the following procedure. One gram of ENTP-4000 was mixed with 10 mg of a photosensitizer, benzoin ethyl ether, and 110 mg of β-D-glucosidase from almonds (3.4 U/mg). The mixture was layered on a sheet of transparent polyester film (thickness, *ca.* 0.5 mm). The layer was covered with transparent thin film and then illuminated with chemical lamps (wavelength range, 300—400 nm) for 3 min. The gel film thus obtained was cut into small pieces (0.5×5×5 mm) and used for the next reaction.

Enzymatic Synthesis of Myrtenyl *O*-β-D-Glucopyranoside (4) A mixture of D-glucose (**3**) (1.1 g, 6.1 mmol), myrtenol (18.0 g, 118 mmol), water (2 ml), and the immobilized β-glucosidase (1.1 g) was incubated for 4 d at 50 °C. The reaction mixture was filtered off and the filtrate was directly chromatographed on silica gel (35 g) to give myrtenyl *O*-β-D-glucopyranoside (**4**, 81 mg, 0.26 mmol, 4.2%) as a white solid from the $CHCl_3$/MeOH=10 : 1 eluent. **4**: $[\alpha]_D^{29}$ −56.6° (*c*=1.2, MeOH); IR (KBr): 3393, 2916, 1369, 1076, 1030 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 0.87 (3H, s), 1.19 (1H, d, *J*=8.6 Hz), 1.30 (3H, s), 2.07—2.13 (1H, m), 2.22—2.26 (1H, m), 2.27—2.32 (2H, m), 2.43 (1H, ddd, *J*=5.6, 5.6, 8.6 Hz), 3.19 (1H, dd, *J*=7.6, 8.5 Hz), 3.21—3.24 (1H, m), 3.26—3.30 (1H, m), 3.33—3.36 (1H, m), 3.66 (1H, dd, *J*=2.3, 11.9 Hz), 3.86 (1H, dd, *J*=2.3, 11.9 Hz), 3.98—4.03 (1H, m), 4.20—4.24 (1H, m), 4.28 (1H, d, *J*=7.6 Hz), 5.55—5.58 (1H, m); ^{13}C-NMR (CD_3OD): δ 21.5, 26.6, 32.2, 32.5, 38.9, 42.2, 44.6, 62.8, 71.7, 72.7, 75.1, 77.9, 78.2, 103.4, 120.8, 146.3; HR-FAB-MS [*m*-nitrobenzyl alcohol (NBA)] *m/z*: Calcd for $C_{16}H_{27}O_6$: 315.1808 $(M+1)^+$, Found: 315.1803.

Enzymatic Synthesis of Neryl *O*-β-D-Glucopyranoside (10) A mixture of D-glucose (**3**) (1.1 g, 6.1 mmol), nerol (18.0 g, 117 mmol), water (2 ml), and the immobilized β-glucosidase (1.1 g) was incubated for 4 d at 50 °C. The reaction mixture was filtered off and the filtrate was directly chromatographed on silica gel (35 g) to give neryl *O*-β-D-glucopyranoside (**10**, 139 mg, 0.44 mmol, 7.2%) as a white solid from the $CHCl_3$/MeOH=10 : 1 eluent. **10**: $[\alpha]_D^{29}$ −18.9° (*c*=0.49, MeOH); IR (KBr):

3408, 2920, 1079, 1042 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 1.61 (3H, s), 1.67 (3H, s), 1.75 (3H, s), 2.06—2.19 (4H, m), 3.17 (1H, dd, J=7.8, 7.8 Hz), 3.20—3.25 (1H, m), 3.26—3.36 (2H, m), 3.67 (1H, dd, J=5.3, 11.9 Hz), 3.85 (1H, dd, J=2.0, 11.9 Hz), 4.21 (1H, dd, J=7.8, 12.0 Hz), 4.27 (1H, d, J=7.8 Hz), 4.32 (1H, dd, J=6.3, 12.0 Hz), 5.09—5.16 (1H, m), 5.35—5.40 (1H, m); ^{13}C-NMR (CD_3OD): δ 17.8, 23.7, 25.9, 27.7, 33.1, 62.7, 66.3, 71.7, 75.1, 77.9, 78.2, 102.9, 122.6, 125.0, 132.8, 141.8; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{16}H_{29}O_6$: 317.1965 (M+1)$^+$, Found: 317.1978.

Myrtenyl 6-*O*-*tert*-Butyldimethylsilyl-β-D-glucopyranoside (5) A mixture of **4** (700 mg, 2.05 mmol), 4-dimethylaminopyridine (DMAP; 6 mg, 0.05 mmol) and TBDMSCl (352 mg, 2.34 mmol) in pyridine (15 ml) was stirred for 16 h at rt. The reaction mixture was evaporated under reduced pressure to give a residue, which was purified by flash column chromatography on silica gel {30 g, *n*-hexane/AcOEt (4 : 1)–AcOEt} to afford **5** (541 mg, 1.26 mmol, 57%) as a colorless syrup. **5**: $[\alpha]_D^{29}$ −50.9° (c=2.2, $CHCl_3$); IR (KBr): 3433, 2927, 1473, 1253, 1048 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 0.10 (3H, s), 0.11 (3H, s), 0.84 (3H, s), 0.91 (9H, s), 1.18 (1H, d, J=8.6 Hz), 1.28 (3H, s), 2.01—2.12 (1H, m), 2.13—2.17 (1H, m), 2.22—2.34 (2H, m), 2.40 (1H, ddd, J=5.6, 5.6, 8.6 Hz), 3.33—3.41 (2H, m), 3.55—3.60 (2H, m), 3.83 (1H, dd, J=6.3, 10.4 Hz), 3.93 (1H, dd, J=5.1, 10.4 Hz), 3.97—3.99 (1H, m), 4.18—4.23 (1H, m), 4.31 (1H, d, J=7.6 Hz), 5.53—5.55 (1H, m); ^{13}C-NMR ($CDCl_3$): δ −4.99[2C], 18.7, 21.7, 26.4[3C], 26.7, 31.8, 32.1, 38.5, 41.3, 44.0, 65.4, 72.4, 73.7, 74.1, 74.5, 76.7, 101.8, 121.3, 144.7; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{22}H_{41}O_6Si$: 429.2672 (M+1)$^+$, Found: 429.2630.

Myrtenyl 2,3,4-Tri-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (6) To a solution of **5** (450 mg, 1.05 mmol) in pyridine (10 ml) was added benzoyl chloride (738 mg, 5.25 mmol) at 0 °C, and the whole was stirred for 14 h at rt. The reaction mixture was diluted with water and extracted with AcOEt. The organic layer was washed with 0.5 N HCl, H_2O and brine. Then the organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was purified by flash column chromatography on silica gel {30 g, *n*-hexane/AcOEt (8 : 1—4 : 1)} to afford **6** (759 mg, 1.02 mmol, 98%) as a colorless syrup. **6**: $[\alpha]_D^{29}$ −24.2° (c=0.59, $CHCl_3$); IR (KBr): 2929, 2359, 1733, 1262, 1091 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.03 (6H, s), 0.77 (3H, s), 0.87 (9H, s), 1.02 (3H, s), 1.05 (1H, d, J=8.6 Hz), 1.93—2.03 (2H, m), 2.14 (1H, ddd, J=5.6, 5.6, 8.6 Hz), 2.10—2.25 (2H, m), 3.79—3.86 (3H, m), 3.98—4.05 (1H, m), 4.23—4.28 (1H, m), 4.79 (1H, d, J=7.8 Hz), 5.44—5.52 (3H, m), 5.83 (1H, dd, J=9.6, 9.6 Hz), 7.24—7.30 (2H, m), 7.34—7.44 (5H, m), 7.48—7.54 (2H, m), 7.80—7.84 (2H, m), 7.90—7.98 (4H, m); ^{13}C-NMR ($CDCl_3$): δ −4.87, −4.82, 18.8, 21.6, 26.3[3C], 31.7, 31.9, 38.2, 39.2, 41.2, 43.7, 63.4, 70.4, 72.3, 72.6, 73.8, 75.8, 100.4, 121.5, 128.7[2C], 128.7[2C], 128.8[2C], 129.5, 129.7, 130.0, 130.2[2C], 130.3[2C], 130.3[2C], 133.5, 133.6, 133.7, 144.6, 165.6, 165.7, 166.4; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{43}H_{53}O_9Si$: 741.3459 (M+1)$^+$, Found: 741.3499.

Myrtenyl 2,3,4-Tri-*O*-benzoyl-β-D-glucopyranoside (7) To a solution of **6** (750 mg, 1.01 mmol) in THF (5 ml) was added 1 N HCl (2.0 ml, 2.0 mmol) and stirred for 1 h at rt. The reaction mixture was extracted with AcOEt. The organic layer was washed with H_2O, brine, dried over Na_2SO_4 and evaporated to give a residue, which was purified by flash column chromatography on silica gel {30 g, *n*-hexane/AcOEt (8 : 1—2 : 1)} to afford **7** (501 mg, 0.8 mmol, 79%) as a colorless oil. **7**: $[\alpha]_D^{29}$ −25.6° (c=0.77, $CHCl_3$); IR (KBr): 3509, 2937, 1733, 1602, 1451, 1093 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.76 (3H, s), 1.04—1.08 (1H, m), 1.04 (3H, s), 1.95—2.20 (2H, m), 2.10—2.26 (3H, m), 3.71—3.90 (3H, m), 3.98—4.03 (1H, m), 4.23—4.29 (1H, m), 4.84 (1H, d, J=7.8 Hz), 5.44—5.48 (1H, m), 4.48—5.55 (2H, m), 5.92 (1H, dd, J=9.6, 9.6 Hz), 7.25—7.31 (2H, m), 7.36—7.45 (5H, m), 7.49—7.56 (2H, m), 7.82—7.86 (2H, m), 7.93—7.98 (4H, m); ^{13}C-NMR ($CDCl_3$): δ 21.5, 26.3, 31.7, 31.9, 38.2, 41.2, 43.7, 61.9, 70.2, 72.4, 73.0, 73.3, 75.1, 100.9, 121.5, 128.8[4C], 129.0[2C], 129.2, 129.4, 130.0, 130.2[2C], 130.3[2C], 130.4[2C], 133.6, 133.7, 134.1, 144.6, 165.5, 166.4, 166.5; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{37}H_{39}O_9$: 627.2594 (M+1)$^+$, Found: 627.2563.

Myrtenyl 2,3,4,2′,3′,4′-*O*-Hexabenzoyl-α-L-arabinopyranosyl-β-D-glucopyranoside (9) To a solution of **7** (335 mg, 0.535 mmol) and 2,3,4-tri-*O*-benzoyl-α-L-arabinopyranosyl bromide (**8**, 561 mg, 1.07 mmol) in CH_2Cl_2 (10 ml) was added tetramethylurea (TMU, 137 mg, 1.18 mmol) at 0 °C under nitrogen atmosphere. AgOTf (275 mg, 1.07 mmol) was added to this reaction mixture at 0 °C under nitrogen atmosphere. The whole was covered with aluminum foil and stirred for 16 h at rt. The reaction mixture was cooled to 0 °C and quenched with 7% aqueous $NaHCO_3$ solution (20 ml). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the organic solvent gave a residue, which was purified by flash column chromatography on silica gel {50 g, *n*-hexane/AcOEt (8 : 1—2 : 1)} to afford **9** (472 mg, 0.403 mmol, 74%) as a colorless amorphous. **9**: $[\alpha]_D^{29}$ +33.9° (c=0.45, $CHCl_3$); IR (KBr): 2937, 1733, 1602, 1451, 1261, 1093 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.69 (3H, s), 0.93—0.98 (1H, m), 0.95 (3H, s), 1.80—1.85 (1H, m), 1.90—1.97 (1H, m), 2.05 (1H, ddd, J=5.6, 5.6, 8.6 Hz), 2.00—2.18 (2H, m), 3.66—3.71 (1H, m), 3.83 (1H, dd, J= 7.3, 11.1 Hz), 3.83—3.91 (2H, m), 3.98—4.05 (1H, m), 4.08 (1H, dd, J=1.8, 11.1 Hz), 4.27 (1H, dd, J=4.3, 12.6 Hz), 4.69 (1H, d, J=8.1 Hz), 4.84 (1H, d, J=6.1 Hz), 5.26—5.30 (1H, m), 5.38 (1H, dd, J=9.6, 9.6 Hz), 5.41 (1H, dd, J=8.1, 9.6 Hz), 5.60 (1H, dd, J=3.5, 8.6 Hz), 5.64—5.69 (1H, m), 5.73 (1H, dd, J=6.1, 8.6 Hz), 5.80 (1H, dd, J=9.6, 9.6 Hz), 7.23—7.28 (2H, m), 7.32—7.45 (11H, m), 7.46—7.59 (5H, m), 7.76—7.80 (2H, m), 7.88—7.96 (6H, m), 7.99—8.04 (4H, m); ^{13}C-NMR ($CDCl_3$): δ 21.1, 25.7, 31.1, 31.4, 37.6, 40.6, 43.1, 62.3, 68.2, 68.4, 69.8, 69.9, 70.3, 71.9[2C], 73.0, 73.8, 100.0, 100.8, 121.4, 128.2[4C], 128.4[2C], 128.4[6C], 128.8, 128.9, 129.1, 129.3, 129.4, 129.4, 129.7[2C], 129.8[2C], 129.9[6C], 129.9[2C], 133.1, 133.1, 133.3[3C], 133.4, 143.6, 164.9, 165.2, 165.3, 165.5, 165.6, 165.8; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{63}H_{59}O_{16}$: 1071.3803 (M+1)$^+$, Found: 1071.3812.

Myrtenyl 6-*O*-α-L-Arabinopyranosyl-β-D-glucopyranoside (Sacranoside A) (1) A mixture of **9** (200 mg, 0.187 mmol) and NaOMe (20 mg, 0.37 mmol) in MeOH–THF (5 : 1; 6 ml) was stirred for 1 h at rt. The reaction mixture was condensed to give a residue, which was purified by flash column chromatography on silica gel {10 g, $CHCl_3$/MeOH (20 : 1—5 : 1)} to afford **1** (37 mg, 0.083 mmol, 44%) as a colorless amorphous. **1**: $[\alpha]_D^{28}$ −52.2° (c=1.55, MeOH); IR (KBr): 3380, 2912, 1652, 1368, 1078 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 0.87 (3H, s), 1.19 (1H, d, J=8.6 Hz), 1.30 (3H, s), 2.06—2.12 (1H, m), 2.21—2.35 (3H, m), 2.42 (1H, ddd, J=5.6, 5.6, 8.6 Hz), 3.17—3.22 (1H, m), 3.33—3.44 (3H, m), 3.51—3.56 (2H, m), 3.59 (1H, dd, J=6.6, 8.8 Hz), 3.73 (1H, dd, J=5.3, 11.4 Hz), 3.79—3.82 (1H, m), 3.87 (1H, dd, J=3.3, 12.4 Hz), 4.00 (1H, dd, J=1.5, 12.4 Hz), 4.08 (1H, dd, J=2.0, 11.4 Hz), 4.20 (1H, dd, J=1.5, 12.4 Hz), 4.28 (1H, d, J=7.8 Hz), 4.32 (1H, d, J=6.6 Hz), 5.56—5.58 (1H, m); ^{13}C-NMR (CD_3OD): δ 21.6, 26.6, 32.2, 32.5, 38.9, 42.2, 44.5, 66.7, 69.4, 69.5, 71.6, 72.4, 72.9, 74.2, 75.0, 76.9, 78.0, 103.4, 105.1, 121.0, 146.3; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{21}H_{35}O_{10}$: 447.2228 (M+1)$^+$, Found: 449.2229.

Neryl 6-*O*-*tert*-Butyldimethylsilyl-β-D-glucopyranoside (11) A mixture of **10** (738 mg, 2.33 mmol), DMAP (14 mg, 0,117 mmol) and TBDMSCl (370 mg, 2.45 mmol) in pyridine (15 ml) was stirred for 14 h at rt. The reaction mixture was evaporated under reduced pressure to give a residue, which was purified by flush column chromatography on silica gel {30 g, *n*-hexane/AcOEt (8 : 1—2 : 1)} to afford **11** (807 mg, 1.87 mmol, 80%) as a white amorphous. **11**: $[\alpha]_D^{29}$ −31.0° (c=3.3, $CHCl_3$); IR (KBr): 3370, 2929, 1461, 1375, 1051 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.10 (3H, s), 0.10 (3H, s), 0.91 (9H, s), 1.60 (3H, s), 1.68 (3H, s), 1.76 (3H, d, J=0.8 Hz), 2.02—2.13 (4H, m), 3.32—3.40 (2H, m), 3.55—3.62 (2H, m), 3.83 (1H, dd, J=6.3, 10.4 Hz), 3.93 (1H, dd, J=5.0, 10.4 Hz), 4.14 (1H, ddd, J= 0.8, 7.8, 11.6 Hz), 4.30 (1H, ddd, J= 0.8, 6.3, 11.6 Hz), 4.31 (1H, d, J= 7.6 Hz), 5.05—5.11 (1H, m), 5.33—5.38 (1H, m); ^{13}C-NMR ($CDCl_3$): δ −5.01[2C], 18.2, 18.7, 24.0, 26.2, 26.3[3C], 27.2, 32.6, 65.4, 65.8, 73.7, 74.0, 74.5, 76.8, 101.6, 121.0, 124.2, 132.6, 142.4; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{22}H_{43}O_6Si$: 431.2829 (M+1)$^+$, Found: 431.2829.

Neryl 2,3,4-Tri-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (12) To a solution of **11** (800 mg, 1.86 mmol) in pyridine (10 ml) was added benzoylchloride (1.07 ml, 9.26 mmol) at 0 °C, and the whole was stirred for 24 h at rt. The reaction mixture was diluted with water and extracted with AcOEt. The organic layer was washed with 0.5 N HCl, H_2O and brine. Then the organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was purified by flash column chromatography on silica gel {30 g, *n*-hexane/AcOEt (16 : 1—4 : 1)} to afford **12** (1.35 g, 1.82 mmol, 98%) as a colorless syrup. **12**: $[\alpha]_D^{27}$ +19.6° (c=3.24, $CHCl_3$); IR (KBr): 2931, 1732, 1453, 1260, 1096 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.02 (6H, s), 0.87 (9H, s), 1.57 (3H, s), 1.66 (3H, s), 1.69 (3H, d, J=0.8 Hz), 2.00—2.08 (4H, m), 3.79—3.87 (3H, m), 4.23 (1H, ddd, J=0.8, 7.8, 12.0 Hz), 4.29 (1H, ddd, J=0.8, 6.0, 12.0 Hz), 4.80 (1H, d, J=7.8 Hz), 4.99—5.04 (1H, m), 5.19—5.25 (1H, m), 5.44 (1H, dd, J=7.8, 9.8 Hz), 5.48 (1H, dd, J=9.8, 9.8 Hz), 5.83 (1H, dd, J=9.8, 9.8 Hz), 7.24—7.29 (2H, m), 7.34—7.50 (5H, m), 7.48—7.53 (2H, m), 7.79—7.83 (2H, m), 7.90—7.97 (4H, m); ^{13}C-NMR ($CDCl_3$): δ −4.90, −4.87, 18.2, 18.8, 23.9, 26.2, 26.3[3C], 27.1, 32.6, 63.4, 65.7, 70.4, 72.6, 73.9, 75.8, 99.9, 121.2, 124.2, 128.7[2C], 128.7[2C], 128.8[2C], 129.6, 129.8, 130.1, 130.2[4C], 130.3[2C], 132.4, 133.5, 133.5, 133.7, 142.1, 165.6, 165.6, 166.4 ; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{43}H_{55}O_9Si$: 743.3615 (M+1)$^+$, Found: 743.3624.

Neryl 2,3,4-Tri-*O*-benzoyl-β-D-glucopyranoside (13) To a solution of **12** (1.30 g, 0.82 mmol) in THF (20 ml) was added 1 N HCl (4.0 ml, 4 mmol)

and stirred for 16 h at rt. The reaction mixture was extracted with AcOEt. The organic layer was washed with H_2O, brine, dried over Na_2SO_4 and evaporated to give a residue, which was purified by flash column chromatography on silica gel {30 g, *n*-hexane/AcOEt (8 : 1—2 : 1)} to afford **13** (1.03 g, 1.63 mmol, 93%) as a colorless oil. **13**: $[\alpha]_D^{26}$ +21.6° (*c*=2.38, $CHCl_3$); IR (KBr): 3444, 2966, 1731, 1453, 1262, 1097 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 1.57 (3H, s), 1.66 (3H, s), 1.70 (3H, d, *J*=1.0 Hz), 1.95—2.05 (4H, m), 2.48—2.55 (1H, m), 3.71—3.79 (2H, m), 3.81—3.89 (1H, m), 4.25—4.30 (2H, m), 4.86 (1H, d, *J*=7.8 Hz), 5.00—5.04 (1H, m), 5.20—5.24 (1H, m), 5.48 (1H, dd, *J*=9.8, 9.8 Hz), 5.49 (1H, dd, *J*=7.8, 9.8 Hz), 5.92 (1H, dd, *J*=9.8, 9.8 Hz), 7.27—7.29 (2H, m), 7.33—7.42 (5H, m), 7.48—7.56 (2H, m), 7.74—7.88 (2H, m), 7.80—7.90 (4H, m); ^{13}C-NMR ($CDCl_3$): δ 18.2, 23.9, 26.2, 27.1, 32.7, 61.9, 65.0, 70.2, 72.4, 73.4, 75.2, 100.0, 120.9, 124.1, 128.8[4C], 129.0[2C], 129.2, 129.4, 130.0, 130.3[2C], 130.3[2C], 130.4[2C], 132.7, 133.6, 133.7, 134.1, 142.5, 165.6, 166.4, 166.5; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{37}H_{41}O_9$: 629.2751 $(M+1)^+$, Found: 629.2752.

Neryl 2,3,4,2′,3′,4′-*O*-Hexabenzoyl-α-L-arabinopyranosyl-β-D-glucopyranoside (14) To a solution of **13** (275 mg, 0.437 mmol) and 2,3,4-tri-*O*-benzoyl-α-L-arabinopyranosyl bromide (**8**, 460 mg, 0.874 mmol) in CH_2Cl_2 (10 ml) was added TMU (111 mg, 0.96 mmol) at 0 °C under nitrogen atmosphere. AgOTf (225 mg, 0.874 mmol) was added to this reaction mixture at 0 °C under a nitrogen atmosphere. The whole was covered with aluminum foil and stirred for 14 h at rt. The reaction mixture was cooled to 0 °C and quenched with 7% aqueous $NaHCO_3$ solution (20 ml). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the organic solvent gave a residue, which was purified by flash column chromatography on silica gel {20 g, *n*-hexane/AcOEt (8 : 1—2 : 1)} to afford **14** (452 mg, 0.421 mmol, 96%) as a colorless amorphous. **14**: $[\alpha]_D^{26}$ +69.5° (*c*=0.81, $CHCl_3$); IR (KBr): 2934, 1729, 1453, 1261, 1095 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 1.53 (3H, d, *J*=0.8 Hz), 1.61 (3H, s), 1.64 (3H, s), 1.87—2.00 (4H, m), 3.82 (1H, dd, *J*=6.6, 11.4 Hz), 3.85 (1H, dd, *J*=2.3, 12.6 Hz), 3.95—4.06 (3H, m), 4.10 (1H, dd, *J*=2.0, 11.4 Hz), 4.26 (1H, dd, *J*=4.8, 12.6 Hz), 4.73 (1H, d, *J*=7.8 Hz), 4.84 (1H, d, *J*=5.8 Hz), 4.94—5.00 (1H, m), 5.07—5.13 (1H, m), 5.37 (1H, dd, *J*=7.8, 9.6 Hz), 5.41 (1H, dd, *J*=9.2, 9.6 Hz), 5.61 (1H, dd, *J*=3.5, 8.1 Hz), 5.63—5.67 (1H, m), 5.71 (1H, dd, *J*=5.8, 8.1 Hz), 5.81 (1H, dd, *J*=9.6, 9.6 Hz), 7.23—7.28 (2H, m), 7.31—7.59 (16H, m), 7.75—7.79 (2H, m), 7.86—7.94 (4H, m), 7.95—8.04 (6H, m); ^{13}C-NMR ($CDCl_3$): δ 18.1, 23.8, 26.2, 27.1, 32.4, 62.3, 65.6, 68.6[2C], 70.2, 70.3, 70.6, 72.4, 73.6, 74.3, 100.0, 101.1, 120.7, 124.2, 128.7[2C], 128.7[2C], 128.8[2C], 128.9[4C], 129.0[2C], 129.3, 129.4, 129.7, 129.8, 129.9, 130.0, 130.2[2C], 130.3[2C], 130.3[4C], 130.4[4C], 132.3, 133.5, 133.6, 133.8, 133.8, 133.9[2C], 142.7, 165.5, 165.6, 165.7, 166.0, 166.1, 166.3; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{63}H_{61}O_{16}$: 1073.3959 $(M+1)^+$, Found: 1073.3994.

Neryl 6-*O*-α-L-Arabinopyranosyl-β-D-glucopyranoside (Sacranoside B) (2) A mixture of **14** (200 mg, 0.186 mmol) and NaOMe (20 mg, 0.37 mmol) in MeOH–THF (1 : 1; 10 ml) was stirred for 3 h at rt. The reaction mixture was condensed to give a residue, which was purified by flash column chromatography on silica gel {10 g, CH_2Cl_2/MeOH (9 : 1—5 : 1)} to afford **2** (40 mg, 0.09 mmol, 48%) as a colorless amorphous. **2**: $[\alpha]_D^{26}$ −34.9° (*c*=1.85, MeOH); IR (KBr): 3379, 2921, 1659, 1444, 1258 cm^{-1}; ^{1}H-NMR (CD_3OD): δ 1.61 (3H, s), 1.68 (3H, s), 1.75 (3H, d, *J*=1.0 Hz), 2.04—2.16 (4H, m), 3.18 (1H, dd, *J*=7.8, 9.0 Hz), 3.33—3.39 (3H, m), 3.52 (1H, dd, *J*=3.5, 8.8 Hz), 3.53 (1H, dd, *J*=1.8, 12.4 Hz), 3.60 (1H, dd, *J*= 6.6, 8.8 Hz), 3.74 (1H, dd, *J*=4.5, 11.4 Hz), 3.79—3.82 (1H, m), 3.87 (1H, dd, *J*=3.3, 12.4 Hz), 4.08 (1H, dd, *J*=1.7, 11.4 Hz), 4.17 (1H, dd, *J*=7.6, 11.4 Hz), 4.27 (1H, d, *J*=7.8 Hz), 4.31 (1H, d, *J*=6.6 Hz), 4.28—4.35 (1H, m), 5.09—5.15 (1H, m), 5.35–5.41 (1H, m); ^{13}C-NMR (CD_3OD): δ 17.8, 23.7, 25.9, 27.7, 33.1, 66.4, 66.6, 69.3, 69.4, 71.5, 72.3, 74.2, 75.0, 76.7, 77.9, 103.1, 105.1, 122.5, 125.0, 132.8, 141.8; HR-FAB-MS (NBA) *m/z*: Calcd for $C_{21}H_{36}NaO_{10}$: 471.2206 $(M+Na)^+$. Found: 471.2213.

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10) According to a private communication from Prof. M. Yoshikawa, the opposite sign of the reported optical rotation of natural **2** in comparison to that of synthetic **2** was presumably attributed to contamination by a small amount of impurity.