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CHEMOENZYMATIC SYNTHESIS OF NATURALLY OCCURRING GERANYL 6-*O*-GLYCOSYL- β -D-GLUCOPYRANOSIDES

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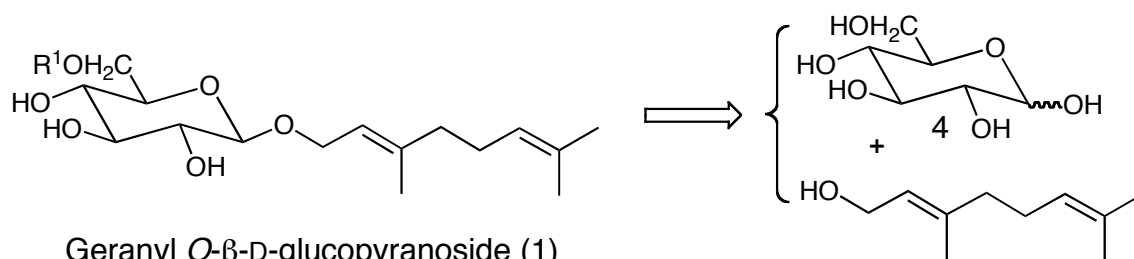
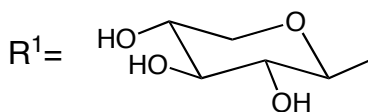
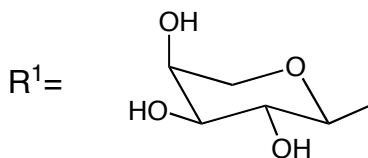
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Abstract- Direct β -glucosidation between geranyl alcohol and *D*-glucose (**4**) using the immobilized β -glucosidase from almonds with the synthetic prepolymer ENTP-4000 gave geranyl *O*- β -*D*-glucoside (**1**) in 11% yield. The coupling of the geranyl *O*- β -*D*-glucopyranoside congener (**7**) with 2,3,4-tri-*O*-benzoyl- α -*D*-xylopyranoside bromide (**8**) or 2,3,4-tri-*O*-benzoyl- α -*L*-arabinopyranosyl bromide (**10**) afforded the coupled products (**9** and **11**), respectively. Deprotection of the coupled products (**9** and **11**) using MeONa in MeOH-THF gave the synthetic geranyl 6-*O*- β -*D*-xylopyranosyl- β -*D*-glucopyranoside (**2**) and geranyl 6-*O*- α -*L*-arabinopyranosyl- β -*D*-glucopyranoside (Kenposide A, **3**).

Monoterpene glycosides are a group of water soluble natural products widely distributed in the plant kingdom.¹ Among them, two kinds of naturally occurring geranyl 6-*O*-glucosyl- β -*D*-glucopyranoside congeners, geranyl 6-*O*- β -*D*-xylopyranosyl- β -*D*-glucopyranoside (**2**)² and geranyl 6-*O*- α -*L*-arabinopyranosyl- β -*D*-glucopyranoside (Kenposide A, **3**)³⁻⁵ were isolated from a methanol extract of *Camellia sinensis* var. *sinensis* cv Shuixian,² and a ethanol extract of *Hovenia dulcis* var. *tomentella*³ respectively. The biological activity of some compounds have been undergone and **3** is reported to indicate immunomodulatory properties.⁴ For the purpose of investigation of pharmacological activity of these β -*D*-glucopyranoside congeners, the synthesis of the above-mentioned β -*D*-glucopyranoside congeners has aroused our interest. In this paper, we describe the synthesis of geranyl β -*D*-glucopyranoside (**1**) and its naturally occurring geranyl 6-*O*-glycosyl- β -*D*-glucopyranoside congeners (**2** and **3**) based on the selective β -glycosidation between *D*-glucose (**4**) and geranyl alcohol catalyzed by the immobilized β -glucosidase (EC 3.2.1.21) from almonds.

Geranyl *O*- β -D-glucopyranoside (**1**)Geranyl 6-*O*- β -D-xylopyranosyl- β -D-glucopyranoside (**2**)Geranyl 6-*O*- α -L-arabinopyranosyl- β -D-glucopyranoside (Kenposide A, **3**)

Enzymatic β -glycosidation

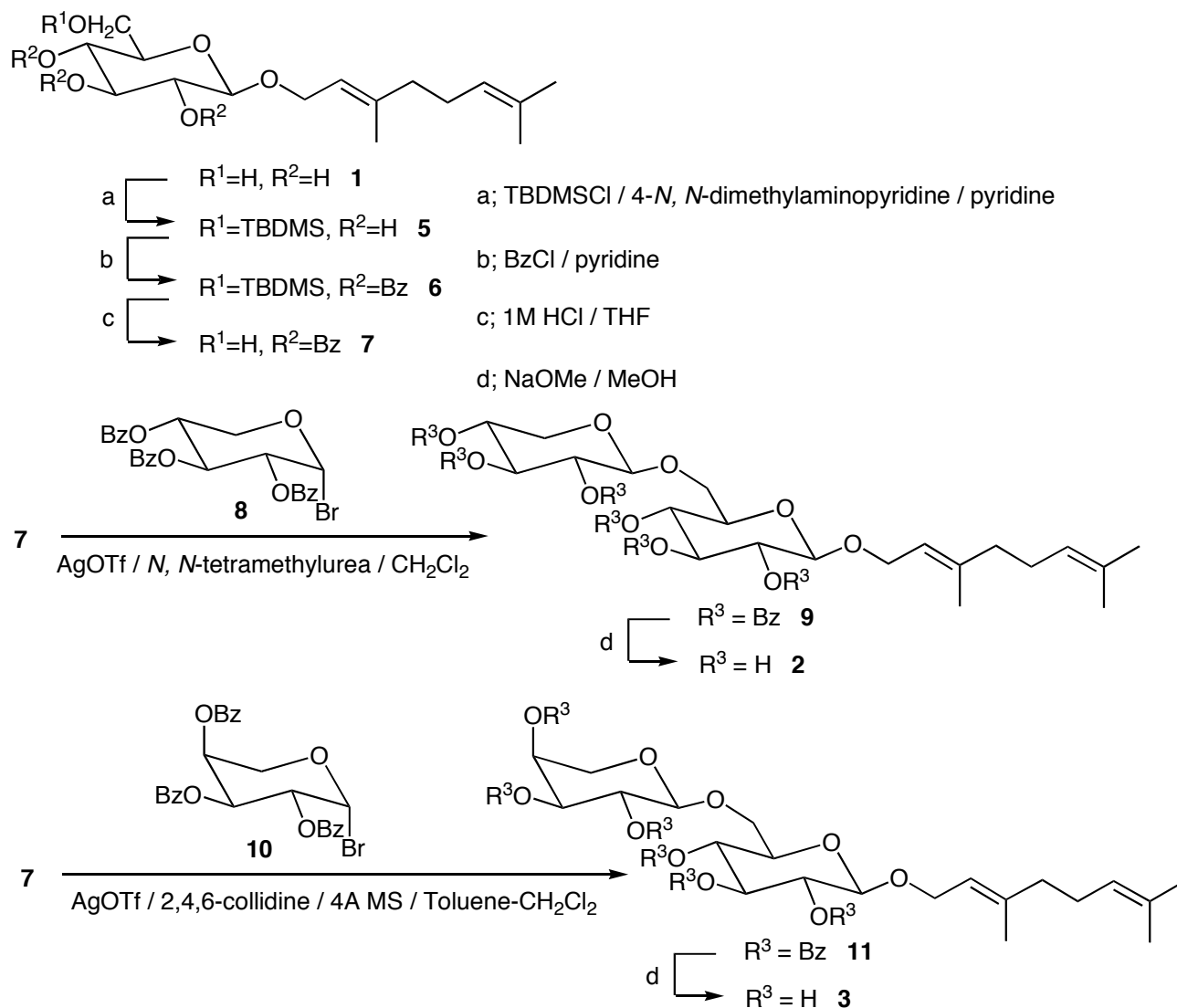
In case of the direct β -glycosidation between *D*-glucose (**4**) and primary alcohols using β -glucosidase (EC 3.2.1.21) from almonds under thermodynamic conditions, a high concentration of alcohol or a medium with low water activity is reported to be effective.⁶ On the other hand, we reported the effectiveness of immobilization of β -glucosidase (EC 3.2.1.21) from almonds with a photocross-linkable resin prepolymer (ENTP-4000) in the direct β -glucosidation between *D*-glucose (**4**) and 1,8-octanediol.⁷ Then we examined the direct β -glycosidation between *D*-glucose (**4**) and geranyl alcohol using the reported immobilized β -glucosidase (EC 3.2.1.21)⁷ from almonds. When a large amount of geranyl alcohol (19.2 equivalent) was used as an acceptor for *D*-glucose (**4**) in the presence of the immobilized β -glucosidase to give a 11% yield of geranyl *O*- β -D-glucopyranoside (**1**).⁸ As the length of alkyl or alkenyl chain of alcohol become long, the yield of β -D-glucopyranoside decreases gradually in spite of an increase of the number of enzyme units. This tendency was observed in the literature.^{7,9}

Synthesis of geranyl 6-*O*- β -D-xylopyranosyl- β -D-glucopyranoside (**2**)

Tert-butyldimethylsilylation of **1** gave a silyl ether (**5**; 63% yield), which was subjected to benzylation to give an benzoate (**6**) in 71% yield. Desilylation of **6** using 1M HCl to provide the desired **7** in 99% yield. By applying the reported procedure,¹⁰ coupling reaction of geranyl β -D-glucopyranoside congener (**7**) with 2,3,4-tri-*O*-benzoyl- α -D-xylopyranosyl bromide (**8**)¹¹ in the presence of silver triflate (AgOTf) and 1,2-tetramethylurea (TMU) gave the coupled product (**9**) in 92% yield. Finally, treatment of **9** with NaOMe in MeOH provided the synthetic geranyl 6-*O*- β -D-xylopyranosyl- β -D-glucopyranoside (**2**) in 85% yield. The spectral data (¹³C-NMR) and specific rotation ($[\alpha]_D^{28} -61.7^\circ$ ($c=2.3$, MeOH)) of the synthetic (**2**) were identical with those (¹³C-NMR and $[\alpha]_D^{20} -51^\circ$ ($c=0.69$, MeOH)) of natural product (**2**).²

Synthesis of geranyl 6-*O*- α -L-arabinopyranosyl- β -D-glucopyranoside (**3**)

By following the reported procedure,¹² coupling reaction of **7** with 2,3,4-tri-*O*-benzoyl- α -L-arabinopyranosyl bromide (**10**)¹³ in the presence of silver triflate (AgOTf) and 2,4,6-collidine gave the coupled product (**11**) in 57% yield. Finally, treatment of **11** with NaOMe in MeOH provided the synthetic Geranyl 6-*O*- α -L-arabinopyranosyl- β -D-glucopyranoside (Kenposide A, **3**) in 85% yield. The spectral data (¹H- and ¹³C-NMR) and specific rotation ($[\alpha]_D^{22} -34.6^\circ$ (c=2.1, MeOH)) of the synthetic **3** were identical with those (¹³C-NMR and $[\alpha]_D -33.4^\circ$ (c=6.8, MeOH)) of natural product **3**.³



Conclusion

In conclusion, direct β -glucosidation between geranyl alcohol and *D*-glucose (**4**) using the immobilized β -glucosidase from almonds with the synthetic prepolymer ENTP-4000 gave a geranyl *O*- β -*D*-glucoside (**1**) in 11% yield. The coupling of the geranyl *O*- β -*D*-glucopyranoside congener (**7**) with 2,3,4-tri-*O*-benzoyl- α -*D*-xylopyranoside bromide (**8**) and 2,3,4-tri-*O*-benzoyl- α -*L*-arabinopyranosyl bromide (**10**) gave the coupled products (**9**, and **11**), respectively. Deprotection of the coupled products (**9** and **11**) afforded the synthetic geranyl 6-*O*- β -*D*-xylopyranosyl- β -*D*-glucopyranoside (**2**) and geranyl 6-*O*- α -*L*-arabinopyranosyl- β -*D*-glucopyranoside (Kenposide A, **3**), respectively.

EXPERIMENTAL

^1H - 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 , CD_3OD or pyridine- d_6 with Me_4Si as an internal reference. High-resolution mass spectra (HR-MS) and the fast atom bombardment MS spectrum (FAB MS spectrum) were obtained with a JEOL JMS 600H spectrometer. Specific 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 while for flash column chromatography, silica gel (Silica gel 60N, spherical, neutral, 40-50 μM) 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 β -D-glucosidase from almonds 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 units/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 X 5 X 5 mm) and used for the bioconversion reaction.

Enzymatic synthesis of geranyl *O*- β -D-glucopyranoside (**1**)

A mixture of *D*-glucose (**4**) (1.1 g, 6.1 mmol), geraniol (18.0 g, 117 mmol), water (2 mL), and the immobilized β -glucosidase was incubated for 4 days at 50°C. The reaction mixture was filtered off and the filtrate was directly chromatographed on silica gel (35 g) to give geranyl *O*- β -D-glucopyranoside (**1**, 212 mg, 11%) as white solid from the $\text{CHCl}_3/\text{MeOH} = 10:1$ eluent. **1**: $[\alpha]_{\text{D}}^{22} -39.8^\circ$ ($c=0.28$, MeOH); IR (KBr): 3418, 2914, 1075, 1027 cm^{-1} , ^1H -NMR (CD_3OD): δ 1.60 (3H, s), 1.67 (3H, d, $J=1.0$ Hz), 1.68 (3H, s), 2.02-2.07 (2H, m), 2.08-2.14 (2H, m), 3.17 (1H, dd, $J=7.8$, 7.8 Hz), 3.21-3.36 (3H, m), 3.67 (1H, dd, $J=5.6$, 12.0 Hz), 3.86 (1H, dd, $J=2.3$, 12.0 Hz), 4.25 (1H, dd, $J=7.6$, 11.5 Hz), 4.28 (1H, d, $J=7.8$ Hz), 4.35 (1H, dd, $J=5.8$, 11.5 Hz), 5.08-5.13 (1H, m), 5.34-5.40 (1H, m); ^{13}C -NMR (CD_3OD): δ 16.4, 17.7, 25.9, 27.4, 40.7, 62.8, 66.3, 71.7, 75.1, 78.0, 78.2, 102.7, 121.6, 125.1, 132.5, 141.8; HR FAB-MS (NBA) m/z : Calcd for $\text{C}_{16}\text{H}_{29}\text{O}_6$: 317.1964 ($\text{M}+1$) $^+$, Found: 317.1950.

Geranyl 6-*O*-*tert*-butyldimethylsilyl- β -D-glucopyranoside (**5**)

A mixture of **1** (650 mg, 2.05 mmol), 4-*N,N*-dimethylaminopyridine (DMAP; 12.5 mg, 0.10 mmol) and TBDMSCl (340 mg, 2.26 mmol) in pyridine (15 mL) was stirred for 24 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 (15:1)-AcOEt) to afford **5** (560 mg, 63%) as a colorless syrup. **5**: $[\alpha]_{\text{D}}^{29} -38.5^\circ$ ($c=1.25$, CHCl_3); IR (KBr): 3446, 2929, 2855, 1250, 1056 cm^{-1} , ^1H -NMR (CDCl_3): δ 0.10 (3H, s), 0.10 (3H, s), 0.90 (9H, s), 1.60 (3H, s), 1.67 (3H, s), 1.68 (3H, d, $J=0.8$ Hz), 2.01-2.12 (4H, m), 3.31-3.42 (2H, m), 3.53-3.60 (2H, m), 3.85 (1H, dd, $J=5.6$, 11.0 Hz), 3.91

(1H, dd, $J=5.3, 11.0$ Hz), 4.17 (1H, dd, $J=7.8, 11.6$ Hz), 4.30 (1H, d, $J=7.8$ Hz), 4.33 (1H, dd, $J=6.3, 11.6$ Hz), 5.05-5.11 (1H, m), 5.32-5.38 (1H, m); $^{13}\text{C-NMR}$ (CDCl_3): δ -4.98[2C], 16.9, 18.2, 18.7, 26.2, 26.3[3C], 26.8, 40.1, 65.2, 66.0, 73.3, 74.0, 74.8, 76.8, 101.4, 120.0, 124.3, 132.2, 142.2; HR FAB-MS (NBA) m/z : Calcd for $\text{C}_{22}\text{H}_{43}\text{O}_6\text{Si}$: 431.2829 ($\text{M}+1$)⁺, Found: 431.2817.

Geranyl 2, 3, 4-tri-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl- β -D-glucopyranoside (6)

To a solution of **5** (550 mg, 1.28 mmol) in pyridine (5 mL) was added benzoyl chloride (900 mg, 6.4 mmol) at 0°C, and the whole was stirred for 12 h at rt. The reaction mixture was diluted with water and extracted with AcOEt. The organic layer was washed with 0.5 N HCl, H₂O and brine. Then the organic layer was dried over Na₂SO₄ 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** (671 mg, 71%) as a colorless syrup. **6**: $[\alpha]_{\text{D}}^{28} +6.5^\circ$ ($c=2.65$, CHCl_3); IR (KBr): 2931, 1733, 1260, 1094 cm^{-1} , $^1\text{H-NMR}$ (CDCl_3): δ 0.03 (6H, s), 0.87(9H, s), 1.57 (3H, s), 1.59 (3H, s), 1.67 (3H, d, $J=0.8$ Hz), 1.96-2.06 (4H, m), 3.85-3.79 (3H, m), 4.28-4.31 (2H, m), 4.81 (1H, d, $J=8.1$ Hz), 5.01-5.07 (1H, m), 5.17-5.22 (1H, m), 5.46 (1H, dd, $J=7.8, 9.6$ Hz), 5.47 (1H, dd, $J=9.3, 9.3$ Hz), 5.83 (1H, dd, $J=9.6, 9.6$ Hz), 7.24-7.28 (2H, m), 7.35-7.43 (5H, m), 7.47-7.53 (2H, m), 7.80-7.82 (2H, m), 7.90-7.95 (4H, m); $^{13}\text{C-NMR}$ (CDCl_3): δ -4.91, -4.86, 16.9, 18.2, 18.8, 26.2, 26.3[3C], 26.8, 40.0, 63.5, 65.5, 70.4, 72.5, 73.9, 75.9, 99.5, 120.0, 124.3, 128.7[2C], 128.7[2C], 128.8[2C], 129.5, 129.7, 130.1, 130.2[2C], 130.3[4C], 132.2, 133.5, 133.5, 133.7, 142.5, 165.6, 165.7, 166.4; HR FAB-MS (NBA) m/z : Calcd for $\text{C}_{43}\text{H}_{55}\text{O}_9\text{Si}$: 743.3615 ($\text{M}+1$)⁺, Found: 743.3539.

Geranyl 2, 3, 4-tri-*O*-benzoyl- β -D-glucopyranoside (7)

To a solution of **6** (610 mg, 0.82 mmol) in THF (5 mL) was added 1M HCl (1.0 ml, 1.0 mmol) and stirred for 12 h at rt. The reaction mixture was extracted with AcOEt. The organic layer was washed with H₂O, brine and dried over Na₂SO₄ 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** (516 mg, 0.82 mmol, 99%) as a colorless oil. **7**: $[\alpha]_{\text{D}}^{26} +7.46^\circ$ ($c=1.25$, CHCl_3); IR (KBr): 3427, 2920, 1730, 1260, 1096 cm^{-1} , $^1\text{H-NMR}$ (CDCl_3): δ 1.59 (3H, s), 1.61 (3H, d, $J=0.8$ Hz), 1.69 (3H, d, $J=1.0$ Hz), 1.95-2.07 (4H, m), 2.49-2.56 (1H, m), 3.72-3.79 (2H, m), 3.82-3.90 (1H, m), 4.26-4.35 (2H, m), 4.86 (1H, d, $J=8.0$ Hz), 5.03-5.08 (1H, m), 5.20-5.26 (1H, m), 5.49 (1H, dd, $J=9.8, 9.8$ Hz), 5.50 (1H, dd, $J=8.0, 9.8$ Hz), 5.92 (1H, dd, $J=9.8, 9.8$ Hz), 7.26-7.30 (2H, m), 7.35-7.45 (5H, m), 7.47-7.56 (2H, m), 7.81-7.86 (2H, m), 7.92-7.98 (4H, m); $^{13}\text{C-NMR}$ (CDCl_3): δ 16.9, 18.2, 26.2, 26.8, 40.0, 62.0, 66.0, 70.2, 72.4, 73.4, 75.2, 99.8, 120.0, 124.3, 128.8[4C], 129.0[2C], 129.2, 129.4, 130.0, 130.2[2C], 130.3[2C], 130.4[2C], 132.3, 133.6, 133.7, 134.1, 142.7, 165.6, 166.4, 166.5; HR FAB-MS (NBA) m/z : Calcd for $\text{C}_{37}\text{H}_{41}\text{O}_9$: 629.2751 ($\text{M}+1$)⁺, Found: 629.2673.

Geranyl 2, 3, 4, 2', 3', 4'-*O*-hexabenzoyl- β -D-xylopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside (9)

To a solution of **7** (290 mg, 0.7 mmol) and 2,3,4-tri-*O*-benzoyl- α -D-xylopyranosyl bromide (**8**) (545 mg, 1.04 mmol) in CH_2Cl_2 (10 mL) was added tetramethylurea (TMU, 132 mg, 1.14 mmol) at 0°C under nitrogen atmosphere. AgOTf (266 mg, 1.04 mmol) was added to the above-mentioned reaction mixture at 0°C under nitrogen atmosphere. The whole was covered with aluminum foil and stirred for 18 h at rt. The reaction mixture was cooled at 0°C and quenched with 7% aqueous NaHCO₃ 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 **9** (520 mg, 0.484 mmol, 93%) as a colorless amorphous. **9**: $[\alpha]_{\text{D}}^{28}$ -20.1° ($c=0.91$, CHCl_3); IR (KBr): 2929, 1730, 1260, 1100 cm^{-1} , $^1\text{H-NMR}$ (CDCl_3): δ 1.52 (3H, s), 1.58 (3H, s), 1.69 (3H, s), 1.91-1.96 (2H, m), 1.97-2.02 (2H, m), 3.68 (1H, dd, $J=6.8$, 12.1 Hz), 3.81 (1H, dd, $J=6.8$, 11.4 Hz), 3.98 (1H, ddd, $J=2.0$, 6.8, 9.6 Hz), 4.02-4.10 (3H, m), 4.40 (1H, dd, $J=4.0$, 12.1 Hz), 4.74 (1H, d, $J=7.8$ Hz), 4.91 (1H, d, $J=5.3$ Hz), 5.02-5.07 (1H, m), 5.08-5.14 (1H, m), 5.24 (1H, ddd, $J=4.0$, 6.8, 6.8 Hz), 5.38 (1H, dd, $J=5.3$, 7.1 Hz), 5.41 (1H, dd, $J=7.8$, 9.6 Hz), 5.43 (1H, dd, $J=9.6$, 9.6 Hz), 5.73 (1H, dd, $J=7.1$, 7.1 Hz), 5.83 (1H, dd, $J=9.6$, 9.6 Hz), 7.23-7.28 (2H, m), 7.30-7.45 (11H, m), 7.47-7.55 (5H, m), 7.75-7.79 (2H, m), 7.88-8.03 (10H, m); $^{13}\text{C-NMR}$ (CDCl_3): δ 16.8, 18.2, 26.2, 26.8, 40.0, 61.5, 65.5, 68.6, 69.5, 70.3, 70.5, 70.5, 72.4, 73.6, 74.3, 99.5, 100.8, 119.5, 124.3, 128.7[2C], 128.8[2C], 128.8[2C], 128.9[2C], 128.9[2C], 129.0[2C], 129.4, 129.4, 129.6, 129.7, 129.8, 130.0, 130.2[4C], 130.4[8C], 132.2, 133.6, 133.6, 133.7, 133.8, 133.9, 133.9, 143.1, 165.5[2C], 165.8, 165.8, 166.0, 166.3; HR FAB-MS (NBA) m/z : Calcd for $\text{C}_{63}\text{H}_{61}\text{O}_{16}$: 1073.3959 ($\text{M}+1$) $^+$, Found: 1073.3827.

Geranyl 6-*O*- β -D-xylopyranosyl- β -D-glucopyranoside (**2**)

A mixture of **9** (160 mg, 0.15 mmol) and NaOMe (15.9 mg, 0.29 mmol) in MeOH-THF (1:1; 8 mL) was stirred for 30 min at rt. The reaction mixture was condensed to give a residue, which was purified by flash column chromatography on silica gel (10 g, $\text{CHCl}_3/\text{MeOH}$ (4:1)) to afford **2** (47mg, 0.105 mol, 71%) as a colorless amorphous. **2**: $[\alpha]_{\text{D}}^{28}$ -61.7° ($c=2.36$, MeOH); IR (KBr): 3400, 2923, 1642, 1042 cm^{-1} , $^1\text{H-NMR}$ (CD_3OD): δ 1.61 (3H, m), 1.67 (3H, m), 1.69 (3H, s), 2.01-2.08 (2H, m), 2.09-2.17 (2H, m), 3.16-3.23 (3H, m), 3.28-3.37 (3H, m), 3.38-3.43 (1H, m), 3.48 (1H, ddd, $J=5.6$, 8.4, 10.4 Hz), 3.75 (1H, dd, $J=5.6$, 11.2 Hz), 3.86 (1H, dd, $J=5.6$, 11.6 Hz), 4.08 (1H, dd, $J=2.1$, 11.2 Hz), 4.22 (1H, dd, $J=7.3$, 11.6 Hz), 4.28 (1H, d, $J=7.8$ Hz), 4.31 (1H, d, $J=7.6$ Hz), 4.34 (1H, dd, $J=7.3$, 11.6 Hz), 5.07-5.13 (1H, m), 5.34-5.41 (1H, m); $^{13}\text{C-NMR}$ (CD_3OD): δ 16.6, 17.8, 25.9, 27.4, 40.7, 66.5, 66.9, 69.8, 71.2, 71.5, 74.9, 75.0, 77.0, 77.7, 78.0, 102.8, 105.5, 121.5, 125.1, 132.5, 141.9; HR FAB-MS (NBA) m/z : Calcd for $\text{C}_{21}\text{H}_{37}\text{O}_{10}$: 449.2386 ($\text{M}+1$) $^+$. Found: 449.2426.

Geranyl 2, 3, 4, 2', 3', 4'-*O*-hexabenzoyl- α -L-arabinopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside (**11**)

To a solution of **7** (160 mg, 0.254 mmol) and 2,3,4-tri-*O*-benzoyl- α -L-arabinopyranosyl bromide (**10**) (478 mg, 1.41 mmol) in CH_2Cl_2 (10 mL) and toluene (0.4 mL) was added 2,4,6-collidine (40 mg, 0.33 mmol) at -20°C under nitrogen atmosphere. AgOTf (85 mg, 0.33 mmol) was added to the above-mentioned reaction mixture at -20°C under nitrogen atmosphere. The whole was covered with aluminum foil and stirred for 36 h at rt. The reaction mixture was cooled at 0°C and quenched with CH_2Cl_2 (15 mL) and 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 **11** (157 mg, 0.146 mmol, 57%) as a colorless amorphous. **11**: $[\alpha]_{\text{D}}^{28}$ $+63.5^\circ$ ($c=0.74$, CHCl_3); IR (KBr): 2930, 1730, 1261, 1096 cm^{-1} , $^1\text{H-NMR}$ (CDCl_3): δ 1.50 (3H, s), 1.58 (3H, s), 1.69 (3H, s), 1.89-2.03 (4H, m), 3.83 (1H, dd, $J=7.5$, 11.1 Hz), 3.86 (1H, dd, $J=2.5$, 12.6 Hz), 3.96 (2H, d, $J=7.0$ Hz), 4.00 (1H,

ddd, $J=1.6, 7.5, 9.5$ Hz), 4.09 (1H, dd, $J=1.6, 11.1$ Hz), 4.26 (1H, dd, $J=4.5, 12.6$ Hz), 4.70 (1H, d, $J=8.1$ Hz), 4.83 (1H, d, $J=6.1$ Hz), 5.01-5.09 (2H, m), 5.38 (1H, dd, $J=9.5, 9.5$ Hz), 5.38 (1H, dd, $J=8.1, 9.5$ Hz), 5.59 (1H, dd, $J=3.5, 8.5$ Hz), 5.64-5.67 (1H, m), 5.72 (1H, dd, $J=6.1, 8.5$ Hz), 5.81 (1H, dd, $J=9.5, 9.5$ Hz), 7.23-7.28 (2H, m), 7.32-7.59 (16H, m), 7.75-7.79 (2H, m), 7.87-7.97 (6H, m), 7.98-8.03 (4H, m); $^{13}\text{C-NMR}$ (CDCl_3): δ 16.8, 18.2, 26.2, 26.8, 39.9, 62.7, 65.3, 68.7, 69.0, 70.3, 70.4, 70.9, 72.4, 73.6, 74.3, 99.4, 101.4, 119.5, 124.3, 128.7[2C], 128.7[2C], 128.9[2C], 129.0[6C], 129.3, 129.4, 129.6, 129.8, 129.9, 130.0, 130.2[4C], 130.3[2C], 130.3[2C], 130.4[2C], 130.4[2C], 132.2, 133.5, 133.6, 133.8, 133.9[2C], 133.9, 143.1, 165.5, 165.7, 165.8, 166.0, 166.1, 166.3; HR FAB-MS (NBA) m/z : Calcd for $\text{C}_{63}\text{H}_{61}\text{O}_{16}$: 1073.3959 ($\text{M}+1$)⁺, Found: 1073.3983.

Geranyl 6-*O*- α -L-arabinopyranosyl- β -D-glucopyranoside (**3**)

A mixture of **11** (120 mg, 0.112 mmol) and NaOMe (12 mg, 0.24 mmol) in MeOH-THF (1:1; 10 mL) was stirred for 60 min at rt. The reaction mixture was condensed to give a residue, which was purified by flash column chromatography on silica gel (10 g, $\text{CHCl}_3/\text{MeOH}$ (4:1)) to afford **3** (42mg, 0.094 mmol, 84%) as a colorless amorphous. **3**: $[\alpha]_{\text{D}}^{22}$ -34.6° ($c=2.1$, MeOH); IR (KBr): 3394, 2925, 1642, 1075 cm^{-1} , $^1\text{H-NMR}$ (CD_3OD): δ 1.61 (3H, m), 1.67 (3H, m), 1.69 (3H, s), 2.01-2.07 (2H, m), 2.08-2.14 (2H, m), 3.16-3.21 (1H, m), 3.32-3.44 (3H, m), 3.50-3.56 (2H, m), 3.58 (1H, dd, $J=6.5, 8.5$ Hz), 3.73 (1H, dd, $J=5.6, 11.2$ Hz), 3.78-3.82 (1H, m), 3.86 (1H, dd, $J=3.3, 12.4$ Hz), 4.09 (1H, dd, $J=2.0, 11.4$ Hz), 4.21 (1H, dd, $J=7.6, 11.9$ Hz), 4.29 (1H, d, $J=7.8$ Hz), 4.31 (1H, d, $J=6.5$ Hz), 4.35 (1H, dd, $J=6.3, 11.9$ Hz), 5.08-5.14 (1H, m), 5.34-5.41 (1H, m); $^{13}\text{C-NMR}$ (CD_3OD): δ 16.6, 17.8, 25.9, 27.4, 40.7, 66.5, 66.6, 69.4[2C], 71.6, 72.4, 74.2, 75.0, 76.8, 78.0, 102.9, 105.1, 121.5, 125.1, 132.5, 141.8; $^1\text{H-NMR}$ (pyridine- d_5): δ 1.32 (3H, m), 1.41 (6H, m), 1.73-3.80 (2H, m), 1.81-1.89 (2H, m), 3.53 (1H, dd, $J=2.5, 13.0$ Hz), 3.78 (1H, dd, $J=7.8, 8.6$ Hz), 3.82-3.87 (1H, m), 3.91-3.96 (2H, m), 3.97 (1H, dd, $J=8.6, 8.6$ Hz), 4.02-4.11 (3H, m), 4.16 (1H, dd, $J=7.0, 12.0$ Hz), 4.25 (1H, dd, $J=6.6, 8.6$ Hz), 4.48 (1H, dd, $J=6.3, 12.0$ Hz), 4.59 (1H, dd, $J=2.2, 11.0$ Hz), 4.64 (1H, d, $J=7.8$ Hz), 4.72 (1H, d, $J=6.6$ Hz), 4.88-4.94 (1H, m), 5.33-5.38 (1H, m); $^{13}\text{C-NMR}$ (pyridine- d_5): δ 16.5, 17.7, 25.7, 26.7, 39.8, 65.8, 66.6, 69.2, 69.7, 71.9, 72.4, 74.4, 75.1, 77.1, 78.6, 103.5, 105.5, 121.5, 124.6, 131.5, 139.9; HR FAB-MS (NBA) m/z : Calcd for $\text{C}_{21}\text{H}_{37}\text{O}_{10}$: 449.2386 ($\text{M}+1$)⁺, Found: 449.2311.

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