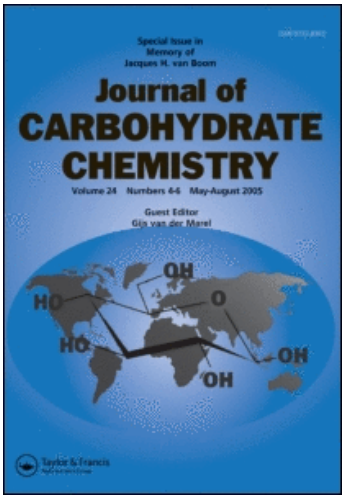

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CHEMICAL SYNTHESIS OF SEVERAL 2'-*O*-, 3'-*O*-GLYCOSYLATED DIOSGENYL β-D-GLUCOPYRANOSIDES

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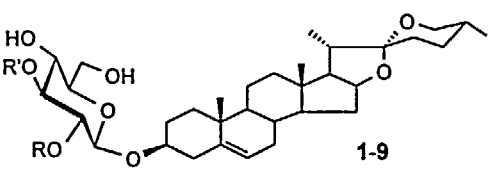
ABSTRACT

Six 2'-*O*-, 3'-*O*-glycosylated diosgenyl β-D-glucopyranosides (**4-9**), which have a typical structural pattern of diosgenyl saponins, were synthesized; their synthetic routes are discussed.

INTRODUCTION

Saponins constitute a structurally diverse class of natural products and demonstrate a wide range of pharmacological activities.[1] The structural diversity of saponins is derived from both the aglycone part and, most importantly, from the sugar pattern. Diosgenyl saponins are the most abundantly existing steroid saponins. One of the typical sugar patterns of the diosgenyl saponins is a β-D-glucopyranose as the first sugar attached to diosgenin, which is further glycosylated at 2'-OH and/or 3'-OH. Saponins **1-9** belong to this group of compounds. Chemical synthesis of saponins and evaluation of their bioactivities are our current interest.[2,3]



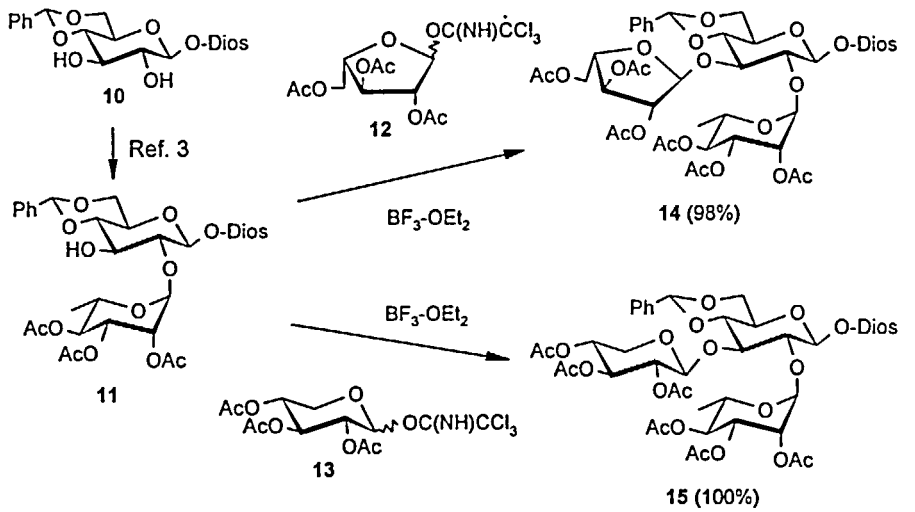
1-9

R	R'	Saponin	Plant sources	Ref.
H	H	1 (Trillin)	*Trillium, Paris, Yucca*	4
α-L-Rha	H	2 (Ophiopogonin C')	*Paris, Ophiopogon, Allium*	5
α-L-Rha	β-D-Glu	3 (Gracillin)	*Paris, Dioscorea, Costacea*	6
α-L-Rha	α-L-Rha	4 (Taccaoside)	*Taccacheancer*	7
α-L-Rha	β-D-Xyl	5 (Ophiopogonin D')	*Ophiopogon*	8
α-L-Rha	α-L-Araf	6	*Paris*	9
H	α-L-Rha	7 (Polyphyllin C)	*Paris*	10
β-D-Glu	H	8	*Solanum*	11
β-D-Glu	β-D-Glu	9		

RESULTS AND DISCUSSION

Diosgenyl saponins **1-3** have been synthesized sequentially through stepwise glycosylation. Trisaccharide **3** was derived from disaccharide **11**, which was synthesized from monosaccharide **10** through mono-protection of the 3'-OH as a TBDMS ether (3'-*O*-TBDMS ether:2'-*O*-TBDMS ether 3:2) followed by glycosylation and then desilylation.[3] Employing **11** as a key intermediate, the trisaccharides **14** and **15** were prepared in excellent yields through glycosylation with trichloroacetimidate donor **12**[2b] and **13**,[12] respectively. (Scheme 1)

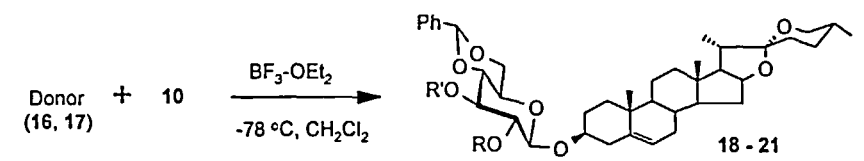
Scheme 1

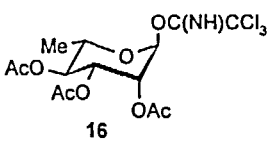
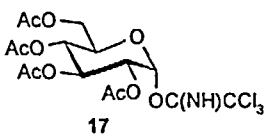


Direct glycosylation of the diol **10** was investigated in order to prepare the mono-glycosylated compounds more efficiently. As shown in Scheme 2, glycosylation of **10** with L-rhamnopyranosyl imidate **16**[13] in a molar ratio **16**:**10** of 1.2 afforded the 2'-*O*-rhamnosylated compound **11** (8%), the 3'-*O*-rhamnosylated compound **18** (32%), and the di-rhamnosylated derivative **19** (17%). The 3'-OH is preferred over 2'-OH in **10** for glycosylation with an L-rhamnopyranosyl donor. When a molar ratio **16**:**10** of 2.1 was used, the di-glycosylated product **19** was obtained in 90% yield. Interestingly, glycosylation of **10** with D-glucopyranosyl imidate **17**[14] in a molar ratio **17**:**10** of 1.5 led to the preferential formation of the 2'-*O*-glycosylated product **20** (17%) and the di-glycosylated compound **21** (19%), without detection of the corresponding 3'-*O*-glycosylated product. When 4.0 equivalents of donor **17** were used, the di-glycosylated product **21** was obtained in 40% yield and **20** in 23% yield. Isomers **11** and **18** were isolated after acetylation to give 3'-OAc and 2'-OAc derivatives **22** and **23** (not shown), respectively.

Protected saponins (**14, 15, 19, 20, 21, 23**) were treated with 80% HOAc and then with NaOMe to remove the benzylidene and acetyl groups, respectively, giving the

Scheme 2

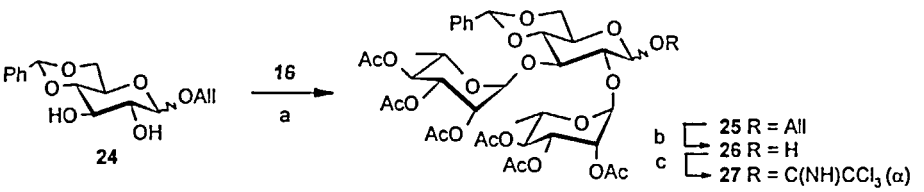


 16	16 :10 = 1.2	11 : R = Ac_3-α-L-Rha, R' = H (8%) 18 : R = H, R' = Ac_3-α-L-Rha (32%) 19 : R = R' = Ac_3-α-L-Rha (17%)
	16 :10 = 2.1	19 (90%)
 17	17 : 10 = 1.5	20 : R = Ac_4-β-D-Glu, R' = H (17%) 21 : R = R' = Ac_4-β-D-Glu (19%)
	17 : 10 = 4.0	20 (23%) 21 (40%)

corresponding saponins **4-9** in good yields (75-91%). The physical data of **4-8** are identical to those reported in the literature.[4-11]

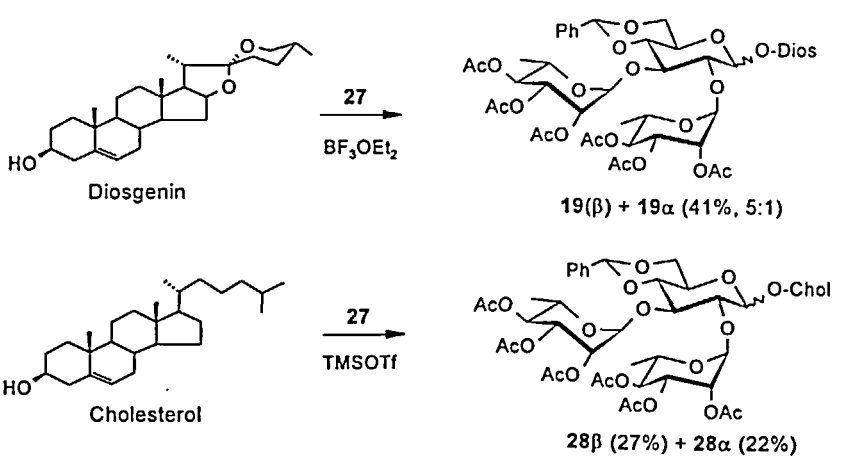
In addition to synthesizing saponins by stepwise glycosylation, they can also be prepared by glycosylation of the aglycone with a fabricated oligosaccharide donor.[2] The later route would facilitate the preparation of a family of saponins with the same sugar unit starting from different aglycones. To examine this strategy, the trisaccharide imidate donor **27** was prepared by reaction of **24** with **16** in the presence of boron trifluoride diethyl etherate to first give **25**, as depicted in Scheme 3. The protected trisaccharide **25** was then deallylated using a method recently developed by us, and consisting of treatment of **25** with $IC_6F_{12}Cl$, $Na_2S_2O_4/NaHCO_3$, followed by Zn, NH_4Cl, EtOH.[15] Resultant **26** was then converted to trisaccharide imidate **27**.

Scheme 3



Reagents and Conditions: (a) $BF_3{\cdot}OEt_2$, CH_2Cl_2, 4Å MS, -60 °C, 100%; (b) 1) $IC_6F_{12}Cl$, $Na_2S_2O_4/NaHCO_3$, CH_3CN/H_2O, rt; 2) Zn, NH_4Cl, EtOH, reflux, 10 min, 70% (two steps); (c) CCl_3CN, DBU, CH_2Cl_2, rt, 88%.

Scheme 4



Unfortunately, glycosylation of diosgenin and cholesterol with the trisaccharide donor **27** under conventional reaction conditions afforded the corresponding glycosides (**19** and **28**) only in low yields and as a mixture of their anomers, presumably due to the absence of a neighboring participating group on the glycosyl donor (Scheme 4). Therefore, at this stage the stepwise glycosylation strategy appears to be a better approach for the preparation of saponins of the type described.

EXPERIMENTAL[16]

Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-2,3,5-tri-*O*-acetyl-α-L-arabinofuranosyl-(1→3)-4,6-*O*-benzylidene-β-D-glucopyranoside (14). To a stirred suspension of **11** (150 mg, 0.16 mmol) and 4Å MS (0.3 g) in dry CH_2Cl_2 (7 mL) at -78 °C under N_2, was added BF_3•OEt_2 (0.1 M in CH_2Cl_2, 0.5 mL) followed by a solution of **12** (195 mg, 0.46 mmol) in CH_2Cl_2 (2 mL). The reaction was allowed to warm to rt, and stirred for 2 h, and then quenched by addition of Et_3N (0.05 mL). The mixture was diluted with CH_2Cl_2 (20 mL) and filtered. The filtrates were concentrated and applied to a silica gel column for chromatography (petroleum ether:EtOAc 3:1) to give **14** as a white solid (187 mg, 98%): R_f 0.43 (1:1 petroleum ether-EtOAc); mp 139-140 °C; $[\alpha]_D^{25}$ -110.2 ° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40-7.30 (m, 5 H), 5.44 (s, 1 H), 5.43 (brd, 1 H), 5.30 (s, 1 H), 5.23-5.17 (m, 2 H), 5.11-5.08 (m, 2 H), 4.94 (s, 1 H), 4.83 (d, 1 H, J = 4.8 Hz), 4.64-4.59 (m, 2 H), 4.42 (m, 1 H), 4.33 (dd, 1 H, J = 4.5, 10.5 Hz), 4.25 (m, 1 H), 4.06 (t, 1 H, J = 9.2 Hz), 3.99 (dd, 1 H, J = 3.3, 12.1 Hz), 3.80-3.62 (m, 4 H), 3.52-3.45 (m, 3 H), 3.38 (t, 1 H, J = 11.0 Hz), 2.14 (s, 3 H), 2.02 (s, 3 H), 2.02, 2.01, 1.97, 1.97 (4s, 12 H), 1.19 (d, 3 H, J = 6.3 Hz), 1.03 (s, 3 H), 0.98 (d, 3 H, J = 7.2 Hz), 0.80 (d, 3 H, J = 6.0 Hz), 0.79 (s, 3H); FAB-MS (*m/z* %): 1195 (M, 1.6), 398 (24.8), 273 (26.0), 259 (44.6), 254 (22.6), 153 (47.1), 139 (100.0).

Anal. Calcd for $C_{63}H_{86}O_{22}$: C, 63.30; H, 7.25. Found: C, 63.29; H, 7.35.

Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl-(1→3)-4,6-*O*-benzylidene-β-D-glucopyranoside (15). A procedure similar to that for the preparation of **14** was employed. Treatment of **11** (173 mg, 0.19 mmol) with BF_3•OEt_2 (2 M in CH_2Cl_2, 0.02 mL) and **13** (249 mg, 0.59 mmol, in 2.0 mL CH_2Cl_2) gave **15** (221 mg, 100%) as a white solid: R_f 0.50 (2:1 petroleum ether-EtOAc);

mp >210 °C; $[\alpha]_D^{25}$ -107.6 ° (*c* 1.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.50-7.30 (m, 5 H), 5.48 (s, 1 H), 5.41 (d, 1 H, J = 4.8 Hz), 5.24-5.19 (m, 3 H), 5.10-5.07(m, 2 H), 4.75 (d, 1 H, J = 6.9 Hz), 4.59 (d, 1 H, J = 7.7 Hz), 4.52 (m, 1 H), 4.41 (m, 1 H), 4.31 (dd, 1 H, J = 4.9, 10.5 Hz), 4.05 (t, 1 H, J = 8.9 Hz), 4.01 (dd, 1 H, J = 5.1, 12.0 Hz), 3.78-3.75 (m, 2 H), 3.65-3.61 (m, 2 H), 3.48-3.36 (m, 3 H), 3.08 (dd, 1 H, J = 9.1, 11.6 Hz), 2.19 (s, 3 H), 2.02 (s, 3 H), 1.99 (s, 3 H), 1.98 (s, 9 H), 1.19 (d, 3 H, J = 6.4 Hz), 1.03 (s, 3 H), 0.97 (d, 3 H, J = 6.9 Hz), 0.79 (d, 3 H, J = 6.4 Hz), 0.78 (s, 3 H); FAB-MS (*m/z* %): 1195 (M, 1.7), 1176 (6.7), 796(15.5), 369(36.6), 273(30.9), 155 (57.0), 139 (47.7), 69 (61.0), 55 (69.4), 42 (100.0).

Anal. Calcd for $C_{63}H_{86}O_{22}$: C, 63.30; H, 7.25. Found: C, 63.04; H, 7.28.

Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4,6-*O*-benzylidene-β-D-glucopyranoside (18), Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-4,6-*O*-benzylidene-β-D-glucopyranoside (11), and Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)]-4,6-*O*-benzylidene-β-D-glucopyranoside (19). A procedure similar to that for the preparation of **14** was employed. Treatment of **10** (500 mg, 0.75 mmol) with $BF_3 \cdot OEt_2$ (0.1 mL, 0.81 mmol) and **16** (400 mg, 0.92 mmol, in 4.0 mL CH_2Cl_2) gave a mixture of **11** and **18** (1:4, 274 mg, 40%), and **19** (158 mg, 17%) as a white solid.

19: R_f 0.49 (1:1 petroleum ether-EtOAc); mp 164-166 °C; $[\alpha]_D^{18}$ -90.0 ° (*c* 1.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.46-7.31 (m, 5 H), 5.48 (s, 1 H), 5.41 (d, 1 H, J = 4.4 Hz), 5.17-5.11 (m, 4 H), 5.07 (t, 1 H, J = 9.7 Hz), 4.97 (s, 1 H), 4.86 (t, 1 H, J = 10.0 Hz), 4.84 (s, 1 H), 4.62-4.58 (m, 1 H), 4.41 (m, 1 H), 4.34 (dd, 1 H, J = 4.9, 10.5 Hz), 4.16-4.11 (m, 1 H), 4.02 (t, 1 H, J = 9.3 Hz), 3.80 (dd, 1 H, J = 8.1, 8.9 Hz), 3.76 (t, 1 H, J = 10.3 Hz), 3.67-3.62 (m, 1 H), 3.58 (t, 1 H, J = 9.5 Hz), 3.49-3.36 (m, 3 H), 2.10, 2.07, 2.01, 1.95, 1.93, 1.89 (6s, 18 H), 1.20 (d, J = 6.1 Hz), 1.03 (s, 3 H), 0.97 (d, 3 H, J = 6.9), 0.79 (d, 3 H, J = 5.3 Hz), 0.79 (s, 3 H), 0.56 (d, 3 H, J = 6.1 Hz); FAB-MS (*m/z* %): 1208 (M, 7.0), 794 (1.0), 397 (50), 283 (8.0), 273 (100), 253 (24.0).

Anal. Calcd for $C_{64}H_{88}O_{22}$: C, 63.56; H, 7.33. Found: C, 63.24; H, 7.36.

Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside (22) and Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside (23). A solution of the above mixture of **11** and **18** in pyridine (2 mL) and Ac_2O (1 mL) was stirred at rt

for 2 h, then poured into water, and extracted with EtOAc. The organic layer was washed with dilute aqueous HCl solution, saturated $NaHCO_3$ solution, and brine, respectively, and then dried over anhydrous $NaSO_4$, and concentrated. The residue was applied to a silica gel column (petroleum ether:EtOAc 4:1) to give **22** and **23** as white solids.

23: R_f 0.38 (2:1 petroleum ether-EtOAc); mp >210 °C; $[\alpha]_D^{24}$ -81.0 ° (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.30 (m, 5 H), 5.53 (s, 1 H), 5.35 (d, 1 H, J = 4.2 Hz), 5.30 (dd, 1 H, J =3 .1, 9.9 Hz), 5.02 (t, 1 H, J = 8.5), 4.95 (dd, 1 H), 4.92 (t, 1 H, J = 10.0 Hz), 4.89 (s, 1 H), 4.53 (d, 1 H, J = 8.0 Hz), 4.40 (m, 1 H), 4.33 (dd, 1 H, J = 4.7, 10.5 Hz), 4.10-4.05 (m, 1 H), 3.88 (t, 1 H, J = 9.3 Hz), 3.80 (dd, 1 H, J = 9.9, 10.6 Hz), 3.66 (t, 1 H, J = 9.2 Hz), 3.50-3.33 (m, 4 H), 2.12, 2.10, 1.97, 1.95 (4 s, 12 H), 0.99 (s, 3 H), 0.96 (d, 3 H, J = 6.9 Hz), 0.78 (d, 3 H, J = 4.7 Hz), 0.77 (s, 3 H), 0.65 (d, 3 H, J = 6.0 Hz); FAB-MS (*m/z* %): 980 (3.8), 979 (13.8), 977 (9.4), 565 (16.3), 397 (76.3), 283 (23.8), 273 (100).

Anal. Calcd for $C_{54}H_{74}O_{16}$: C, 66.24; H, 7.62. Found: C, 66.06; H, 7.81.

22: R_f 0.48 (2:1 petroleum ether-EtOAc); mp 209-210 °C; $[\alpha]_D^{24}$ -69.2° (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.45-7.25 (m, 5 H), 5.44 (s, 1H), 5.42 (d, 1 H, J = 4.2 Hz), 5.39 (dd, 1 H, J = 8.2, 9.6 Hz), 5.25 (dd, 1 H, J = 3.2, 10.0 Hz), 5.07 (t, 1 H, J = 10.0 Hz), 5.05 (dd, 1 H, J = 1.9, 4.9 Hz), 5.03 (s, 1 H), 4.68 (d, 1 H, J = 7.9 Hz), 4.40 (m, 2 H), 4.32 (dd, 1 H, J = 4.3, 10.7 Hz), 3.75 (t, 1 H, J = 9.2 Hz), 3.72 (dd, 1 H, J = 7.5, 9.1 Hz), 3.55 (t, 1 H, J = 9.3 Hz), 3.55-3.32 (m, 4 H), 2.12, 2.10, 2.02, 1.98 (4 s, 12 H), 1.20 (d, 3 H, J = 6.1 Hz), 1.02 (s, 3 H), 0.96 (d, 3 H, J = 6.9 Hz), 0.78 (d, 3 H, J = 2.2 Hz), 0.78 (s, 3 H); FAB-MS (*m/z* %): 980 (0.6), 921 (0.5), 397 (55.9), 282 (62.4), 273 (100), 253 (42.0), 213 (35.6), 171 (26.0), 153 (80.9), 139(39.47).

Anal. Calcd for $C_{54}H_{74}O_{16}$: C, 66.24; H, 7.62. Found: C, 65.66; H, 7.88.

Diosgenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)]-4,6-*O*-benzylidene-β-D-glucopyranoside (20) and Diosgenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)-[2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→3)]-4,6-*O*-benzylidene-β-D-glucopyranoside (21). A procedure similar to that for the preparation of **14** was employed. Treatment of **10** (226 mg, 0.34 mmol) with $BF_3{\cdot}OEt_2$ (0.1 mL, 0.81 mmol) and **17** (676 mg, 1.37 mmol, in 4.0 mL CH_2Cl_2) gave **20** (77 mg, 23%) and **21** (182 mg, 40%) as white solids.

20: R_f 0.43 (2:1 toluene-EtOAc); mp 135-137 °C; $[\alpha]_D^{24}$ -56.9 ° (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.49-7.34 (m, 5 H), 5.51 (s, 1 H), 5.34 (d, 1 H, J = 4.6 Hz), 5.22 (t, 1 H, J = 9.2 Hz), 5.14 (t, 1 H, J = 9.5 Hz), 5.04 (dd, 1 H, J = 8.0, 9.0 Hz), 4.91 (d, 1 H, J = 8.0 Hz), 4.62 (d, 1 H, J = 7.6 Hz), 4.38 (m, 1 H), 4.33-4.28 (m, 2 H), 4.09 (dd, 1 H, J = 1.7, 12.2 Hz), 3.83 (t, 1 H, J = 9.1 Hz), 3.75 (m, 2 H), 3.58-3.37 (m, 6 H), 2.71 (s, 1 H), 2.09, 2.07, 2.04, 2.02 (4 s, 12 H), 1.02 (s, 3 H), 0.97 (d, 3 H, J = 6.9 Hz), 0.79 (d, 3 H, J = 3.8 Hz), 0.78 (s, 3 H); FAB-MS (*m/z* %): 995 (9.8), 993 (2.0), 809 (2.5), 749 (2.5), 663 (13.0), 647 (13.5), 397 (100), 331(84), 271 (24), 253 (50), 213 (32).

Anal. Calcd for $C_{54}H_{74}O_{17}$: C, 65.17; H, 7.50. Found: C, 64.98; H, 7.63.

21: R_f 0.35 (2:1 toluene-EtOAc); mp 124-125 °C; $[\alpha]_D^{20}$ -50.1 ° (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.46-7.16 (m, 5 H), 5.54 (s, 1 H), 5.38 (d, 1 H, J = 4.8 Hz), 5.29-4.86 (m, 8 H), 4.50 (d, 1 H, J = 7.3 Hz), 4.41 (m, 1 H), 4.33-4.26 (m, 2 H), 4.17-3.92 (m, 4 H), 3.84-3.69 (m, 4 H), 3.50-3.32 (m, 5 H), 2.07, 2.06, 2.04, 2.03, 2.02, 2.00, 1.98, 1.96 (8 s, 24 H), 1.02 (s, 3 H), 0.96 (d, 3 H, J = 6.9 Hz), 0.79 (d, 3 H, J = 3.3 Hz), 0.78 (s, 3 H); FAB-MS (*m/z* %): 1324 (3.5), 1068 (3.5), 663 (36.5), 647 (43.5), 397 (100), 331 (82), 271 (34), 253 (71.5).

Anal. Calcd for $C_{54}H_{74}O_{17}$: C, 61.62; H, 7.00. Found: C, 61.42; H, 7.08.

Diosgenyl α-L-rhamnopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside (4). A suspension of **19** (405 mg, 0.34 mmol) in aqueous HOAc (80%, 20 mL) was stirred at 70 °C for 8 h. The solvent was removed by coevaporation with toluene. The residue was dissolved in MeOH/CH_2Cl_2 (5 mL/5 mL), and NaOMe in MeOH (0.1 N, 3.0 mL) was added. After being stirred overnight at rt, the mixture was neutralized with dowex H^+ resin and then filtered. The filtrates were concentrated to a residue, which was purified by silica gel column chromatography (CH_2Cl_2:MeOH 10:1) to give **4** (265 mg, 91%) as a white solid: R_f 0.58 (5:1 CH_2Cl_2-MeOH); mp > 210 °C; $[\alpha]_D^{24}$ -89.4 ° (*c* 1.0, pyridine) [lit.[7] 249-251 °C, $[\alpha]_D^{25}$ -93.4±2 ° (*c* 2.14, DMF)]; IR (KBr) cm^{-1} 3419, 982, 963, 919, 900, 866, 838, 811; ^1H NMR (300 MHz, pyridine-d_5) δ 6.00-5.80 (br, 2 H), 5.39 (d, 1 H, J = 4.3 Hz), 4.99-4.85 (m, 5 H), 4.66-4.37 (m, 7 H), 4.28-4.05 (m, 3 H), 4.05-3.9 (m, 1 H), 3.90-3.84 (m, 1 H), 3.70-3.50 (m, 2 H), 2.90-2.70 (m, 2 H), 1.83 (d, 3 H, J = 6.0 Hz), 1.73 (d, 3 H, J = 6.2 Hz), 1.22 (d, 3 H, J = 6.9 Hz), 1.12 (s, 3 H), 0.91 (s, 3 H), 0.78 (d, 3 H, J = 5.2 Hz); ^{13}C NMR (75 MHz, pyridine-d_5) δ

139.4, 120.4, 107.9, 102.5, 101.2, 98.6, 86.2, 79.7, 77.0, 76.6, 76.5, 72.4, 72.2, 71.4, 71.1, 69.2, 68.6, 68.5, 65.5, 61.6, 60.9, 55.3, 48.9, 40.6, 39.1, 38.5, 37.3, 36.1, 35.8, 30.9, 30.5, 30.4, 29.2, 28.7, 27.9, 19.7, 18.0, 17.3, 17.0, 15.9, 15.0, 13.6; ESI-MS (*m/z* %): 1784 (8.2), 1760 (48.6), 915 (84.3), 892 (97.8), 870 (22.6).

Diosgenyl α-L-rhamnopyranosyl-(1→2)-[β-D-xylopyranosyl-(1→3)]-β-D-glucopyranoside (5). A procedure similar to that for the preparation of **4** was employed. Treatment of **15** (166 mg, 0.14 mmol) gave **5** (98 mg, 83%) as a white solid: R_f 0.36 (4:1 CH_2Cl_2-MeOH); IR (KBr) cm^{-1} 3416, 2937, 1047, 981, 920, 900; mp > 210 °C, [lit.[8] 255-257 °C]; $[\alpha]_D^{26}$ -91.8 ° (*c* 1.0, pyridine), [lit.[8] $[\alpha]_D^{18}$ -41.3 ° (*c* 0.17, Py)]; ^1H NMR (300 MHz, pyridine-d_5) δ 6.40 (s, 1 H), 5.81 (br, 1 H), 5.41 (d, 1 H, J = 4.4 Hz), 5.08-4.95 (m, 4 H), 4.68-4.05 (m, 12 H), 3.95-3.88 (m, 1 H), 3.80-3.58 (m, 3 H), 2.91-2.75 (m, 2 H), 1.84 (d, 3 H, J = 6.1 Hz), 1.22 (d, 3 H, J = 6.9 Hz), 1.14 (s, 3 H), 0.91 (s, 3 H), 0.77 (d, 3 H, J = 5.0 Hz); ^{13}C NMR (75 MHz, pyridine-d_5) δ 143.2, 124.3, 111.7, 107.9, 104.9, 102.4, 90.6, 83.5, 80.8, 80.4, 80.1, 79.8, 77.1, 76.5, 75.3, 74.9, 73.1, 72.1, 71.9, 69.7, 69.3, 65.3, 64.8, 59.1, 52.7, 44.4, 42.9, 42.3, 41.1, 39.9, 39.6, 34.8, 34.7, 34.3, 34.1, 33.0, 32.5, 31.7, 23.5, 21.8, 21.1, 19.8, 18.8, 17.5; ESI-MS (*m/z* %): 878 (M+Na, 100), 856 (16.6).

Diosgenyl α-L-rhamnopyranosyl-(1→2)-[α-L-arabinofuranosyl-(1→3)]-β-D-glucopyranoside (6). A procedure similar to that for the preparation of **4** was employed. Treatment of **14** (158 mg, 0.13 mmol) gave **6** (91 mg, 80%) as a white solid: R_f 0.60 (5:1 CH_2Cl_2-MeOH); mp > 210 °C, [lit.[9] 244-247 °C(dec.)]; $[\alpha]_D^{26}$ -104.7 ° (*c* 1.0, pyridine), [lit.[9] $[\alpha]_D^{24}$ -115.7 ° (*c* 0.51, EtOH)]; IR (KBr) cm^{-1} 3424, 2934, 1047, 981, 920, 899; ^1H NMR (300 MHz, pyridine-d_5) δ 6.09 (s, 1 H), 5.93 (d, 1 H, J = 2.1 Hz), 5.41 (d, 1 H, J = 4.6 Hz), 5.00 (d, 1 H, J = 7.2 Hz), 4.96-4.88 (m, 5 H), 4.66-3.82 (m, 12 H), 3.69-3.50 (m, 2 H), 2.87-2.70 (m, 2 H), 1.84 (d, 3 H, J = 6.2 Hz), 1.22 (d, 3 H, J = 6.9 Hz), 1.13 (s, 3 H), 0.91 (s, 3 H), 0.78 (d, 3 H, J = 5.2Hz); ^{13}C NMR (75 MHz, pyridine-d_5) δ 140.9, 122.0, 110.5, 109.4, 102.6, 100.2, 86.4, 83.1, 81.2, 78.1, 77.7, 74.0, 72.9, 72.5, 70.0, 67.0, 63.0, 62.5, 56.8, 50.4, 42.1, 40.6, 40.0, 38.9, 37.6, 37.3, 32.4, 32.4, 32.0, 31.8, 30.7, 30.2, 29.4, 21.2, 19.5, 18.8, 17.5, 16.5, 15.2; ESI-MS (*m/z* %): 1732 (39.5), 878 (M+Na, 100), 856 (M+1, 12.7).

Diosgenyl α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranoside (7). A procedure similar to that for the preparation of **4** was employed. Treatment of **18** (122 mg, 0.15

mmol) gave **7** (79 mg, 87%) as a white solid: R_f 0.41 (10:1 CH_2Cl_2-MeOH); mp 200-201 °C, [lit.[10] 185-190 °C(decom.)]; $[\alpha]_D^{24}$ -91.0 ° (*c* 1.0, pyridine), [lit.[10] $[\alpha]_D^{27}$ -99 ° (*c* 0.5, pyridine)]; IR (KBr) cm^{-1} 3398, 982, 920, 900, 877, 836, 806; ^1H NMR (300 MHz, pyridine-d_5) δ 6.41 (d, 1 H, J = 1.0 Hz), 5.38 (d, 1 H, J = 4.9 Hz), 5.20-5.10 (m, 2 H), 5.01 (d, 1 H, J = 7.8 Hz), 4.88 (dd, 1 H, J = 1.5, 3.3 Hz), 4.68 (dd, 1 H, J = 3.4, 9.3 Hz), 4.64-4.36 (m, 4 H), 4.33 (t, 1 H, J = 9.2 Hz), 4.11 (t, 1 H, J = 9.0 Hz), 4.00-3.90 (m, 2 H), 3.70-3.55 (m, 2 H), 2.75-2.66 (m, 1 H), 2.50-2.38 (m, 1 H), 1.81 (d, 3 H, J = 6.2 Hz), 1.22 (d, 3 H, J = 6.9 Hz), 0.96 (s, 3 H), 0.91 (s, 3 H), 0.78 (d, 3 H, J = 5.5 Hz); ^{13}C NMR (75 MHz, pyridine-d_5) δ 140.9, 121.9, 109.4, 103.0, 102.5, 83.7, 81.2, 78.5, 78.3, 75.8, 74.3, 72.9, 72.7, 70.0, 69.8, 67.0, 63.0, 62.7, 56.8, 50.4, 42.1, 40.6, 40.0, 39.3, 37.5, 37.2, 32.3, 32.0, 31.8, 30.7, 30.3, 29.4, 21.2, 19.5, 18.2, 17.4, 16.5, 15.2; ESI-MS (*m/z* %): 1468 (61.8), 769 (36.4), 746 (96.6), 724 (30.7).

Diosgenyl β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside (8). A procedure similar to that for the preparation of **4** was employed. Treatment of **20** (140 mg, 0.14 mmol) gave **8** (78 mg, 75%) as a white solid: R_f 0.42 (5:1 CH_2Cl_2-MeOH); mp > 210 °C, [lit.[11] 233-234 °C]; $[\alpha]_D^{24}$ -51.5 ° (*c* 1.0, pyridine), [lit.[11] $[\alpha]_D^{20}$ -65 ° (*c* 1.0, MeOH)]; IR (KBr) cm^{-1} 3401, 982, 962, 921, 900, 865; ^1H NMR (300 MHz, pyridine-d_5) δ 5.41 (d, 1 H, J = 4.7 Hz), 5.38 (d, 1 H, J = 7.7 Hz), 5.15 (d, 1 H, J = 7.6 Hz), 4.70-4.20 (m, 11 H), 4.09-3.88 (m, 3 H), 3.72-3.58 (m, 2 H), 1.22 (d, 3 H, J = 6.9 Hz), 1.07 (s, 3 H), 0.90 (s, 3 H), 0.77 (d, 3 H, J = 5.3 Hz); ^{13}C NMR (75 MHz, pyridine-d_5) δ 141.2, 121.7, 109.4, 106.8, 101.6, 84.9, 81.2, 79.5, 78.8, 78.3, 78.1, 78.0, 77.2, 71.7, 72.6, 67.0, 63.0, 62.8, 56.8, 50.4, 42.1, 40.6, 40.1, 39.4, 37.6, 37.2, 32.4, 32.0, 31.8, 30.7, 30.4, 30.1, 29.4, 21.3, 19.6, 17.4, 16.5, 15.1; ESI-MS (*m/z* %): 740 (2.5), 739 (13.5), 559 (2.0), 461 (7.0), 415 (19), 397 (23), 369 (17.5), 277 (100).

Anal. Calcd for $C_{39}H_{62}O_{13}$: C, 63.39; H, 8.46. Found: C, 63.00; H, 7.95.

Diosgenyl β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranoside (9). A procedure similar to that for the preparation of **4** was employed. Treatment of **21** (144 mg, 0.11 mmol) gave **9** (71 mg, 75%) as a white solid: R_f 0.22 (5:1 CH_2Cl_2-MeOH); mp 211-212 °C; $[\alpha]_D^{24}$ -54.4 ° (*c* 1.0, pyridine); IR (KBr) cm^{-1} 3413, 983, 963, 921, 900, 866; ^1H NMR (300 MHz, pyridine-d_5) δ 5.35 (d, 1 H, J = 7.7 Hz), 5.25 (d, 1 H, J = 5.4 Hz), 5.23 (d, 1 H, J = 7.8 Hz), 4.89 (d, 1 H, J = 7.2 Hz), 4.47-3.72

(m, 2 H), 3.50-3.36 (m, 2 H), 2.68-2.63 (m, 1 H), 2.53-2.45 (m, 1 H), 1.03 (d, 3 H, J = 7.1 Hz), 0.86 (s, 3 H), 0.73 (s, 3 H), 0.60 (d, 3 H, J = 5.5 Hz); ^{13}C NMR (75 MHz, pyridine-d_5) δ 141.5, 112.2, 109.8, 105.6, 105.5, 102.2, 82.3, 81.6, 79.5, 79.1, 79.0, 78.8, 78.4, 78.2, 76.9, 75.7, 72.1, 70.4, 67.4, 63.4, 63.2, 62.9, 57.2, 50.7, 42.5, 41.6, 41.0, 40.4, 39.7, 37.9, 37.5, 32.7, 32.3, 32.1, 31.1, 30.7, 30.5, 29.8, 21.6, 19.1, 17.8, 16.8, 15.5; ESI-MS (*m/z* %): 1825 (14.1), 1034 (14.4), 956 (10.0), 947 (44.2), 924 (100).

Anal. Calcd for $C_{45}H_{72}O_{18}\cdot 3H_2O$: C, 56.59; H, 8.23. Found: C, 56.57; H, 8.05.

Allyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)]-4,6-*O*-benzylidene-α/β-D-glucopyranoside (25). A procedure similar to that for the preparation of **14** was employed. Treatment of **24** (1.32 g, 4.29 mmol) with $BF_3\cdot OEt_2$ (0.5 mL, 4.07 mmol) and **16** (5.63 g, 12.95 mmol, in 6.0 mL CH_2Cl_2) gave **25** (3.66 g, 100%) as white solids.

25α: R_f 0.31 (3:2 petroleum ether-EtOAc); mp 103-105 °C; $[\alpha]_D^{20}$ -16.3 ° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49-7.26 (m, 5 H), 5.60 (m, 1 H), 5.54 (s, 1 H), 5.36 (dd, 1 H, J = 1.3, 17.2 Hz), 5.30-5.18 (m, 5 H), 5.08-4.99 (m, 3 H), 4.95 (t, 1 H, J = 10.1 Hz), 4.88 (s, 1 H), 4.30-4.15 (m, 4 H), 4.08-4.02 (m, 1 H), 3.95-3.85 (m, 2 H), 3.74 (t, 1 H, J = 10.4 Hz), 3.68 (dd, 1 H, J = 3.6, 9.4 Hz), 3.56 (t, 1 H, J = 9.5 Hz), 2.12, 2.09, 2.02, 1.97, 1.95, 1.93 (6 s, 18 H), 1.17 (d, 3 H, J = 6.0 Hz), 0.74 (d, 3 H, J = 6.0 Hz); ESI-MS (*m/z* %): 871 (100), 273 (26.9), 153 (70.6), 111 (38.1).

Anal. Calcd for $C_{40}H_{52}O_{20}$: C, 56.33; H, 6.15. Found: C, 56.46; H, 6.32.

25β: R_f 0.47 (3:2 petroleum ether-EtOAc); mp 212-214 °C; $[\alpha]_D^{20}$ -89.3 ° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.28 (m, 5 H), 5.59 (m, 1 H), 5.49 (s, 1 H), 5.36-5.08 (m, 5 H), 5.08-4.81 (m, 4 H), 4.51 (d, 1 H, J = 7.7 Hz, H-1'), 4.41-4.26 (m, 3H), 4.18-4.06 (m, 2H), 4.01 (t, 1 H, J = 9.1 Hz), 3.82-3.71 (m, 2 H), 3.59 (t, 1 H, J = 9.3 Hz), 3.52-3.41 (m, 1 H), 2.09, 2.07, 2.02, 1.95, 1.93, 1.90 (6 s, 18 H), 1.15 (d, 3 H, J = 6.0 Hz), 0.55 (d, 3 H, J = 6.1 Hz).

Anal. Calcd for $C_{40}H_{52}O_{20}$: C, 56.33; H, 6.15. Found: C, 57.42; H, 6.08.

2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)]-4,6-*O*-benzylidene-α/β-D-glucopyranose (26). To a mixture of **25** (3.33 g, 3.90 mmol) in CH_3CN/H_2O (4:1, 150 mL), was added $IC_6F_{12}Cl$ (2.17 g, 4.68 mmol) followed by addition of a mixture of $Na_2S_2O_4$ (408 mg, 2.34 mmol) and $NaHCO_3$

(197 mg, 2.34 mmol). After being stirred at rt for 1 h, the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous $NaSO_4$, and then concentrated to give a residue (3.74 g). To a solution of the above residue (2.59 g, 1.97 mmol) in dry EtOH (70 mL) was added Zn powder (645 mg, 9.86 mmol) and NH_4Cl (264 mg, 1.97 mmol). After being refluxed for 10 min, the mixture was filtered. The filtrates were concentrated and then purified by silica gel column chromatography (petroleum ether : EtOAc 2:1-1:1) to give **26** (1.53 g, 70%) as a white foamy solid: **26α**: R_f 0.52 (2:3 petroleum ether-EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.28 (m, 5 H), 5.50-4.70 (m, 9 H), 4.40-3.40 (m, 10 H), 2.20-1.80 (m, 18 H), 1.30-1.15 (m, 3 H), 0.78-0.55 (d, 3 H); FAB-MS (*m/z* %): 835 (M+Na, 4.7), 796 (8.2), 725 (8.2), 273 (58.8), 171 (32.9), 153 (100).

2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)]-4,6-*O*-benzylidene-α-D-glucopyranosyl trichloroacetimidate (27). To a solution of **26** (545 mg, 0.67 mmol) in dry CH_2Cl_2 (15 mL) at -20 °C, was added CCl_3CN (0.4 mL, 3.95 mmol) and DBU (0.04 mL, 0.13 mmol). The mixture was stirred at 0 °C for 3 h, and then concentrated to a residue, which was purified by silica gel column chromatography (petroleum ether: EtOAc 3:2) to give **27** (567 mg, 88%) as a foamy solid: R_f 0.40 (1:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ -18.0 ° (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.76 (s, 1 H), 7.50-7.30 (m, 5 H), 6.41 (d, 1 H, J = 3.9 Hz), 5.30-5.10 (m, 4 H), 5.06-4.90 (m, 4 H), 4.37-4.10 (m, 3 H), 4.06-3.80 (m, 3 H), 3.80-3.63 (m, 2 H), 2.11, 2.08, 1.99, 1.96, 1.95, 1.93 (6 s, 18 H), 1.15 (d, 3 H, J = 6.3 Hz), 0.75 (d, 3 H, J = 6.3 Hz); ESI-MS (*m/z* %): 978 (100), 795 (31.3).

Anal. Calcd for $C_{39}H_{48}O_{20}NCCl_3$: C, 48.94; H, 5.05; N, 1.46. Found: C, 49.73; H, 5.19; N, 1.41.

Cholest-5(6)-en-3β-yl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)]-4,6-*O*-benzylidene-α/β-D-glucopyranoside (28). A procedure similar to that for the preparation of **14** was employed. Treatment of cholesterol (49 mg, 0.13 mmol) and **27** (100 mg, 0.1 mmol) with TMSOTf (0.008 mL, 0.044 mmol) gave **28β** (33 mg, 27%) and **28α** (27 mg, 22%) as white solids.

28α: R_f 0.29 (3:2 petroleum ether-EtOAc); mp 131-133 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 7.50-7.30 (m, 5 H), 5.54 (s, 1 H), 5.38 (d, 1 H), 5.28-5.21 (m, 4 H), 5.06-5.03

(m, 2 H), 5.01 (d, 1 H, J = 1.2 Hz), 4.95 (t, 1 H), 4.89 (s, 1 H), 4.29-4.20 (m, 3 H), 3.99-3.94 (m, 2 H), 3.72 (t, 1 H, J = 10.8 Hz), 3.65 (dd, 1 H, J = 3.6, 9.6 Hz), 3.55 (t, 1 H, J = 9.6 Hz), 3.42-3.40 (m, 1 H), 2.12, 2.09, 2.03, 1.96, 1.96, 1.94 (6 s, 18 H), 1.20 (d, 3 H, J = 6.6 Hz), 1.05 (s, 3 H), 0.92 (d, 3 H, J = 6.6 Hz), 0.88 (d, 3 H, J = 2.4 Hz), 0.87 (d, 3 H, J = 2.4 Hz), 0.75 (d, 3 H, J = 6.6 Hz), 0.69 (s, 3 H).

28β: R_f 0.55 (3:2 petroleum ether-EtOAc); mp 139-140 °C; $[\alpha]_D^{18}$ -67.7 ° (*c* 0.31, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.30 (m, 5 H), 5.48 (s, 1 H), 5.41 (d, 1H), 5.20-5.00 (m, 5 H), 4.97 (s, 1 H), 4.90-4.80 (m, 2 H), 4.66-4.54 (m, 2 H), 4.34 (dd, 1 H, J = 4.8, 10.6 Hz), 4.18-4.08 (m, 1 H), 4.02 (t, 1 H, J = 9.1 Hz), 3.84-3.40 (m, 5 H), 2.09, 2.06, 2.00, 1.94, 1.92, 1.89 (6 s, 18 H), 1.20 (d, 3 H, J = 6.3 Hz), 1.00 (s, 3 H), 0.91 (d, 3 H, J = 6.5 Hz), 0.87 (d, 3 H, J = 1.3 Hz), 0.85 (d, 3 H, J = 1.2 Hz), 0.67 (s, 3 H), 0.55 (d, 3 H, J = 6.1 Hz); ESI-MS (*m/z* %): 1227 (M+2Na, 100), 1204 (M+Na, 92.5).

Anal. Calcd for $C_{64}H_{92}O_{20}$: C, 65.07; H, 7.85. Found: C, 65.13; H, 8.19.

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