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SYNTHESIS OF 20*S*-PROTOPANAXADIOL *β*-D-GALACTOPYRANOSIDES

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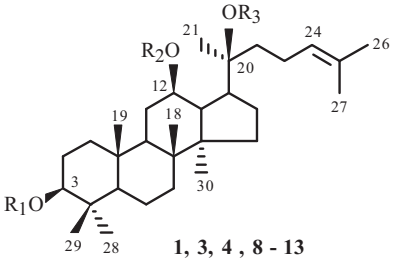
UDC 547.917+547.918+547.597

*20*S*-Protopanaxadiol (3*β*,12*β*,20*S*-trihydroxydammar-24-ene) 3-, 12-, and 20-*O*-*β*-D-galactopyranosides were synthesized for the first time. Condensation of 12*β*-acetoxy-3*β*,20*S*-dihydroxydammar-24-ene (**1**) and 2,3,4,6-tetra-*O*-acetyl-*α*-D-galactopyranosylbromide (*α*-acetobromogalactose) (**2**) under Koenigs–Knorr conditions with subsequent removal of the protecting groups resulted in regio- and stereoselective formation of 20*S*-protopanaxadiol 3-*O*-*β*-D-galactopyranoside, an analog of the natural ginsenoside Rh_2. Glycosylation of 12*β*,20*S*-dihydroxydammar-24-en-3-one (**5**) by **2** with subsequent treatment of the reaction products with $NaBH_4$ in isopropanol and deacetylation with NaOMe gave 20*S*-protopanaxadiol 12- and 20-*O*-*β*-D-galactopyranosides.*

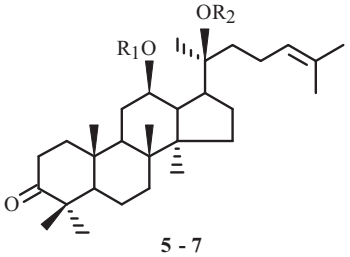
Keywords: dammarane triterpenoids, 20*S*-protopanaxadiol, glycosylation, *Panax ginseng*, 20*S*-protopanaxadiol 3-*O*-*β*-D-galactopyranoside, 20*S*-protopanaxadiol 12-*O*-*β*-D-galactopyranoside, 20*S*-protopanaxadiol 20-*O*-*β*-D-galactopyranoside.

Triterpene glycosides are constituents of the root extract of ginseng (*Panax ginseng* C. A. Meyer) and constantly attract attention because of the broad spectrum and variety of physiological activity. They have been the subject of numerous investigations [1–11]. Although the properties of ginseng glycosides have been extensively studied and the active constituents have been identified, the mechanism of action of these compounds is not fully known and the chemical structure–biological activity relationship remains an open question. The biological properties and mechanism of action of 20*S*-protopanaxadiol 3-*O*-*β*-D-glucopyranoside (ginsenoside Rh_2) [3–9] and 20*S*-protopanaxadiol 20-*O*-*β*-D-glucopyranoside, one of the principal metabolites of *P. ginseng* glycosides (compound K, M1) [1, 4, 7, 10, 11], have been continuously studied for the last several years. We developed semi-synthetic preparative methods for preparing these compounds [12–14] that were based on chemical transformation of betulafolientriol, a dammarane triterpenoid and one of the constituents extracted from birch leaves (*Betula pendula* Roth., *B. platyphylla* Sukacz).

Herein we continue research on the synthesis of glycosides of dammarane tetracyclic triterpenoids. We considered it advantageous to synthesize 20*S*-protopanaxadiol *β*-D-galactopyranosides that are close structural analogs of ginsenoside Rh_2 and metabolite M1 (compound K) in order to obtain new data on the structure–activity relationship of dammarane glycosides.



1, 3, 4 , 8 - 13



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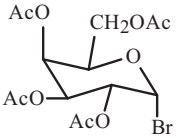

2

1: $R_1 = R_3 = H$, $R_2 = Ac$; **3:** $R_1 = GalAc_4$, $R_2 = Ac$, $R_3 = H$; **4:** $R_1 = Gal$, $R_2 = R_3 = H$; **5:** $R_1 = R_2 = H$
6: $R_1 = GalAc_4$, $R_2 = H$; **7:** $R_1 = H$, $R_2 = GalAc_4$; **8:** $R_1 = R_3 = H$, $R_2 = GalAc_4$
9: $R_1 = R_2 = H$, $R_3 = GalAc_4$; **10:** $R_1 = R_2 = Ac$, $R_3 = GalAc_4$; **11:** $R_1 = Ac$, $R_2 = GalAc_4$, $R_3 = H$
12: $R_1 = R_3 = H$, $R_2 = Gal$; **13:** $R_1 = R_2 = H$, $R_3 = Gal$

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TABLE 1. ^{13}C NMR Chemical Shifts for **1**, **3**, **4**, **8**-**13** (δ, ppm vs. TMS)

C atom	**1**	**3**	**4**	**8**	**9**	**10**	**11**	**12**	**13**
1	38.82	38.75	39.21	39.11	38.92	38.47	38.79	38.96	39.58
2	27.24	25.89	26.87	27.22	27.47	23.57	23.55	28.17	28.44
3	78.72	90.45	88.68	78.72	78.93	80.64	80.50	77.90	78.22
4	38.92	39.05	39.72	38.95	38.93	37.88	37.88	39.46	39.72
5	55.82	56.11	56.43	55.82	55.87	55.89	55.92	56.26	56.53
6	18.22	18.09	18.47	18.19	18.31	18.16	18.07	18.60	18.93
7	34.59	34.54	35.19	34.52	34.72	34.44	34.45	34.92	35.35
8	39.71	39.69	40.04	39.64	39.75	39.55	39.67	39.89	40.25
9	50.02	49.97	50.43	49.77	49.75	49.86	49.70	50.27	50.49
10	37.15	36.87	37.01	37.21	37.13	36.99	37.13	37.39	37.53
11	28.24	28.23	32.12	27.48	30.10	29.04	27.48	27.78	31.14
12	76.67	76.53	71.02	78.13	70.02	75.20	78.01	77.07	70.21
13	44.88	44.82	48.61	46.00	48.65	45.63	46.00	46.70	49.69
14	52.74	52.67	51.73	51.97	51.25	53.04	51.95	52.13	51.57
15	31.47	31.42	31.36	30.71	30.25	31.61	30.74	31.36	30.94
16	27.15	27.12	26.83	26.70	26.45	26.36	26.72	27.17	26.82
17	52.89	52.90	54.84	53.63	52.74	47.84	53.57	53.80	51.66
18	15.58	15.56	16.76	15.84	15.76	15.44	15.84	15.63	16.22
19	16.18	16.07	16.39	16.12	15.97	16.16	16.19	16.31	16.50
20	73.66	73.66	72.95	72.66	84.90	83.21	72.65	72.67	83.28
21	26.21	26.19	27.12	26.25	22.35	21.69	26.28	27.06	22.44
22	36.11	36.04	35.91	35.77	35.39	39.00	35.78	36.48	36.34
23	22.25	22.22	23.02	22.32	22.95	22.72	22.32	22.92	23.28
24	125.18	125.14	126.35	125.82	124.50	124.53	125.84	126.64	126.21
25	131.30	131.33	130.74	130.62	131.50	131.51	130.63	130.39	131.03
26	25.73	25.73	25.81	25.77	25.63	25.64	25.78	25.72	25.90
27	17.66	17.66	17.68	17.64	17.72	17.75	17.65	17.63	17.92
28	27.98	27.62	28.18	27.99	28.05	27.96	27.95	28.57	28.84
29	15.32	16.14	15.86	15.35	15.35	16.46	16.48	16.17	16.47
30	17.30	17.22	17.06	17.39	16.99	17.96	17.36	17.40	17.61
$\underline{C}H_3CO$	21.51	21.51		20.78	20.54	21.82	21.27		
		20.83		20.66	20.54	21.26	20.78		
		20.74		20.66	20.69	20.91	20.67		
		20.68		20.53	20.84	20.72	20.67		
		20.58				20.61	20.54		
						20.57			
$CH_3\underline{C}O$	169.64	170.42		170.41	170.43	170.86	170.92		
		170.35		170.36	170.36	170.49	170.43		
		170.18		170.13	170.13	170.40	170.34		
		169.67		168.62	168.93	170.23	170.13		
		169.31				170.19	168.61		
						169.05			

We synthesized 20*S*-protopanaxadiol 3-*O*-*β*-D-galactopyranoside (**4**) using the approach developed by us for regioselective glycosylation of the C-3 equatorial hydroxyl of 20*S*-protopanaxadiol with acetyl protection of the 12*β*-OH group, the steric position of which prevents simultaneously glycosylation of the tertiary C-20-OH group [12, 13]. Condensation of 12*β*-acetoxy-3*β*,20*S*-dihydroxydammar-24-ene (**1**) with 2,3,4,6-tetra-*O*-acetyl-*α*-D-galactopyranosylbromide (*α*-acetobromogalactose) (**2**) in the presence of silver oxide (Ag_2O) and 4-Å molecular sieves in dichloroethane at room temperature formed the corresponding acetylated 3-*O*-*β*-D-galactoside (**3**) (51.8% yield), subsequent deacetylation of which by NaOMe in MeOH gave in quantitative yield free 20*S*-protopanaxadiol 3-*O*-*β*-D-galactopyranoside (**4**). A previous attempt by us to perform regio- and stereoselective glycosylation of the C-20 tertiary hydroxyl in 20*S*-protopanaxadiol 3,12-diacetate was unsuccessful [15, 16]. Condensation of 20*S*-protopanaxadiol 3,20-diketone with *α*-acetobromoglucose with subsequent reduction of both C-3 and C-12 ketones also did not give the desired result [14].

TABLE 2. ^{13}C NMR Chemical Shifts of the Sugar Component for **3**, **4**, **8**–**13** (δ, ppm vs. TMS)

Compound	C atom					
	1′	2′	3′	4′	5′	6′
3	103.53	69.25	70.95	67.14	70.53	61.45
4	107.58	73.20	75.49	70.34	76.89	62.52
8	97.10	68.78	70.95	66.69	70.99	60.94
9	95.25	69.50	71.13	67.11	70.97	61.68
10	95.25	69.48	71.33	67.36	70.57	61.79
11	97.06	68.84	70.97	66.74	71.02	60.99
12	100.75	72.47	75.51	69.84	77.22	62.11
13	98.99	72.77	76.37	70.24	76.95	62.29

We studied condensation of 12*β*,20*S*-dihydroxydammar-24-en-3-one (**5**) with **2** in order to prepare dammarane tetracyclic triterpenoids containing C-12 and C-20 galactopyranosides. The reaction formed a mixture of acetylated 12*β*,20*S*-dihydroxydammar-24-en-3-one 12- and 20-*O*-*β*-D-galactopyranosides (**6**) and (**7**) (59% yield, ~6:1 ratio), treatment of which with $NaBH_4$ in isopropanol produced 20*S*-protopanaxadiol 12- and 20-*O*-*β*-D-galactopyranoside tetraacetates (**8**) and (**9**). The mixture of these compounds was treated with Ac_2O in pyridine at 90° for 2–3 h in order to simplify chromatographic separation of the reduction products **8** and **9**. Because the C-20 tertiary OH group in **8** was not acetylated, such treatment produced a mixture of 20-*O*-*β*-D-galactopyranoside hexaacetate (**10**) and 12-*O*-*β*-D-galactopyranoside pentaacetate (**11**), chromatographic separation of which was facile. Compounds **8** and **9** were deacetylated by NaOMe solution (0.1 N) in MeOH; compounds **10** and **11**, by KOH solution (10%) in MeOH. This produced in quantitative yields the corresponding free 12- and 20-*O*-*β*-D-galactopyranosides **12** and **13**.

The structures of all compounds were established using IR, PMR, ^{13}C NMR, and 2D spectroscopy. Doublets for anomeric protons of the sugar components of acetylated galactosides **3** and **6**–**11** appeared in PMR spectra in $CDCl_3$ at δ 4.51–4.78 ppm ($J_{1',2'}$ = 7.7–8.0 Hz). Doublets for anomeric protons of galactose in free galactosides **4**, **12**, and **13** were observed in PMR spectra in deuteropyridine at δ 4.88–5.18 ppm ($J_{1',2'}$ = 7.7 Hz). Chemical shifts and spin–spin coupling constants of galactose anomeric protons were indicative of the *trans*-configuration of the glycoside bond in all galactosides. The site of attachment of the galactose unit was confirmed by comparing ^{13}C NMR spectra of **1**, **3**, **4**, and **8**–**13** (Tables 1 and 2).

EXPERIMENTAL

PMR and ^{13}C NMR spectra of **1** and **3**–**11** were recorded in $CDCl_3$; of **4**, **12**, and **13**, in Py-d_5 on a Bruker Avance-700 spectrometer at operating frequency 700 MHz (^1H) and 175 MHz (^{13}C) at 30°C. Chemical shifts are given on the δ scale vs. TMS. Multiplicity of ^{13}C resonances were found using DEPT-135 experiments by the standard method. Homonuclear ^1H–^1H COSY-45 and heteronuclear HSQC and HMBC 2D correlation spectra were also obtained using standard methods. HMBC experiments were optimized for $^nJ_{HC}$ ~ 5 Hz. IR spectra were recorded in $CHCl_3$ solution on a Bruker Vector 22 spectrophotometer. Optical rotation was determined on a Perkin–Elmer 343 Polarimeter in a 10-cm cuvette at 20°C. Melting points were measured on a Boetius stage. Column chromatography was performed over KSK silica gel (120–150 mesh) using hexane:acetone (20:1→6:1). The purity of compounds was monitored using TLC on Sorbfil plates (Russia) and solvent systems hexane:acetone (3:1) and C_6H_6:$CHCl_3$:MeOH (6:4:1 and 3:2:1) with detection by H_2SO_4 in EtOH (10%) followed by heating at 100–200°C. Elemental analyses of all newly prepared compounds agreed with those calculated.

12*β*-Acetoxy-3*β*,20*S*-dihydroxydammar-24-ene (1) was prepared by the literature method [12, 13].

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.777 (3H, s, Me-29), 0.858 (3H, s, Me-19), 0.951 (3H, s, Me-30), 0.978 (3H, s, Me-28), 1.011 (3H, s, Me-18), 1.131 (3H, s, Me-21), 1.640 (3H, s, Me-27), 1.709 (3H, s, Me-26), 2.047 (3H, s, OAc), 3.01 (1H, s, OH-20), 3.20 (1H, dd, J = 11.6, 4.3, H-3*α*), 4.73 (1H, td, J = 10.6, 10.6, 5.0, H-12*α*), 5.16 (1H, tt, J = 7.0, 7.0, 1.4, 1.4, H-24).

12*β*,20*S*-Dihydroxydammar-24-en-3-one (5) was prepared as before [15, 16], mp 196–198°C (acetone), lit. [17] mp 196–199°C.

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.899 (3H, s, Me-30), 0.985 (3H, s, Me-19), 1.030 (3H, s, Me-18), 1.046 (3H, s, Me-29), 1.085 (3H, s, Me-28), 1.207 (3H, s, Me-21), 1.641 (3H, s, Me-27), 1.700 (3H, s, Me-26), 3.60 (1H, td, J = 10.4, 10.4, 5.2, H-12α), 5.17 (1H, tt, J = 7.1, 7.1, 1.5, 1.5, H-24).

2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosylbromide (2) was prepared by the literature method [18], mp 84–85°C (Et_2O), lit. [19] mp 84–85°C.

Condensation of 1 and 2. A mixture of **1** (0.48 g, 0.95 mmol), **2** (1.03 g, 2.5 mmol), and Ag_2O (0.70 g, 3 mmol) in anhydrous dichloroethane (10 mL) was stirred at room temperature for 6 h, diluted with $CHCl_3$, and filtered to remove insoluble silver compounds. The solvent was distilled at reduced pressure. The solid was worked up with hot water to remove water-soluble galactose derivatives and dried. The dry solid was chromatographed over a column of silica gel with elution by hexane:acetone (15:1→8:1) to afford starting acetate **1** (0.08 g, 16.5%) and **3** (0.41 g, 51.8%).

12β-Acetoxy-3β-(22,32,42,62-tetra-*O*-acetyl-β-D-galactopyranosyloxy)-20*S*-hydroxydammar-24-ene (3), $C_{46}H_{72}O_{13}$, amorphous, $[\alpha]_D^{20}$ +11.2° (*c* 0.9, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1720 (CH_3C=O), 1756 (CH_3C=O), 3535 (OH).

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.755 (3H, s, Me-29), 0.852 (3H, s, Me-19), 0.912 (3H, s, Me-28), 0.939 (3H, s, Me-30), 1.000 (3H, s, Me-18), 1.129 (3H, s, Me-21), 1.638 (3H, s, Me-27), 1.708 (3H, s, Me-26), 1.982 (3H, s, OAc), 2.044 (3H, s, OAc), 2.047 (3H, s, OAc), 2.061 (3H, s, OAc), 2.143 (3H, s, OAc), 3.08 (1H, dd, J = 11.8, 4.8, H-3α), 3.90 (1H, td, J = 6.8, 6.8, 1.0, H-5′), 4.11 (1H, dd, J = 11.1, 6.6, H-6′), 4.16 (1H, dd, J = 11.1, 6.8, H-6′), 4.51 (1H, d, $J_{1',2'}$ = 7.9, H-1′), 4.73 (1H, td, J = 10.6, 10.6, 5.0, H-12α), 5.02 (1H, dd, J = 10.3, 3.5, H-3′), 5.16 (1H, tt, J = 7.0, 7.0, 1.5, 1.5, H-24), 5.25 (1H, dd, J = 10.6, 7.9, H-2′), 5.37 (1H, dd, J = 3.5, 1.0, H-4′).

3-*O*-β-D-Galactopyranosyl-3β,12β,20*S*-trihydroxydammar-24-ene (4) was prepared by deacetylation of **3** by NaOMe in MeOH (0.1 N) at 20°C for 1–1.5 h. $C_{36}H_{62}O_8$, amorphous, $[\alpha]_D^{20}$ +7.8° (*c* 0.87, C_5H_5N).

PMR spectrum (700 MHz, C_5D_5N, δ, ppm, J/Hz): 0.829 (3H, s, Me-19), 0.976 (3H, s, Me-29), 0.984 (6H, s, Me-18, Me-30), 1.322 (3H, s, Me-28), 1.438 (3H, s, Me-21), 1.635 (3H, s, Me-27), 1.663 (3H, s, Me-26), 3.40 (1H, dd, J = 11.8, 4.5, H-3α), 3.93 (1H, td, J = 10.5, 10.5, 5.0, H-12α), 4.11 (1H, td, J = 6.2, 6.2, 1.2, H-5′), 4.17 (1H, dd, J = 9.5, 3.5, H-3′), 4.47 (3H, m, H-2′, 2H-6′), 4.58 (1H, d, J = 2.8, H-4′), 4.88 (1H, d, $J_{1',2'}$ = 7.7, H-1′), 5.33 (1H, tt, J = 7.1, 7.1, 1.3, 1.3, H-24).

Condensation of 5 and 2. A mixture of **5** (0.62 g, 1.35 mmol), **2** (1.23 g, 3 mmol), Ag_2O (0.70 g, 3 mmol), and 4-Å molecular sieves (1.0 g) in anhydrous dichloroethane (10 mL) was stirred at room temperature for 4–5 h until **2** disappeared (TLC monitoring) and filtered to remove insoluble silver compounds and molecular sieves. The solvent was distilled at reduced pressure. The solid was dried, worked up three times with hot water to remove galactose derivatives, dried, and chromatographed over a column of silica gel with elution by hexane:acetone (10:1) to afford **5** (0.02 g, 3.2%), **6** (0.35 g, 32.8%), and a mixture of **6** and **7** (0.28 g, 26.2%).

12β-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-20*S*-hydroxydammar-24-en-3-one (6). $C_{44}H_{68}O_{12}$, amorphous, $[\alpha]_D^{20}$ +20.0° (*c* 1.0, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1697 (C=O), 1754 (CH_3C=O), 3474 (OH).

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.908 (3H, s, Me-30), 0.971 (3H, s, Me-19), 1.008 (3H, s, Me-18), 1.055 (3H, s, Me-29), 1.104 (3H, s, Me-28), 1.126 (3H, s, Me-21), 1.654 (3H, s, Me-27), 1.717 (3H, s, Me-26), 1.974 (3H, s, OAc), 2.035 (3H, s, OAc), 2.053 (3H, s, OAc), 2.151 (3H, s, OAc), 3.87 (1H, td, J = 10.6, 10.6, 5.1, H-12α), 3.89 (1H, ddd, J = 7.8, 6.0, 1.2, H-5′), 4.13 (1H, dd, J = 11.2, 8.0, H-6′), 4.22 (1H, dd, J = 11.2, 6.0, H-6′), 4.71 (1H, d, $J_{1',2'}$ = 8.0, H-1′), 5.05 (1H, dd, J = 10.4, 3.4, H-3′), 5.12 (1H, dd, J = 10.4, 8.0, H-2′), 5.22 (1H, tt, J = 7.0, 7.0, 1.4, 1.4, H-24), 5.36 (1H, dd, J = 3.4, 1.2, H-4′).

Reduction of the Mixture of 6 and 7. A suspension of $NaBH_4$ (100 mg) in isopropanol (10 mL) was treated dropwise with a solution of **6** and **7** (280 mg) in isopropanol (5 mL) and stirred at room temperature for 1 h until they disappeared (TLC monitoring). The excess of $NaBH_4$ was decomposed by adding dropwise a dilute solution (1:1) of acetic acid. The reaction mixture was poured into a cylinder with ground ice and extracted with $CHCl_3$. The $CHCl_3$ extract was evaporated. The solid was dried and chromatographed over a column of silica gel with elution by hexane:acetone (10:1) to afford **8** (23 mg), a mixture of **8** and **9** (175 mg), and **9** (12 mg).

3β,20*S*-Dihydroxy-12β-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyloxy)dammar-24-ene (8). $C_{44}H_{70}O_{12}$, amorphous, $[\alpha]_D^{20}$ +6.2° (*c* 1.1, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1754 (CH_3C=O), 3474 (OH), 3634 (OH).

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.792 (3H, s, Me-29), 0.876 (3H, s, Me-19), 0.894 (3H, s, Me-30), 0.966 (3H, s, Me-18), 0.992 (3H, s, Me-28), 1.120 (3H, s, Me-21), 1.651 (3H, s, Me-27), 1.714 (3H, s, Me-26), 1.971 (3H, s, OAc), 2.036 (3H, s, OAc), 2.050 (3H, s, OAc), 2.147 (3H, s, OAc), 3.22 (1H, dd, J = 11.7, 4.5, H-3α), 3.85 (1H, td, J = 10.5, 10.5, 5.0, H-12α), 3.88 (1H, ddd, J = 7.9, 5.9, 1.1, H-5′), 4.13 (1H, dd, J = 11.3, 7.9, H-6′), 4.22 (1H, dd, J = 11.3, 5.9, H-6′),

4.70 (1H, d, $J_{1',2'}$ = 7.9, H-1′), 5.04 (1H, dd, J = 10.4 ,3.5, H-3′), 5.12 (1H, dd, J = 10.4, 7.9, H-2′), 5.21 (1H, tt, J = 7.0, 7.0, 1.5, 1.5, H-24), 5.36 (1H, dd, J = 3.5, 1.1, H-4′).

3β,12β-Dihydroxy-20*S*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyloxy)dammar-24-ene (9). $C_{44}H_{70}O_{12}$, amorphous, $[\alpha]_D^{20}$ +21.0° (*c* 0.9, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1754 (CH_3C=O), 3474 (OH), 3634 (OH).

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.779 (3H, s, Me-29), 0.869 (3H, s, Me-30), 0.879 (3H, s, Me-19), 0.979 (6H, s, Me-18, Me-28), 1.257 (3H, s, Me-21), 1.606 (3H, s, Me-27), 1.674 (3H, s, Me-26), 1.970 (3H, s, OAc), 2.008 (3H, s, OAc), 2.045 (3H, s, OAc), 2.149 (3H, s, OAc), 3.20 (1H, dd, J = 11.4, 4.8, H-3α), 3.55 (1H, td, J = 10.2, 10.2, 5.4, H-12α), 3.87 (1H, t, J = 6.6, 6.6, H-5′), 4.07 (1H, dd, J = 11.4, 6.8, H-6′), 4.14 (1H, dd, J = 11.3, 6.4, H-6′), 4.78 (1H, d, J = 7.7, H-1′), 5.05 (1H, dd, J = 10.4, 3.4, H-3′), 5.07 (1H, m, H-24), 5.11 (1H, dd, J = 10.4, 7.7, H-2′), 5.35 (1H, dd, J = 3.4, 1.0, H-4′).

Acetylation of the Mixture of 8 and 9. The mixture of **8** and **9** (90 mg) was dissolved in anhydrous pyridine (3 mL), treated with Ac_2O (2 mL), held at 90°C for 3 h (TLC monitoring), and poured onto ice. The resulting precipitate was filtered, washed with cold H_2O, dried, and chromatographed over a column of silica gel with elution by hexane:acetone (10:1) to afford **10** (20 mg) and **11** (50 mg).

3β,12β-Diacetoxy-20*S*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyloxy)dammar-24-ene (10). $C_{48}H_{74}O_{14}$, mp 179–181°C (EtOH), $[\alpha]_D^{20}$ +18.7° (*c* 0.44, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1718 (CH_3C=O), 1756 (CH_3C=O).

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.848 (3H, s, Me-29), 0.850 (3H, s, Me-28), 0.877 (3H, s, Me-19), 0.925 (3H, s, Me-30), 0.979 (3H, s, Me-18), 1.172 (3H, s, Me-21), 1.595 (3H, s, Me-27), 1.655 (3H, s, Me-26), 1.968 (3H, s, OAc), 1.982 (3H, s, OAc), 2.031 (3H, s, OAc), 2.036 (3H, s, OAc), 2.057 (3H, s, OAc), 2.159 (3H, s, OAc), 3.85 (1H, ddd, J = 7.0, 6.0, 1.0, H-5′), 4.07 (1H, dd, J = 11.4, 7.0, H-6′), 4.11 (1H, dd, J = 11.4, 6.1, H-6′), 4.48 (1H, dd, J = 11.4, 3.7, H-3α), 4.63 (1H, d, J = 7.8, H-1′), 4.83 (1H, td, J = 10.7, 10.7, 5.1, H-12α), 5.014 (1H, dd, J = 10.4, 3.5, H-3′), 5.015 (1H, m, H-24), 5.12 (1H, dd, J = 10.4, 7.8, H-2′), 5.35 (1H, dd, J = 3.5, 1.0, H-4′).

3β-Acetoxy-20*S*-hydroxy-12β-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyloxy)dammar-24-ene (11). $C_{48}H_{72}O_{13}$, amorphous, $[\alpha]_D^{20}$ +20.1° (*c* 0.66, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1720 (CH_3C=O), 1756 (CH_3C=O), 3474 (OH).

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.866 (3H, s, Me-29), 0.869 (3H, s, Me-28), 0.890 (3H, s, Me-30), 0.900 (3H, s, Me-19), 0.967 (3H, s, Me-18), 1.120 (3H, s, Me-21), 1.651 (3H, s, Me-27), 1.713 (3H, s, Me-26), 1.970 (3H, s, OAc), 2.040 (3H, s, OAc), 2.047 (3H, s, OAc), 2.055 (3H, s, OAc), 2.150 (3H, s, OAc), 3.86 (1H, td, J = 10.5, 10.5, 5.0, H-12α), 3.89 (1H, ddd, J = 7.6, 6.1, 1.2, H-5′), 3.95 (1H, s, OH-20), 4.15 (1H, dd, J = 11.3, 7.7, H-6′), 4.21 (1H, dd, J = 11.3, 6.0, H-6′), 4.49 (1H, dd, J = 11.8, 4.7, H-3α), 4.70 (1H, d, J = 7.9, H-1′), 5.04 (1H, dd, J = 10.3, 3.5, H-3′), 5.11 (1H, dd, J = 10.3, 7.9, H-2′), 5.21 (1H, tt, J = 7.0, 7.0, 1.5, 1.5, H-24), 5.35 (1H, dd, J = 3.4, 1.1, H-4′).

12-*O*-β-D-Galactopyranosyl-3β,12β,20*S*-trihydroxydammar-24-ene (12) was prepared by deacetylation of **8** by NaOMe in MeOH (0.1 N) or deacetylation of **11** using KOH solution (10%) in MeOH at 20°C. $C_{36}H_{62}O_8$, amorphous, $[\alpha]_D^{20}$ +1.3° (*c* 0.75, C_5H_5N).

PMR spectrum (700 MHz, C_5D_5N, δ, ppm, J/Hz): 0.789 (3H, s, Me-19), 0.838 (3H, s, Me-18), 0.843 (3H, s, Me-30), 1.025 (3H, s, Me-29), 1.227 (3H, s, Me-28), 1.351 (3H, s, Me-21), 1.633 (3H, s, Me-27), 1.639 (3H, s, Me-26), 3.43 (1H, dd, J = 11.5, 4.9, H-3α), 4.13 (1H, td, J = 6.1, 6.1, 1.0, H-5′), 4.24 (1H, dd, J = 9.3, 3.4, H-3′), 4.32 (1H, m, H-12α), 4.42 (2H, d, J = 6.2, 2H-6′), 4.50 (1H, dd, J = 9.3, 7.7, H-2′), 4.55 (1H, dd, J = 3.4, 1.0, H-4′), 5.18 (1H, d, $J_{1',2'}$ = 7.7, H-1′), 5.33 (1H, tt, J = 7.2, 7.2, 1.3, 1.3, H-24).

20-*O*-β-D-Galactopyranosyl-3β,12β,20*S*-trihydroxydammar-24-ene (13) was prepared by deacetylation of **9** by NaOMe in MeOH (0.1 N) or deacetylation of **10** using KOH solution (10%) in MeOH at 20°C. $C_{36}H_{62}O_8$, amorphous, $[\alpha]_D^{20}$ +29.8° (*c* 0.8, C_5H_5N).

PMR spectrum (700 MHz, C_5D_5N, δ, ppm, J/Hz): 0.899 (3H, s, Me-19), 0.967 (3H, s, Me-30), 0.997 (3H, s, Me-18), 1.044 (3H, s, Me-29), 1.234 (3H, s, Me-28), 1.593 (3H, s, Me-27), 1.614 (3H, s, Me-26), 1.637 (3H, s, Me-21), 3.42 (1H, dd, J = 11.1, 4.6, H-3α), 4.06 (1H, td, J = 6.2, 6.2, 0.9, H-5′), 4.18 (1H, dd, J = 9.2, 3.4, H-3′), 4.18 (1H, m, H-12α), 4.37 (1H, dd, J = 6.2, 10.9, H-6′), 4.43 (1H, dd, J = 9.2, 7.8, H-2′), 4.44 (1H, dd, J = 6.2, 10.9, H-6′), 4.57 (1H, d, J = 3.3, H-4′), 5.10 (1H, d, $J_{1',2'}$ = 7.7, H-1′), 5.27 (1H, t, J = 7.2, 7.2, H-24).

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