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SYNTHESIS OF DIGLYCOSIDES OF 3*β*,20*S*-DIHYDROXYDAMMAR-24-EN-12-ONE

L. N. Atopkina* and V. A. Denisenko

UDC 547.917+547.918+547.597

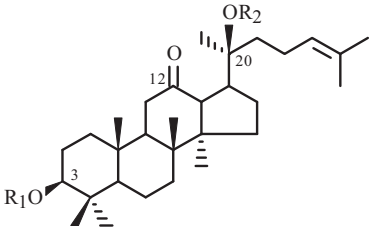
*The 3-*O*-β-D-galactopyranosyl-20-O-β-D-glucopyranoside and 3-*O*-β-D-glucopyranosyl-20-*O*-β-D-galactopyranoside of 3β,20*S*-dihydroxydammar-24-en-12-one, which are structural analogs of chikusetsusaponin-LT$_8$ (**1**), a minor glycoside from* Panax japonicus*, were synthesized for the first time.*

Keywords: dammarane-type triterpenoids, 20*S*-hydroxydammar-24-en-3,12-dione, glycosylation, chikusetsusaponin-LT$_8$, 3,20-di-*O*-*β*-D-glucopyranoside of 3*β*-20*S*-dihydroxydammar-24-en-12-one, 3-*O*-*β*-D-galactopyranosyl-20-*O*-*β*-D-glucopyranoside of 3*β*,20*S*-dihydroxydammar-24-en-12-one, 3-*O*-*β*-D-glucopyranosyl-20-*O*-*β*-D-galactopyranoside of 3*β*,20*S*-dihydroxydammar-24-en-12-one.

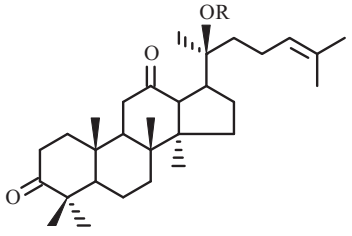
One of the dammarane glycosides that is rarely encountered in nature is chikusetsusaponin-LT$_8$ (**1**). Its aglycon is the 12-keto-derivative of 20*S*-protopanaxadiol (3*β*,20*S*-dihydroxydammar-24-en-12-one) (**2**), which was first isolated from leaves of *Panax japonicus* C. A. Meyer [1]. We proposed a preparative synthesis of this compound that was based on chemical transformation of betulafolientriol (3*α*,12*β*,20*S*-trihydroxydammar-24-ene), a component of birch leaf extract, into the 12-keto-derivative **2** and its glycosylation [2]. Diglucoside **1** is more toxic against tumor cells [3] than the 3,20-di-*O*-*β*-D-glucopyranoside of 20*S*-protopanaxadiol (ginsenoside-F$_2$), in which a hydroxyl is located on C-12. However, **1** does not exhibit hemolytic activity [4].

The method proposed by us for preparing **1** [2] does not allow diglycosylated derivatives of 3*β*,20*S*-dihydroxydammar-24-ene-12-one with different carbohydrate units on C-3 and C-20 to be synthesized. Therefore, we considered it advisable to develop a synthesis of 3*β*,20*S*-dihydroxydammar-24-en-12-one derivatives containing not only the same but also different carbohydrate units on C-3 and C-20, e.g., glucose and galactose.

Regio- and stereoselective glycosylation of the tertiary hydroxyl on C-20 was performed by condensation of 20*S*-hydroxydammar-24-en-3,12-dione (**5**) [5] with 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranosylbromide (**3**) under Koenigs–Knorr reaction conditions [5]. The product was the diketone (**6**) 20-*O*-*β*-D-glucopyranoside tetraacetate, which was reduced by $NaBH_4$ in *i*-PrOH. This led to selective reduction of only the C-3 carbonyl and formed 3*β*,20*S*-dihydroxydammar-24-en-12-one 20-*O*-*β*-D-glucopyranoside (**7**) (83.6% yield) [5].



1, 2, 7 - 9, 11 - 14



5, 6, 10

1: $R_1 = R_2 =$ *β*-D-Glc; **2:** $R_1 = R_2 =$ H; **5:** R = H; **6**: R = *β*-D-GlcAc_4; **7:** $R_1 =$ H, $R_2 =$ *β*-D-GlcAc_4
8: $R_1 =$ *β*-D-GalAc_4, $R_2 =$ *β*-D-GlcAc_4; **9:** $R_1 = R_2 =$ *β*-D-GlcAc_4; **10:** R = *β*-D-GalAc_4
11: R_1 = H, $R_2 =$ *β*-D-GalAc_4; **12:** $R_1 =$ *β*-D-GlcAc_4, $R_2 =$ *β*-D-GalAc_4
13: $R_1 =$ *β*-D-Gal, $R_2 =$ *β*-D-Glc; **14**: $R_1 =$ *β*-D-Glc, $R_2 =$ *β*-D-Gal

Pacific Institute of Bioorganic Chemistry, Far-East Branch, Russian Academy of Sciences, 690022, Vladivostok, Prosp. 100-Letiya Vladivostoka, 159, fax: 7-(4232) 31 40 50, e-mail: atopkina@mail.ru. Translated from *Khimiya Prirodnykh Soedinenii*, No. 1, January–February, 2012, pp. 63–67. Original article submitted June 9, 2011.

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TABLE 1. ^{13}C Chemical Shifts of **1** and **8**–**14** (δ, ppm, 0 = TMS)

C atom	**1**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
1	38.85	38.60	38.59	39.27	38.63	38.55	38.90	38.84
2	26.60	25.88	25.73	33.79	27.18	25.72	26.67	26.60
3	88.51	90.32	90.21	216.88	78.61	90.24	88.47	88.50
4	39.65	39.08	39.06	47.36	38.93	39.05	39.67	39.65
5	56.21	56.12	56.08	55.18	55.79	56.03	56.24	56.19
6	18.55	18.27	18.25	19.78	18.37	18.23	18.56	18.53
7	34.80	34.44	34.43	33.79	34.46	34.42	34.82	34.76
8	40.91	40.55	40.54	40.50	40.56	40.54	40.92	40.88
9	54.83	54.59	54.59	53.92	54.61	54.60	54.86	54.82
10	37.50	37.39	37.37	37.31	37.65	37.36	37.20	37.48
11	40.11	39.79	39.78	39.90	39.78	39.79	40.12	40.09
12	211.13	211.83	211.86	211.22	211.82	212.01	211.13	211.18
13	56.46	55.55	55.54	55.64	55.56	55.52	56.47	56.46
14	56.23	56.23	56.22	56.28	56.26	56.28	56.26	56.20
15	32.31	31.69	31.67	31.71	31.69	31.66	32.32	32.29
16	24.60	23.54	23.53	23.76	23.50	23.47	24.60	24.62
17	42.65	41.04	41.02	41.16	41.12	41.05	42.67	42.69
18	15.95	15.59	15.58	15.28	15.61	15.59	15.95	15.91
19	16.26	16.07	16.06	15.81	16.10	16.07	16.28	16.25
20	81.37	82.18	82.17	82.09	82.11	82.06	81.38	81.26
21	22.46	23.33	23.31	23.49	23.35	23.37	22.46	22.41
22	40.61	38.83	38.82	38.87	38.89	38.89	40.62	40.61
23	23.96	23.74	23.73	23.49	23.72	23.72	23.96	23.95
24	125.81	124.30	124.29	124.28	124.31	124.28	125.82	125.85
25	130.84	131.63	131.62	131.67	131.58	131.64	130.84	130.84
26	25.76	25.66	25.65	25.65	25.62	25.68	25.76	25.77
27	17.77	17.67	17.66	17.67	17.64	17.68	17.77	17.78
28	28.06	27.65	27.62	26.71	27.98	27.60	28.07	28.05
29	16.65	16.10	16.06	21.00	15.27	16.07	16.61	16.64
30	17.02	16.75	16.73	16.78	16.81	16.77	17.03	17.00
$\underline{C}H_3CO$		20.82	20.81	20.99	20.93	20.99		
		20.82	20.75	20.74	20.72	20.79		
		20.68	20.67	20.54	20.52	20.79		
		20.68	20.61	20.50	20.48	20.71		
		20.61	20.61			20.64		
		20.61	20.59			20.61		
		20.58	20.58			20.58		
		20.58	20.58			20.54		
$CH_3\underline{C}O$		170.59	170.59	170.42	170.41	170.63		
		170.36	170.59	170.34	170.34	170.49		
		170.31	170.32	169.98	169.98	170.41		
		170.20	170.20	169.19	169.12	170.35		
		170.16	169.54			170.06		
		169.53	169.39			169.42		
		169.27	169.11			169.15		
		169.00	169.00			169.15		

Compound **7**, which had a free hydroxyl on C-3, was a key synthon for 3*β*,20*S*-dihydroxydammar-24-en-12-one diglycosides because it could act as starting material for subsequent condensation with any other glycosyl donor, in particular, 2,3,4,6-tetra-*O*-acetyl-*α*-D-galactopyranosylbromide (**4**). The reaction of **7** and **4** in the presence of Ag_2O in dichloroethane formed the diglycoside (**8**) (89.7% yield) in which a galactose unit was located on C-3; a glucose, on C-20. The reaction of **7** with glycosyl donor **3** under the same conditions gave accordingly the acetylated 3*β*,20*S*-dihydroxydammar-24-en-12-one 3,20-di-*O*-*β*-D-glucopyranoside (**9**) (67% yield), which was identical to the diglucoside synthesized by us earlier [2]. Condensation of diketone **5** with *α*-acetobromogalactose (**4**) and subsequent treatment of the reaction product **10** with $NaBH_4$ in *i*-PrOH afforded 3*β*,20*S*-dihydroxydammar-24-en-12-one 20-*O*-*β*-D-galactopyranoside tetraacetate (**11**). Reaction of **11** and **3** gave diglycoside **12**, with a glucose on C-3; a galactose, C-20.

TABLE 2. ^{13}C Chemical Shifts of Sugar Components of **1** and **8**–**14** (δ, ppm, 0 = TMS)

Compound	Carbohydrate unit	C atom					
		1′ 1″	2′ 2″	3′ 3″	4′ 4″	5′ 5″	6′ 6″
1	3-Glc	106.98	75.80	78.78	72.00	78.43	63.16
	20-Glc	98.51	75.74	79.25	71.95	77.99	63.05
8	3-$GalAc_4$	103.59	69.27	70.98	67.15	70.54	61.42
	20-$GlcAc_4$	94.61	71.96	73.23	68.99	71.57	62.67
9	3-$GlcAc_4$	102.97	71.66	72.85	68.76	71.61	62.26
	20-$GlcAc_4$	94.60	71.94	73.21	68.97	71.56	62.66
10	20-$GalAc_4$	95.15	69.60	71.25	67.31	70.70	61.87
11	20-$GalAc_4$	95.13	69.54	71.25	67.30	70.66	61.87
12	3-$GlcAc_4$	102.98	71.58	72.80	68.69	71.60	62.22
	20-$GalAc_4$	95.11	69.46	71.21	67.24	70.63	61.87
13	3-Gal	107.57	73.19	75.49	70.37	76.95	62.60
	20-Glc	98.52	75.74	79.25	72.02	77.97	63.07
14	3-Glc	106.99	75.81	78.78	71.94	78.43	63.16
	20-Gal	99.03	73.22	76.01	70.19	76.58	62.21

Glc = -*β*-D-glucopyranosyl; Gal = -*β*-D-galactopyranosyl.

Deacetylation of **8**, **9**, and **12** was carried out using sodium methoxide solution (0.1 N) and formed the corresponding free diglycosides **1**, **13**, and **14**.

The structures of all compounds were established by spectral methods. Doublets for the sugar anomeric protons of acetylated glycosides **6–12** appeared in PMR spectra in $CDCl_3$ at δ 4.49–4.60 ppm ($J_{1',2'}$ = 7.8–8.1 Hz). Doublets for the anomeric protons of glucose and galactose for free glycosides **1**, **13**, and **14** were observed in PMR spectra in Py-d_5 at δ 4.95–5.12 ppm ($J_{1',2'}$ = 7.6–7.7 Hz). The chemical shifts and spin–spin coupling constants of the glucose and galactose anomeric protons were indicative of the *trans*-configuration of the glycoside bond in all these glycosides. The sites of attachment of the carbohydrates were confirmed by comparing ^{13}C NMR spectra of **1** and **5–14** (Tables 1 and 2).

The synthetic pathway to 3*β*,20*S*-dihydroxydammar-24-en-12-one diglycosides proposed by us is simpler and shorter than that published earlier [2]. It allows diglycosylated derivatives containing the same or different carbohydrate units on C-3 and C-20 to be prepared.

EXPERIMENTAL

PMR and ^{13}C NMR spectra of **5-12** (in $CDCl_3$) and **1**, **13**, and **14** (in Py-d_5) were recorded on Avance-500 (500 MHz for ^1H and 125 MHz for ^{13}C) and Avance-700 (700 MHz for ^1H and 175 MHz for ^{13}C) spectrometers (Bruker). Chemical shifts are given on the δ-scale vs. TMS. Multiplicities of ^{13}C resonances were established using DEPT-135 experiments by the standard method. Homonuclear 2D ^1H–^1H COSY-45 correlation spectra and heteronuclear 2D HSQC and HMBC correlation spectra were also obtained using standard methods. HMBC experiments were optimized for $^nJ_{HC} \cong 5$ Hz. IR spectra were recorded in $CDCl_3$ solutions on a Vector 22 spectrophotometer (Bruker). Optical rotation was measured on a 343 Polarimeter (Perkin–Elmer) in a 10-cm cuvette at 20°C. Melting points were taken on a Boetius stage. Column chromatography was performed over KSK silica gel (120–150 mesh) using solvent systems hexane:acetone (15:1→4:1). The purity of compounds was monitored using TLC on Sorbfil plates (Russia) and solvent systems hexane:acetone (2:1), benzene:$CHCl_3$:MeOH (6:4:1 and 2:2:1). Detection used H_2SO_4 (10%) in EtOH with heating at 100–200°C. Elemental analyses of all newly prepared compounds agreed with those calculated.

2,3,4,6-Tetra-*O*-acetyl-*α*-D-glucopyranosylbromide (**3**) was prepared by the literature method [6], mp 88–89°C (Et_2O) (lit. [6] mp 88–89°C).

2,3,4,6-Tetra-*O*-acetyl-*α*-D-galactopyranosylbromide (**4**) was prepared by the literature method [6], mp 84–85°C (Et_2O) (lit. [7] mp 84–85°C).

20*S*-Hydroxydammar-24-en-3,12-dione (**5**) was prepared by oxidation of betulafolientriol according to the previously reported method [5], mp 151–152°C (MeOH) (lit. [5] mp 151–152°C).

20*S*-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glycopyranosyloxy)dammar-24-en-3,12-dione (**6**) was prepared by condensation of diketone **5** with α-acetobromoglucose (**3**) in the presence of Ag_2O and 4-Å molecular sieves according to the previously reported method [5], mp 200–202°C (EtOH) (lit. [5] mp 200–202°C).

3β-Hydroxy-20*S*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)dammar-24-en-12-one (**7**) was prepared by treatment of glycoside **6** with $NaBH_4$ in *i*-PrOH according to the previously reported method [5], mp 199–200.5°C (MeOH) (lit. [5] mp 199–200.5°C).

Condensation of 7 with 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosylbromide (4) in the Presence of Ag_2O. A mixture of **7** (0.11 g, 0.138 mmol), Ag_2O (0.12 g, 0.5 mmol), and α-acetobromogalactose (**4**) in anhydrous dichloroethane (5 mL) was stirred at room temperature for 2 h until **4** disappeared (TLC monitoring), diluted with $CHCl_3$, and filtered to remove insoluble silver salts. The solvent was distilled at reduced pressure. The solid was washed with hot water, dried, and crystallized from EtOH to afford **8** (0.14 g, 89.7%).

3β-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-20*S*-(2″,3″,4″,6″-tetra-*O*-acetyl-β-D-glucopyranosyloxy)dammar-24-en-12-one (8). $C_{58}H_{86}O_{21}$, mp 204–204.5°C (EtOH), $[\alpha]_D^{20}$ +11.2° (*c* 0.4, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1704 (C=O), 1755 (CH_3C=O).

PMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.718 (3H, s, Me-30), 0.777 (3H, s, Me-29), 0.916 (3H, s, Me-28), 0.936 (3H, s, Me-19), 1.028 (3H, s, Me-21), 1.192 (3H, s, Me-18), 1.608 (3H, s, Me-27), 1.656 (3H, s, Me-26), 1.978 (3H, s, OAc), 1.985 (3H, s, OAc), 1.986 (3H, s, OAc), 2.025 (3H, s, OAc), 2.047 (6H, s, 2OAc), 2.053 (3H, s, OAc), 2.144 (3H, s, OAc), 2.454 (1H, td, J = 10.1, 10.1, 5.1, H-17), 3.016 (1H, d, J = 9.5, H-13), 3.067 (1H, dd, J = 11.6, 4.6, H-3α), 3.660 (1H, ddd, J = 10.1, 6.7, 2.3, glucose H-5″), 3.885 (1H, t, J = 6.8, 6.8, galactose H-5′), 4.080 (1H, dd, J = 12.0, 3.0, glucose H-6″^{a}), 4.089 (1H, dd, J = 11.2, 6.8, galactose H-6′^{a}), 4.155 (1H, dd, J = 12.0, 6.7, glucose H-6″^{b}), 4.182 (1H, dd, J = 11.2, 6.9, galactose H-6′^{b}), 4.493 (1H, d, $J_{1',2'}$ = 8.1, galactose H-1′), 4.603 (1H, d, $J_{1'',2''}$ = 7.8, glucose H-1″), 4.935 (1H, dd, J = 9.5, 7.9, glucose H-2″), 4.983 (1H, t, J = 9.8, 9.8, glucose H-4″), 5.017 (1H, dd, J = 10.4, 3.4, galactose H-3′), 5.044 (1H, t, J = 6.8, 6.8, H-24), 5.183 (1H, t, J = 9.4, 9.4, glucose H-3″), 5.252 (1H, dd, J = 10.5, 8.1, galactose H-2′), 5.371 (1H, d, J = 3.5, galactose H-4′).

3-*O*-β-D-Galactopyranosyl-20-*O*-β-D-glucopyranoside of 3β,20*S*-dihydroxydammar-24-en-12-one (13) was prepared by deacetylation of **8** using NaOMe in MeOH (0.1 N) at 20°C. $C_{42}H_{70}O_{13}\cdot 2H_2O$, amorph., $[\alpha]_D^{20}$ +7.0° (*c* 0.9, C_5H_5N).

PMR spectrum (700 MHz, C_5D_5N, δ, ppm, J/Hz): 0.818 (3H, s, Me-19), 0.930 (3H, s, Me-30), 0.962 (3H, s, Me-29), 1.294 (3H, s, Me-18), 1.297 (3H, s, Me-28), 1.573 (3H, s, Me-21), 1.623 (3H, s, Me-26), 1.643 (3H, s, Me-27), 2.948 (1H, td, J = 9.8, 9.8, 4.6, H-17), 3.349 (1H, dd, J = 11.8, 4.3, H-3α), 3.607 (1H, d, J = 9.4, H-13), 3.901 (1H, ddd, J = 9.1, 5.3, 2.7, glucose H-5″), 3.996 (1H, t, J = 8.0, 8.0, glucose H-2″), 4.126 (1H, t, J = 6.2, 6.2, galactose H-5′), 4.173 (1H, dd, J = 9.5, 3.4, galactose H-3′), 4.204 (1H, t, J = 9.0, 9.0, glucose H-3″), 4.230 (1H, t, J = 8.9, 8.9, glucose H-4″), 4.342 (1H, m, glucose H-6″^{a}), 4.454 (1H, t, J = 9.0, 9.0, galactose H-2′), 4.495 (3H, m, glucose H-6″^{b}, galactose H-6′^{a} and H-6′^{b}), 4.587 (1H, d, J = 3.2, galactose H-4′), 4.867 (1H, d, $J_{1',2'}$ = 7.7, galactose H-1′), 5.099 (1H, d, $J_{1'',2''}$ = 7.6, glucose H-1″), 5.220 (1H, tt, J = 7.0, 7.0, 1.3, 1.3, H-24).

Condensation of 7 with 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosylbromide (3) in the Presence of Ag_2O and 4-Å Molecular Sieves. A mixture of **7** (0.21 g, 0.27 mmol), Ag_2O (0.23 g, 1.0 mmol), 4-Å molecular sieves (0.5 g), and α-acetobromoglucose (**3**, 0.41 g, 1.0 mmol) in anhydrous dichloroethane (10 mL) was stirred at room temperature for 2 h until **3** disappeared (TLC monitoring), diluted with $CHCl_3$, and filtered to remove insoluble silver salts. The solvent was distilled at reduced pressure. The solid was washed with hot water, dried, and chromatographed over a column of SiO_2 with elution by hexane:acetone (6:1→4:1) to afford **7** (0.03 g, 14.3%) and **9** (0.20 g, 67.1%).

3β,20*S*-Di-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)dammar-24-en-12-one (9), mp 232–234°C (MeOH), $[\alpha]_D^{20}$ +11.0° (*c* 1.0, $CHCl_3$) (lit. [2] mp 232–234°C).

PMR spectrum (700 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.715 (3H, s, Me-30), 0.759 (3H, s, Me-29), 0.912 (3H, s, Me-28), 0.934 (3H, s, Me-19), 1.027 (3H, s, Me-21), 1.192 (3H, s, Me-18), 1.608 (3H, d, J = 1.0, Me-27), 1.656 (3H, d, J = 1.0, Me-26), 1.975 (3H, s, OAc), 1.983 (3H, s, OAc), 2.001 (3H, s, OAc), 2.020 (6H, s, 2OAc), 2.029 (3H, s, OAc), 2.049 (3H, s, OAc), 2.073 (3H, s, OAc), 2.454 (1H, td, J = 10.0, 10.0, 5.4, H-17), 3.014 (1H, d, J = 9.6, H-13), 3.059 (1H, dd, J = 11.9, 4.6, H-3α), 3.659 (1H, ddd, J = 10.0, 6.9, 2.6, glucose H-5″ on C-20), 3.674 (1H, ddd, J = 10.0, 5.5, 2.6, glucose H-5′ on C-3), 4.082 (1H, dd, J = 12.0, 2.5, glucose H-6″^{a} on C-20), 4.108 (1H, dd, J = 12.1, 2.6, glucose H-6′^{a} on C-3), 4.151 (1H, dd, J = 12.0, 6.8, glucose H-6″^{b} on C-20), 4.236 (1H, dd, J = 12.1, 5.5, glucose H-6′^{b} on C-3), 4.524 (1H, d, $J_{1',2'}$ = 8.0, glucose H-1′ on C-3), 4.604 (1H, d, $J_{1'',2''}$ = 7.9, glucose H-1″ on C-20), 4.931 (1H, dd, J = 9.6, 7.8, glucose H-2″ on C-20), 4.980 (1H, t, J = 9.7, 9.7,

glucose H-4″ on C-20), 5.021 (1H, dd, J = 9.7, 8.1, glucose H-2′ on C-3), 5.036 (1H, t, J = 9.7, 9.7, glucose H-4′ on C-3), 5.044 (1H, m, H-24), 5.180 (1H, t, J = 9.4, 9.4, glucose H-3″ on C-20), 5.198 (1H, t, J = 9.5, 9.5, glucose H-3′ on C-3).

3,20-Di-*O*-β-D-glucopyranoside of 3β,20*S*-dihydroxydammar-24-en-12-one (1) was prepared by deacetylation of **9** using NaOMe in MeOH (0.1 N) at 20°C, mp 243–248°C (MeOH) (lit. [2] mp 243–248°C).

PMR spectrum (700 MHz, C_5D_5N, δ, ppm, J/Hz): 0.806 (3H, s, Me-19), 0.924 (3H, s, Me-30), 0.991 (3H, s, Me-29), 1.293 (3H, s, Me-18), 1.304 (3H, s, Me-28), 1.573 (3H, s, Me-21), 1.622 (3H, s, Me-26), 1.642 (3H, s, Me-27), 2.946 (1H, td, J = 9.7, 9.7, 4.6, H-17), 3.349 (1H, dd, J = 11.7, 4.4, H-3α), 3.605 (1H, d, J = 9.4, H-13), 3.900 (1H, ddd, J = 9.0, 5.3, 2.7, glucose H-5″ on C-20), 3.995 (1H, t, J = 8.2, 8.2, glucose H-2″ on C-20), 4.028 (1H, ddd, J = 9.3, 5.5, 2.6, glucose H-5′ on C-3), 4.046 (1H, t, J = 8.2, 8.2, glucose H-2′ on C-3), 4.203 (1H, t, J = 8.9, 8.9, glucose H-3″ on C-20), 4.212 (1H, t, J = 8.9, 8.9, glucose H-4′ on C-3), 4.216 (1H, t, J = 8.9, 8.9, glucose H-4″ on C-20), 4.256 (1H, t, J = 8.9, 8.9, glucose H-3′ on C-3), 4.340 (1H, dd, J = 11.5, 5.3, glucose H-6″^{b} on C-20), 4.432 (1H, dd, J = 11.6, 5.4, glucose H-6′^{b} on C-3), 4.488 (1H, dd, J = 11.5, 2.6, glucose H-6″^{a} on C-20), 4.630 (1H, dd, J = 11.6, 2.2, glucose H-6′^{a} on C-3), 4.949 (1H, d, $J_{1',2'}$ = 7.8, glucose H-1′ on C-3), 5.098 (1H, $J_{1'',2''}$ = 7.8, glucose H-1″ on C-20), 5.219 (1H, tt, J = 7.0, 7.0, 1.4, 1.4, H-24).

Condensation of 5 with 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosylbromide (4) in the Presence of Ag_2O. A mixture of **5** (0.20 g, 0.44 mmol), α-acetobromogalactose (**4**, 0.62 g, 1.5 mmol), and Ag_2O (0.35 g, 1.5 mmol) in dichloroethane (5 mL) was stirred at room temperature for 5 h, treated with more α-acetobromogalactose (0.20 g, 0.5 mmol) and Ag_2O (0.12 g, 0.5 mmol), stirred for 3 h until **4** disappeared (TLC monitoring), and filtered to remove insoluble silver salts. The solvent was distilled at reduced pressure. The dry solid was washed with hot water (3×), dried, and chromatographed over a column of silica gel with elution by hexane:acetone (15:1→6:1) to afford **5** (0.03 g, 15.0%) and **10** (0.24 g, 69.5%).

20*S*-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)dammar-24-en-3,12-dione (10). $C_{44}H_{66}O_{12}$, mp 182–184°C (EtOH), $[\alpha]_D^{20}$ +43.6° (*c* 0.6, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1704 (C=O), 1753 (CH_3C=O).

PMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.747 (3H, s, Me-30), 1.047 (6H, s, Me-19, Me-21), 1.070 (3H, s, Me-29), 1.099 (3H, s, Me-28), 1.280 (3H, s, Me-18), 1.613 (3H, s, Me-27), 1.664 (3H, s, Me-26), 1.958 (3H, s, OAc), 1.988 (3H, s, OAc), 2.022 (3H, s, OAc), 2.173 (3H, s, OAc), 2.159 (1H, dd, J = 12.7, 3.6, H-11α), 2.264 (1H, t, J = 12.9, 12.9, H-11β), 2.476 (3H, m, H-2α, H-2β, H-17), 3.084 (1H, d, J = 9.6, H-13), 3.848 (1H, ddd, J = 7.4, 5.5, 1.2, H-5′), 4.089 (1H, dd, J = 11.3, 5.7, H-6′^{a}), 4.132 (1H, dd, J = 11.5, 7.4, H-6′^{b}), 4.565 (1H, d, $J_{12,22}$ = 7.9, H-1′), 5.004 (1H, dd, J = 10.3, 3.6, H-3′), 5.049 (1H, tt, J = 7.0, 7.0, 1.4, 1.4, H-24), 5.091 (1H, dd, J = 10.3, 7.7, H-2′), 5.356 (1H, dd, J = 3.6, 1.2, H-4′).

Reduction of Galactoside 10. A suspension of $NaBH_4$ (0.15 g) in *i*-PrOH (5 mL) was treated at room temperature with a solution of **10** (0.12 g, 0.15 mmol) in *i*-PrOH (10 mL), stirred for 1 h until starting **10** disappeared (TLC monitoring), treated with dilute HOAc (1:1), and poured into a beaker with ground ice. The resulting precipitate was filtered off, washed with icewater, dried, and crystallized from EtOH to afford **11** (0.08 g, 66.7%).

3β-Hydroxy-20*S*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyloxy)dammar-24-en-12-one (11). $C_{44}H_{68}O_{12}$, mp 197–198°C (EtOH), $[\alpha]_D^{20}$ +25.7° (*c* 0.7, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1701 (C=O), 1752 (CH_3C=O), 3612 (OH).

PMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.735 (3H, s, Me-30), 0.806 (3H, s, Me-29), 0.952 (3H, s, Me-19), 0.989 (3H, s, Me-28), 1.042 (3H, s, Me-21), 1.234 (3H, s, Me-18), 1.611 (3H, s, Me-27), 1.661 (3H, s, Me-26), 1.957 (3H, s, OAc), 1.983 (3H, s, OAc), 2.023 (3H, s, OAc), 2.172 (3H, s, OAc), 2.464 (1H, td, J = 10.2, 10.2, 5.2, H-17), 3.045 (1H, d, J = 9.7, H-13), 3.195 (1H, dd, J = 11.2, 4.7, H-3α), 3.845 (1H, ddd, J = 7.3, 5.7, 1.0, H-5′), 4.088 (1H, dd, J = 11.2, 5.7, H-6′^{a}), 4.127 (1H, dd, J = 11.2, 7.3, H-6′^{b}), 4.565 (1H, d, $J_{1',2'}$ = 7.8, H-1′), 4.999 (1H, dd, J = 10.4, 3.7, H-3′), 5.047 (1H, tt, J = 7.0, 7.0, 1.3, 1.3, H-24), 5.091 (1H, dd, J = 10.4, 7.8, H-2′), 5.352 (1H, dd, J = 3.7, 1.0, H-4′).

Condensation of 11 with 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosylbromide (3) in the Presence of Ag_2O. A mixture of **11** (0.09 g, 0.114 mmol), Ag_2O (0.12 g, 0.5 mmol), and α-acetobromoglucose (**3**, 0.21 g, 0.5 mmol) in anhydrous dichloroethane (5 mL) was stirred at room temperature for 2 h, treated with more Ag_2O (0.12 g, 0.5 mmol) and **3** (0.21 g, 0.5 mmol), stirred for 2 h until **3** disappeared (TLC monitoring), diluted with $CHCl_3$, and filtered to remove insoluble silver salts. The solvent was distilled in vacuo. The solid was washed with hot water and dried to afford **12** (0.10 g, 78.3%).

3β-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-20*S*-(2″,3″,4″,6″-tetra-*O*-acetyl-β-D-galactopyranosyloxy)dammar-24-en-12-one (12). $C_{58}H_{86}O_{21}$, mp 172–174°C (EtOH), $[\alpha]_D^{20}$ +7.2° (*c* 0.3, $CHCl_3$). IR spectrum (ν, cm^{-1}): 1704 (C=O), 1755 (CH_3C=O).

PMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.721 (3H, s, Me-30), 0.763 (3H, s, Me-29), 0.914 (3H, s, Me-28), 0.943 (3H, s, Me-19), 1.036 (3H, s, Me-21), 1.222 (3H, s, Me-18), 1.610 (3H, s, Me-27), 1.661 (3H, s, Me-26), 1.959 (3H, s, OAc), 1.982 (3H, s, OAc), 2.006 (3H, s, OAc), 2.024 (6H, s, 2OAc), 2.033 (3H, s, OAc), 2.078 (3H, s, OAc), 2.175 (3H, s, OAc), 2.456 (1H, td, J = 10.1, 10.1, 5.3, H-17), 3.040 (1H, d, J = 9.3, H-13), 3.065 (1H, dd, J = 11.9, 4.7, H-3α), 3.678 (1H,

ddd, J = 9.9, 5.5, 2.6, glucose H-5′), 3.845 (1H, t, J = 6.6, 6.6, galactose H-5″), 4.082 (1H, dd, J = 11.3, 5.6, galactose H-6″^{a}), 4.106 (1H, dd, J = 12.1, 2.5, glucose H-6′^{a}), 4.131 (1H, dd, J = 11.3, 7.5, galactose H-6″^{b}), 4.241 (1H, dd, J = 12.2, 5.5, glucose H-6′^{b}), 4.527 (1H, d, $J_{1',2'}$ = 8.1, glucose H-1′), 4.559 (1H, d, $J_{1'',2''}$ = 7.8, galactose H-1″), 4.996 (1H, dd, J = 10.3, 3.6, galactose H-3″), 5.029 (1H, dd, J = 9.7, 8.0, glucose H-2′), 5.038 (1H, t, J = 9.7, 9.7, glucose H-4′), 5.047 (1H, m, H-24), 5.092 (1H, dd, J = 10.3, 7.7, galactose H-2″), 5.202 (1H, t, J = 9.5, 9.5, glucose H-3′, 5.354 (1H, d, J = 3.6, galactose H-4″).

3-*O*-β-D-Glucopyranosyl-20-*O*-β-D-galactopyranosyd of 3β,20*S*-dihydroxydammar-24-en-12-one (14) was prepared by deacetylation of **12** using NaOMe in MeOH (0.1 N) at 20°C. $C_{42}H_{70}O_{13}\cdot 2H_2O$, amorph., $[\alpha]_D^{20}$ +22.0° (*c* 0.9, C_5H_5N).

PMR spectrum (700 MHz, C_5D_5N, δ, ppm, J/Hz): 0.802 (3H, s, Me-19), 0.910 (3H, s, Me-30), 0.986 (3H, s, Me-29), 1.243 (3H, s, Me-18), 1.299 (3H, s, Me-28), 1.561 (3H, s, Me-21), 1.631 (3H, s, Me-26), 1.648 (3H, s, Me-27), 2.939 (1H, td, J = 10.0, 10.0, 4.5, H-17), 3.346 (1H, dd, J = 11.8, 4.4, H-3α), 3.572 (1H, d, J = 9.6, H-13), 4.037 (3H, m, glucose H-2′ and H-5′, galactose H-5″), 4.130 (1H, dd, J = 9.4, 3.5, galactose H-3″), 4.213 (1H, t, J = 9.0, 9.0, glucose H-4′), 4.256 (1H, t, J = 8.9, 8.9, glucose H-3′), 4.359 (1H, dd, J = 10.8, 6.1, galactose H-6″^{b}), 4.377 (1H, dd, J = 9.4, 7.5, galactose H-2″), 4.433 (1H, dd, J = 11.7, 5.4, glucose H-6′^{b}), 4.453 (1H, dd, J = 10.8, 6.2, galactose H-6″^{a}), 4.572 (1H, d, J = 3.5, galactose H-4″), 4.630 (1H, dd, J = 11.8, 2.6, glucose H-6′^{a}), 4.947 (1H, d, $J_{1',2'}$ = 7.7, glucose H-1′), 5.000 (1H, d, $J_{1'',2''}$ = 7.6, galactose H-1″), 5.238 (1H, tt, J = 7.0, 7.0, 1.3, 1.3, H-24).

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