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SEMISYNTHETIC ANALOGUES OF GINSENOSIDES, GLYCOSIDES FROM GINSENG

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ABSTRACT

Glycosylation of the dammar-24-ene-3,12β,20(*S*)-triols with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (*A*) in the presence of silver oxide in dichloromethane gives a mixture of the acetylated 3-, 12-, 20-, 3,12-di-, and 3,20-di-*O*-β-D-glucopyranosyl derivatives in a total yield of 83–84.5%. Under similar conditions, the 3-*O*-acetyl derivatives of dammar-24-ene-3,12β,20(*S*)-triols give a mixture of 12- and 20-*O*-β-D-glucopyranosyl derivatives. Condensation of betulafolienetriol [dammar-24-ene-3α,12β,20(*S*)-triol] both with the glycosyl bromide *A* in the presence of mercuric cyanide in nitromethane and with 3,4,6-tri-*O*-acetyl-β-D-glucopyranose 1,2-(*tert*-butyl orthoacetate) in the presence of 2,4,6-trimethylpyridinium perchlorate in chlorobenzene under azeotropic distillation results in dehydration and 20-dehydroxyglucosides are formed.

INTRODUCTION

Glycosides of the dammarane series[1,2] are major components of the extract of ginseng root, the stimulating and adaptogenic properties of which are well known. The biological effects are dependent[3] on the structure of the aglycon and on the type, number, and positions of the carbohydrate residues. The 3-*O*-β-D-glucopyranosyl derivative of 20(*S*)-protopanaxadiol[4], obtained by hydrolysis of ginsenosides R_b, R_c, and R_d, has antitumor activity.

Recent advances in structural studies and the biological activity of the dammarane saponines have been reviewed[3]. Dammarane saponins are classified into two groups, namely, 20(*S*)-protopanaxadiol (**1**) and 20(*S*)-protopanaxatriol[5].

The triterpene of the dammarane series, betulafolienetriol [dammar-24-ene-3α,12β,20(*S*)-triol (**2**)], first isolated[6] from the common birch *Betula alba* and later identified[7] in the leaves of Far-East species of the genus *Betula*, differs from the native sapogenin **1** only in the configuration at C-3.

The scarcity of the natural ginsenosides has prompted a search for routes of synthesis from the relatively accessible betulafolienetriol **2** and its 3-epimer **1**, which is obtainable readily from **2** *via* the 3-keto derivative **3**.

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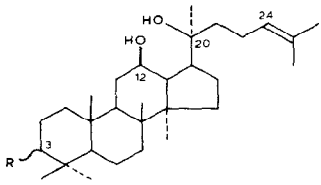
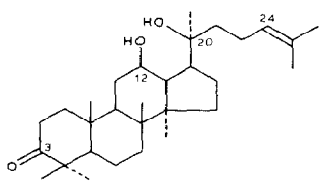


1 R = —OH
2 R = ---OH



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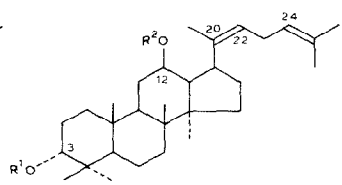


4 R^1 = Ac, R^2 = Glc(Ac)$_4$
5 R^1 = R^2 = Glc(Ac)$_4$
6 R^1 = R^2 = H
7 R^1 = H, R^2 = Glc(Ac)$_4$

Although the synthesis of steroid and triterpene glycosides by the orthoester method[8] gives such by-products as ethers and acetates, it is highly stereoselective for the glycoside.

RESULTS AND DISCUSSION

Condensation of **2** with 3,4,6-tri-*O*-acetyl-D-glucose 1,2-(*tert*-butyl orthoacetate) in chlorobenzene in the presence of 2,4,6-trimethylpyridinium perchlorate (2,4,6-collidinium perchlorate) under azeotropic distillation results in dehydration of the side chain to give the 20-dehydroxyglucosides **4** and **5**. When **2** was heated with a catalytic amount of 2,4,6-collidinium perchlorate under the conditions of chlorobenzene azeotropic distillation for 15 min, a mixture of weakly polar products was obtained, in which dammar-20(22),24-diene-3α,12β-diol (**6**), formed *via* side-chain dehydration of the parent alcohol, preponderated (58.3% yield).

Attempts at glycosylation of **2** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (α-acetobromoglucose) in the presence of mercuric cyanide in nitromethane[9] were unsuccessful, and the 20-dehydroxyglucosides **4**, **5**, and **7** were

TABLE I

CONDITIONS AND RESULTS FOR CONDENSATION OF **1**, **2**, **8**, AND **9** WITH α-ACETOBROMOGLUCOSE IN THE PRESENCE OF SILVER OXIDE

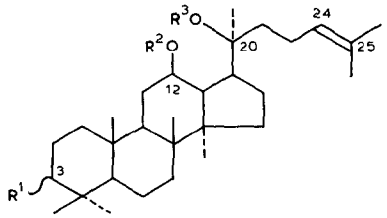
Run	*Initial reactants (mmol)*			*Reaction products (%)*[a]		
	Alcohol	*α-Aceto-bromoglucose*	Ag_2O	*Monoglucosides*	*Diglucosides*	*Recycling (%)*
1	**1**, 5	15	15	48 **15:16:17** 4.5:2.5:1	35 **18:19** 1.5:1	
2	**2**, 5	15	15	50 **10:11:12** 1:4:2	34.5 **13:14** 1.5:1	
3	**8**, 2	3	3	32.6 **22**, 24.4 **23**		20.9
4	**9**, 1	1.5	1.5	27.3 **20**, 26.3 **24**		31.0

[a]Yields as obtained for chromatographically homogeneous mixtures. The glucoside ratio was determined after supplementary chromatography.

obtained from **2** using the orthoester and Helferich methods. In the latter method, mercuric cyanide does not affect **2**, but in the presence of mercuric bromide, produced by interaction of acetobromoglucose and mercuric cyanide, the aglycon was converted into a mixture of weakly polar products.

However, the condensation of **1** and **2** and their acetyl derivatives **8** and **9** with α-acetobromoglucose under Koenigs–Knorr conditions gave results that are summarized in Table I.

On the basis of elemental analysis and ^{1}H- and ^{13}C-n.m.r. data, the products were assigned the following structures: 3- (**10**), 12- (**11**), 20- (**12**), 3,12-di- (**13**), and 3,20-di- (**14**) -*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) derivatives of dammar-24-ene-3α,12β,20(*S*)-triol, and 3- (**15**), 12- (**16**), 20- (**17**), 3,12-di- (**18**), and 3,20-di- (**19**) -*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) derivatives of dammar-24-ene-3β,12β,20(*S*)-triol.



8 R^1 = ---OAc, R^2 = R^3 = H
9 R^1 = —OAc, R^2 = R^3 = H
10 R^1 = ---OGlc(Ac)$_4$, R^2 = R^3 = H
11 R^1 = ---OH, R^2 = Glc(Ac)$_4$, R^3 = H
12 R^1 = ---OH, R^2 = H, R^3 = Glc(Ac)$_4$
13 R^1 = ---OGlc(Ac)$_4$, R^2 = Glc(Ac)$_4$, R^3 = H
14 R^1 = ---OGlc(Ac)$_4$, R^2 = H, R^3 = Glc(Ac)$_4$
15 R^1 = —OGlc(Ac)$_4$, R^2 = R^3 = H
16 R^1 = —OH, R^2 = Glc(Ac)$_4$, R^3 = H
17 R^1 = —OH, R^2 = H, R^3 = Glc(Ac)$_4$
18 R^1 = —OGlc(Ac)$_4$, R^2 = Glc(Ac)$_4$, R^3 = H
19 R^1 = —OGlc(Ac)$_4$, R^2 = H, R^3 = Glc(Ac)$_4$
20 R^1 = —OAc, R^2 = Glc(Ac)$_4$, R^3 = H
21 R^1 = —OAc, R^2 = Ac, R^3 = Glc(Ac)$_4$
22 R^1 = ---OAc, R^2 = Glc(Ac)$_4$, R^3 = H
23 R^1 = ---OAc, R^2 = H, R^3 = Glc(Ac)$_4$
24 R^1 = —OAc, R^2 = H, R^3 = Glc(Ac)$_4$
25 R^1 = ---OAc, R^2 = Ac, R^3 = H
26 R^1 = —OAc, R^2 = Ac, R^3 = H
27 R^1 = ---OAc, R^2 = Ac R^3 = Glc(Ac)$_4$
28 R^1 = ---OGlc, R^2 = R^3 = H
29 R^1 = ---OH, R^2 = Glc, R^3 = H
30 R^1 = ---OH, R^2 = H, R^3 = Glc
31 R^1 = ---OGlc, R^2 = Glc, R^3 = H
32 R^1 = ---OGlc, R^2 = H, R^3 = Glc
33 R^1 = —OGlc, R^2 = R^3 = H
34 R^1 = —OH, R^2 = Glc, R^3 = H
35 R^1 = —OH, R^2 = H, R^3 = Glc
36 R^1 = —OGlc, R^2 = Glc, R^3 = H
37 R^1 = —OGlc, R^2 = H, R^3 = Glc

The mixture of **16** and **17** was amenable to fractionation after acetylation (→ **20** and **21**, respectively). The hexa-acetate **21** was identical (physical constants and spectra) with the hexa-acetate of the 20-β-D-glucoside of 20(*S*)-protopanaxadiol (compound K), obtained[9] by enzymic hydrolysis of ginsenosides R_{b1}, R_{b2}, and R_c, and **19** is ginsenoside F_2 octa-acetate isolated[10] from the leaves of *Panax ginseng*.

TABLE II

^{13}C CHEMICAL SHIFT DATA[a]

Atom	**2**	**10**	**11**	**12**	**13**	**14**
C-3	76.0	82.0	75.6	76.3	82.1	82.4
C-12	70.8	71.0	78.2	70.2	78.4	70.3
C-20	73.8	74.8	72.7	85.2	72.9	85.2
Atom	**1**	**15**	**16**	**17**	**18**	**19**
C-3	79.0	90.6	78.8	79.0	90.2	90.8
C-12	70.9	70.9	78.4	70.1	78.2	70.1
C-20	74.2	74.1	72.8	85.1	73.0	85.1

Atom	**8**	**9**	**26**	**20**	**21**	**22**	**23**	**24**
C-3	78.3	80.8	80.5	80.8	80.8	78.2	78.4	80.9
C-12	70.8	70.6	76.5	77.9	75.3	78.4	70.1	70.1
C-20	73.8	73.7	73.7	72.8	83.4	72.9	85.2	85.2

Atom	**4**	**5**	**6**	**7**
C-3	77.9	82.1	76.0	76.0
C-12	78.1	78.4	77.7	73.4
C-20	137.4	137.6	137.6	140.2

[a] δ scale, referenced to internal Me_4Si

The doublets at δ 4.50–4.85 ($J_{1',2'}$ 7.8–8.0 Hz) for the anomeric protons of the sugar components of **10–19** are indicative of β linkages. The locations of the carbohydrate moieties were determined by comparing the ^{13}C-n.m.r. spectra of the parent triols **1** and **2** with those of the derived glucosides **10–19** (see Table II).

The non-stereoselective location of glucosylation under Koenigs–Knorr conditions results in the formation of almost all of the possible products.

Condensation of the 3-acetates **8** and **9** with α-acetobromoglucose under the above conditions (Table I, runs 3 and 4) yielded mixtures of the corresponding 12- and 20-*O*-β-D-glucopyranosyl derivatives (**20, 22–24**). Attempted glucosylation of the diacetates **25** and **26** was unsuccessful.

EXPERIMENTAL

I.r. spectra were recorded with a Specord 75 spectrophotometer on solutions in chloroform. N.m.r. spectra were recorded with a Bruker WM-250 spectrometer at 250 MHz for ^1H and 62.9 MHz for ^{13}C, for solutions in $CHCl_3$ (internal Me_4Si) at 30°; the accuracies were ±1.5 Hz for ^{13}C and ±0.15 Hz for ^1H. ^{13}C resonances were assigned by the off-resonance spin-decoupling technique, with reference to data in the literature[10]. Optical rotations were measured with a Perkin–Elmer 141 instrument, using a 10-cm cell at 20°. M.p.s. were determined on a Boetius table.

Column chromatography was performed on KSK silica gel (120–150 mesh), using hexane–acetone (15:1 → 5:1) and benzene–methanol (250:1 → 80:1).

Compounds were checked for homogeneity by t.l.c. on silica gel, using benzene–chloroform–methanol (6:4:1), benzene-ethanol (10:1), and hexane–acetone (2:1; 3:2), and detection by charring with sulfuric acid.

Deacetylation of **10–19** with methanolic 0.1M sodium methoxide gave the corresponding products **28–37** in yields of 90–95%.

Dammar-24-ene-3α,12β,20(*S*)-triol (**2**), isolated from an ethereal extract of the leaves *Betula platyphylla,* followed by chromatography on silica gel and crystallization from acetone, had m.p. 195–196°; lit.[6] m.p. 197–198°.

Dammar-24-ene-12β,20(*S*)-diol-3-one (**3**), obtained by oxidation of **2** with chromic anhydride in pyridine, had m.p. 196–198° (from acetone); lit.[6] m.p. 202–203° (from methanol); lit.[11] m.p. 196–199° (from acetone).

Dammar-24-ene-3β,12β,20(*S*)-triol (**1**), obtained by reducing **3** with sodium borohydride in 2-propanol, had m.p. 197–198° (from acetone), $[\alpha]_D^{20}$ +21° (*c* 1, chloroform); lit.[12] 197–200° (from benzene).

3,12-Di-*O*-acetyldammar-24-ene-3α,12β,20(*S*)-triol (**25**), obtained by conventional acetylation of **2** with acetic anhydride in pyridine, was amorphous, $[\alpha]_D^{20}$ −15° (*c* 1, chloroform); ν_{max} 1598, 1720, and 3535 cm^{-1}. ^{1}H-N.m.r. data: δ 0.84 (s, 3 H), 0.88 (s, 3 H), 0.89 (s, 3 H), 0.99 (s, 3 H), 1.02 (s, 3 H), 1.14 (s, 3 H), 1.64 (s, 3 H), 1.72 (s, 3 H), 2.06 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 3.11 (s, 1 H, OH), 4.63 (t, 1 H, 2 *J* 1.8 Hz, H-3*e*), 4.74 (td, 1 H, *J* 10.0, 10.0, and 5.0 Hz, H-12*a*), 5.16 (t, 1 H, *J* 6.3 and 6.3 Hz, H-24).

3-*O*-Acetyldammar-24-ene-3α,12β,20(*S*)-triol (**8**), obtained by partial deacetylation of **25** with methanolic 0.1M sodium methoxide for 4–5 h at room temperature, had m.p. 216–218° (from acetone), $[\alpha]_D^{20}$ −7° (*c* 1, chloroform); lit.[13] m.p. 216–218° (from acetone).

3,12-Di-*O*-acetyldammar-24-ene-3β,12β,20(*S*)-triol (**26**), obtained by conventional acetylation of **1** with acetic anhydride in pyridine, had m.p. 172–173° (from acetone), $[\alpha]_D^{20}$ +10° (*c* 1, chloroform); ν_{max} 1598, 1720, and 3535 cm^{-1}. ^{1}H-N.m.r. data: δ 0.85 (s, 6 H), 0.88 (s, 3 H), 0.95 (s, 3 H), 1.01 (s, 3 H), 1.13 (s, 3 H), 1.64 (s, 3 H), 1.71 (s, 3 H), 2.04 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 3.04 (s, 1 H, OH), 4.48 (m, 1 H, H-3*a*), 4.73 (td, 1 H, *J* 10.0, 10.0, and 5.0 Hz, H-12*a*), 5.16 (t, 1 H, *J* 6.5 and 6.5 Hz, H-24).

Anal. Calc. for $C_{34}H_{56}O_5$: C, 74.95; H, 10.36. Found: C, 74.87; H, 10.38.

3-*O*-Acetyldammar-24-ene-3β,12β,20(*S*)-triol (**9**), obtained by partial deacetylation of **26** as above, had m.p. 175–177° (from acetone), $[\alpha]_D^{20}$ +34° (*c* 1, chloroform); ν_{max} 1600, 1718, 3372, and 3600 cm^{-1}. ^{1}H-N.m.r. data: δ 0.86 (s, 6 H), 0.89 (s, 3 H), 0.91 (s, 3 H), 0.99 (s, 3 H), 1.20 (s, 3 H), 1.64 (s, 3 H), 1.70 (s, 3 H), 2.07 (s, 3 H, OAc), 3.60 (td, 1 H, *J* 10.0, 10.0, and 5.0 Hz, H-12*a*), 4.48 (m, 1 H, H-3*a*), 5.17 (t, 1 H, *J* 6.3 and 6.3 Hz, H-24).

Anal. Calc. for $C_{32}H_{54}O_4$: C, 76.44; H, 10.83. Found: C, 76.36; H, 10.81.

Condensation of **2** *with 3,4,6-tri-*O*-acetyl-*β*-*D*-glucopyranose 1,2-(*tert*-butyl*

orthoacetate) in the presence of 2,4,6-collidinium perchlorate. — A solution of **2** (460 mg) in chlorobenzene (10 mL) was boiled under azeotropic distillation for 10 min and then, in 3 portions every 20 min, 2,4,6-trimethylpyridinium (2,4,6-collidinium) perchlorate (4 mg) and the ortho-ester (1 mmol) were added. The mixture was boiled for a further 20 min and then concentrated to dryness. Column chromatography (hexane–acetone 40:1 →5:1) of the residue gave **4** (180 mg, 22.1%) and **5** (530 mg, 48.1%).

3-*O*-Acetyl-12-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-20(22),24-diene-3α,12β-diol (**4**); ν_{max} 1600, 1625, 1725, and 1750 cm^{-1}. ^{1}H-N.m.r. data: δ 4.42 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′).

Anal. Calc. for $C_{46}H_{70}O_{12}$: C, 67.78; H, 8.66. Found: C, 67.86; H, 8.59.

3,12-Di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-20(22),24-diene-3α,12β-diol (**5**), ν_{max} 1600, 1625, and 1725 cm^{-1}. ^{1}H-N.m.r. data: δ 4.53 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′ at C-3), 4.42 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1′ at C-12).

Anal. Calc. for $C_{58}H_{86}O_{20}$: C, 63.14; H, 7.86. Found: C, 63.38; H, 7.90.

Condensation of **2** *with α-acetobromoglucose in the presence of mercuric cyanide.* — A mixture of **2** (460 mg, 1 mmol), α-acetobromoglucose (820 mg, 2 mmol), and mercuric cyanide (500 mg, 2 mmol) in nitromethane (10 mL) was agitated for 4 h at room temperature, then diluted with chloroform, washed with water, dried, and concentrated. Column chromatography (hexane–acetone, 40:1 → 5:1) of the residue gave **4** (70 mg, 8.6%), **7** (150 mg, 19.4%), and **5** (290 mg, 26.3%).

12-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-20(22),24-diene-3α,12β-diol (**7**); ν_{max} 1610, 1630, 1750, and 3600 cm^{-1}. ^{1}H-N.m.r. data: δ 4.42 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1′).

Anal. Calc. for $C_{44}H_{88}O_{11}$: C, 68.36; H, 8.87. Found: C, 68.65; H, 8.78.

A mixture of **2** (150 mg) and 2,4,6-collidinium perchlorate (2 mg) in chlorobenzene (5 mL) was boiled under azeotropic distillation for 15 min and then concentrated to dryness. Column chromatography (hexane–acetone, 30:1) of the residue gave **6** (84 mg, 58.3%). ^{1}H-N.m.r. data: δ 0.84 (s, 3 H), 0.89 (s, 6 H), 0.94 (s, 3 H), 1.02 (s, 3 H), 1.61 (s, 3 H), 1.66 (s, 6 H), 3.39 (t, 1 H, *J* 3.0 Hz, H-3*e*), 3.74 (m, 1 H, H-12*a*), 5.06 (t, 1 H, *J* 7.2 and 7.2 Hz, H-24).

Anal. Calc. for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38. Found: C, 81.87; H, 11.31.

Condensations in the presence of silver oxide. — A mixture of the alcohol (2.30 g, 5 mmol), silver oxide (1.17 g), α-acetobromoglucose (2.06 g), and dichloromethane (25 mL) was agitated until the α-acetobromoglucose had reacted (t.l.c.) and then the remaining silver oxide (2.34 g) and α-acetobromoglucose (4.11 g) were added in two portions. The reaction was continued until the alcohol was consumed. The solvent was evaporated and the dry residue was subjected to column chromatography. The following compounds were obtained in this way.

3-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3α,12β,-20(*S*)-triol (**10**), m.p. 214–217° (from ethanol), $[\alpha]_D^{20}$ −21° (*c* 1, chloroform); ν_{max} 1594, 1751, 3366, and 3594 cm^{-1}. ^{1}H-N.m.r. data: δ 4.50 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1′).

Anal. Calc. for $C_{44}H_{70}O_{12}$: C, 66.80; H, 8.92. Found: C, 66.31; H, 8.97.

12-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3α,12β,-20(*S*)-triol (**11**) had $[\alpha]_D^{20}$ −23° (*c* 1, chloroform); ν_{max} 1599, 1754, 3474, and 3634 cm^{-1}. ^{1}H-N.m.r. data: δ 4.73 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1′).

Anal. Calc. for $C_{44}H_{70}O_{12}$: C, 66.80; H, 8.92. Found: C, 66.62; H, 8.94.

Acetylation of **11** with acetic anhydride–pyridine gave a product identical with **22** (Table I, run no. 3).

20-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3α,12β,-20(*S*)-triol (**12**) had $[\alpha]_D^{20}$ −19° (*c* 1, chloroform); ν_{max} 1599, 1754, 3474, and 3634 cm^{-1}. ^{1}H-N.m.r. data: δ 4.85 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′).

Anal. Calc. for $C_{44}H_{70}O_{12}$: C, 66.80; H, 8.92. Found: C, 66.58; H, 8.85.

Acetylation of **12** with acetic anhydride in pyridine for 7 h at 90° gave the 3,12-diacetate **27**, m.p. 108–110° (from hexane), $[\alpha]_D^{20}$ −22° (*c* 0.8, chloroform).

Anal. Calc. for $C_{48}H_{74}O_{14}$: C, 65.88; H, 8.52. Found: C, 66.01; H, 8.49.

3,12-Di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3α,12β,20(*S*)-triol (**13**), m.p. 158–160° (from ethanol), $[\alpha]_D^{20}$ −23° (*c* 0.66, chloroform); ν_{max} 1600, 1752, and 3474 cm^{-1}. ^{1}H-N.m.r. data: δ 4.53 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′ at C-3), 4.71 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′ at C-12).

Anal. Calc. for $C_{58}H_{88}O_{21}$: C, 62.12; H, 7.91. Found: C, 62.43; H, 7.69.

3,20-Di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3α,12β,20(*S*)-triol (**14**) had m.p. 169–173° (from hexane), $[\alpha]_D^{20}$ −12° (*c* 1, chloroform); ν_{max} 1600, 1755, and 3470 cm^{-1}. ^{1}H-N.m.r. data: δ 4.49 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′ at C-3), 4.85 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1′ at C-20).

Anal. Calc. for $C_{58}H_{88}O_{21}$: C, 62.12; H, 7.91. Found: C, 62.56; H, 7.98.

3-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3β,12β,-20(*S*)-triol (**15**) had m.p. 212–214° (from ethanol), $[\alpha]_D^{20}$ +12.5° (*c* 1, chloroform); ν_{max} 1595, 1750, 3367, and 3595 cm^{-1}. ^{1}H-N.m.r. data: δ 4.53 (d, 1 H, $J_{1',2'}$ 7.9 Hz, H-1′).

Anal. Calc. for $C_{44}H_{70}O_{12}$: C, 66.80; H, 8.92. Found: C, 66.33; H, 8.92.

Acetylation of the mixture of **16** *and* **17**. — The mixture (280 mg) was acetylated with acetic anhydride (0.7 mL) in pyridine (1.5 mL) for 72 h at room temperature. Column chromatography (hexane–acetone, 10:1) of the product gave **21** (74 mg, 30.1%) and **20** (164 mg, 69.9%).

3,12-Di-*O*-acetyl-20-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3β,12β,20(*S*)-triol (**21**) had m.p. 176–177° (from ethanol), $[\alpha]_D^{20}$ +7.5° (*c* 0.8, chloroform); lit.[14] m.p. 177–178°. The melting point was undepressed on admixture with the authentic sample.

3-*O*-Acetyl-12-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3β,12β,20(*S*)-triol (**20**) had m.p. 137–140° (from ethanol), $[\alpha]_D^{20}$ +20° (*c* 0.75, chloroform); ν_{max} 1600, 1718, 1752, and 3474 cm^{-1}. ^{1}H-N.m.r. data: δ 4.74 (d, 1 H, $J_{1',2'}$ 8.2 Hz, H-1′).

Anal. Calc. for $C_{46}H_{72}O_{13}$: C, 66.32; H, 8.71. Found: C, 66.15; H, 8.69.

3,12-Di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-

3β,12β,20(*S*)-triol (**18**) had m.p. 193–195° (from ethanol), $[\alpha]_D^{20}$ +9° (*c* 1, chloroform); ν_{max} 1600, 1752, and 3474 cm^{-1}. ^{1}H-N.m.r. data: δ 4.50 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′ at C-3), 4.73 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′ at C-12).

Anal. Calc. for $C_{58}H_{88}O_{21}$: C, 62.12; H, 7.91. Found: C, 61.97; H, 7.92.

3,20-Di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3β,12β,20(*S*)-triol (**19**) had m.p. 120–125° (from hexane–acetone), $[\alpha]_D^{20}$ +20° (*c* 0.75, chloroform); ν_{max} 1600, 1755, and 3470 cm^{-1}. ^{1}H-N.m.r. data: δ 4.53 (d, 1 H, $J_{1',2'}$ 7.0 Hz, H-1′ at C-3), 4.85 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′ at C-20).

Anal. Calc. for $C_{58}H_{88}O_{21}$: C, 62.12; H, 7.91. Found: C, 62.46; H, 7.86.

3-*O*-Acetyl-12-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3α,12β,20(*S*)-triol (**22**) had m.p. 188–191° (from ethanol), $[\alpha]_D^{20}$ −19° (*c* 0.9, chloroform); ν_{max} 1597, 1718, 1751, and 3469 cm^{-1}. ^{1}H-N.m.r. data: δ 4.74 (d, 1 H, $J_{1',2'}$ 7.2 Hz, H-1′).

Anal. Calc. for $C_{46}H_{72}O_{13}$: C, 66.32; H, 8.71. Found: C, 66.18; H, 8.75.

3-*O*-Acetyl-20-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3α,12β,20(*S*)-triol (**23**) had m.p. 168–172° (from ethanol), $[\alpha]_D^{20}$ −19° (*c* 1, chloroform); ν_{max} 1597, 1718, 1751, and 3469 cm^{-1}. ^{1}H-N.m.r. data: δ 4.85 (d, 1 H, $J_{1',2'}$ 8.2 Hz, H-1′).

Anal. Calc. for $C_{46}H_{72}O_{13}$: C, 66.32; H, 8.71. Found: C, 66.04; H, 8.75.

3-*O*-Acetyl-20-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)dammar-24-ene-3β,12β,20(*S*)-triol (**24**) had $[\alpha]_D^{20}$ +21.5° (*c* 1, chloroform); ν_{max} 1597, 1718, 1753, and 3472 cm^{-1}. ^{1}H-N.m.r. data: δ 4.87 (d, 1 H, $J_{1',2'}$ 7.0 Hz, H-1′).

Anal. Calc. for $C_{46}H_{72}O_{13}$: C, 66.32; H, 8.71. Found: C, 66.67; H, 8.64.

Deacetylation of **10–15**, **18**, and **19** was performed in methanolic 0.1M sodium methoxide, and **20** and **21** were deacetylated in methanolic 10% KOH.

3-*O*-β-D-Glucopyranosyldammar-24-ene-3α,12β,20(*S*)-triol (**28**) had $[\alpha]_D^{20}$ −17.5° (*c* 0.75, pyridine).

Anal. Calc. for $C_{36}H_{62}O_8 \cdot 0.5\ H_2O$: C, 68.42; H, 10.05. Found: C, 68.23; H, 10.03.

12-*O*-β-D-Glucopyranosyldammar-24-ene-3α,12β,20(*S*)-triol (**29**) had m.p. 160–165° (from methanol), $[\alpha]_D^{20}$ −3.5° (*c* 1, pyridine).

Anal. Calc. for $C_{36}H_{62}O_8 \cdot 0.5\ H_2O$: C, 68.42; H, 10.05. Found: C, 68.11; H, 9.89.

20-*O*-β-D-Glucopyranosyldammar-24-ene-3α,12β,20(*S*)-triol (**30**) had $[\alpha]_D^{20}$ +4° (*c* 1, pyridine).

Anal. Calc. for $C_{36}H_{62}O_8 \cdot H_2O$: C, 67.46; H, 10.06. Found: C, 67.19; H, 9.91.

3,12-Di-*O*-β-D-glucopyranosyldammar-24-ene-3α,12β,20(*S*)-triol (**31**) had m.p. 190–200° (from methanol), $[\alpha]_D^{20}$ −18° (*c* 0.9, pyridine).

Anal. Calc. for $C_{42}H_{72}O_{13} \cdot 3.5\ H_2O$: C, 59.47; H, 9.38. Found: C, 59.55; H, 8.96.

3,20-Di-*O*-β-D-glucopyranosyldammar-24-ene-3α,12β,20(*S*)-triol (**32**) had $[\alpha]_D^{20}$ −12° (*c* 1.25, pyridine).

Anal. Calc. for $C_{42}H_{72}O_{13} \cdot 3\ H_2O$: C, 60.11; H, 9.37. Found: C, 60.23; H, 8.88.

3-*O*-β-D-Glucopyranosyldammar-24-ene-3β,12β,20(*S*)-triol (**33**) had m.p. 220–225° (from methanol), $[\alpha]_D^{20}$ +8° (*c* 1.1, pyridine).

Anal. Calc. for $C_{36}H_{62}O_8 \cdot 1.5\ CH_3OH$: C, 67.12; H, 10.21. Found: C, 67.00; H, 9.93.

12-*O*-β-D-Glucopyranosyldammar-24-ene-3β,12β,20(*S*)-triol (**34**) had $[\alpha]_D^{20}$ −6.5° (*c* 0.75, pyridine).

Anal. Calc. for $C_{36}H_{62}O_8 \cdot H_2O$: C, 67.46; H, 10.06. Found: C, 67.05; H, 9.78.

20-*O*-β-D-Glucopyranosyldammar-24-ene-3β,12β,20(*S*)-triol (**35**) had $[\alpha]_D^{20}$ +31° (*c* 0.5, pyridine).

Anal. Calc. for $C_{36}H_{62}O_8 \cdot 1.5\ H_2O$: C, 66.52; H, 10.09. Found: C, 66.12; H, 9.84.

3,12-Di-*O*-β-D-glucopyranosyldammar-24-ene-3β,12β,20(*S*)-triol (**36**) had $[\alpha]_D^{20}$ −9° (*c* 1.1, pyridine).

Anal. Calc. for $C_{42}H_{72}O_{13} \cdot 2\ H_2O$: C, 61.44; H, 9.33. Found: C, 61.60; H, 9.03.

3,20-Di-*O*-β-D-glucopyranosyldammar-24-ene-3β,12β,20(*S*)-triol (**37**) had $[\alpha]_D^{20}$ +9° (*c* 1.5, pyridine).

Anal. Calc. for $C_{42}H_{72}O_{13} \cdot 2\ H_2O$: C, 61.44; H, 9.33. Found: C, 61.42; H, 9.22.

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