SYNTHESIS OF GLYCOSIDES OF LUPANE-TYPE TRITERPENE ACIDS

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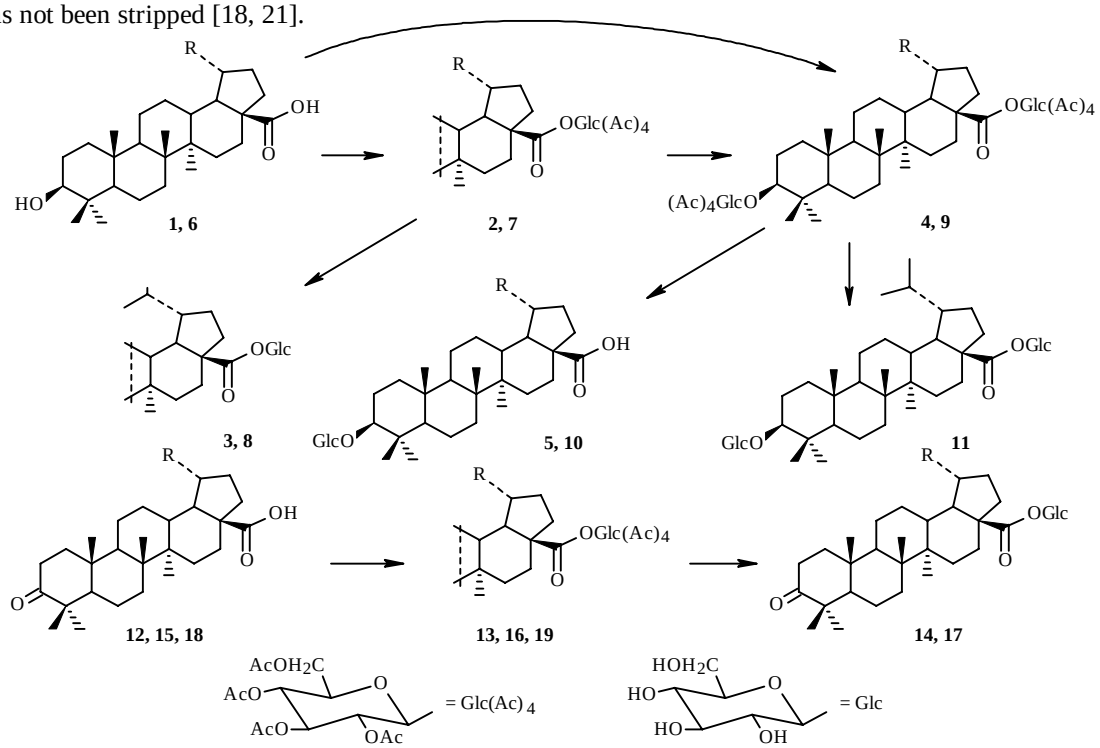
A preparative synthesis of glucosides of the lupane-type triterpene acids betulinic, dihydrobetulinic, betulonic, dihydrobetulonic, and 3,20-dioxo-30-norlupan-28-oic was proposed. Glycosylation of 3-hydroxyacids by α-acetobromoglucose (ABG) with Ag_2O was performed in pyridine (Py) to form glycosides at C-28, repeated glycosylation of which by these same reagents but in CH_2Cl_2 generated a glycoside bond at C-3 to form bisglucosides. 28-Glucosides of ketoacids were formed in high yields in both Py and CH_2Cl_2.

Key words: betulin, betulinic acid, glucosides, PMR and ^{13}C NMR.

The biological activities of betulinic and platanic acids as anti-HIV agents that was previously reported [1] have stimulated interest in the synthesis of other lupane derivatives with potentially interesting biological activities [2-11]. Several glycosides of lupane derivatives were synthesized [3, 5, 11-16]. It should be noted that glycosides of many triterpenoids and steroids are biologically more available to living organisms than their starting aglycons [17]. The platform compound in most syntheses based on lupane triterpenes is betulin, 20(29)-lupen-3β,28-diol, which occurs in significant quantities in the outer bark of various white-birch species, from which it is easily isolated pure and reproducibly as a natural product [18-21]. It must be emphasized that betulin can be obtained in significant quantities as a side product during processing of birch wood from which the bark has not been stripped [18, 21].



1-5, **12-14**: R=-CH(CH$_3$)=CH$_2$; **6-11**, **15-17**: R=-CH(CH$_3$)$_2$; **18**, **19**: -C(CH$_3$)=O

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TABLE 1. ^{13}C NMR Spectra of **2**, **4**, **5**, **7**, **9**, **10**, **12**, and **13**

C atom	Compound							
	2	**4**	**5**	**7**	**9**	**10**	**12**	**13**
1	39.0	39.0	39.2	39.1	39.1	39.2	39.6	39.6
2	27.7	25.9	26.3	27.7	27.2	26.3	34.2	34.2
3	79.0	90.7	88.9	79.1	90.7	88.7	218.4	218.0
4	39.0	39.2	39.2	39.1	39.1	38.8	47.4	47.4
5	55.6	56.0	56.1	55.7	56.0	55.7	55.0	55.0
6	18.5	18.5	18.6	18.6	18.5	18.2	19.7	19.7
7	34.7	34.8	34.9	34.9	34.9	34.6	33.6	33.8
8	41.0	41.0	41.2	41.1	41.1	40.9	39.6	39.6
9	50.8	50.9	51.0	50.7	50.7	50.4	49.9	49.9
10	37.5	37.2	37.5	37.5	37.2	37.5	37.1	37.0
11	21.2	21.2	21.3	21.2	21.3	21.0	21.4	21.4
12	25.8	26.1	26.8	27.2	26.2	27.1	25.5	25.6
13	38.5	38.5	38.7	38.5	38.4	38.2	38.6	38.3
14	42.6	42.7	42.9	42.9	42.9	42.7	42.5	42.6
15	30.7	30.7	31.4	30.0	30.0	29.7	30.6	30.6
16	32.0	32.0	33.0	32.0	32.0	32.4	32.2	31.7
17	57.0	57.0	56.6	57.5	57.5	56.6	56.5	56.8
18	46.9	46.9	47.8	49.0	49.0	49.0	47.4	46.8
19	49.5	49.6	50.0	44.4	44.4	44.5	49.9	49.9
20	150.1	150.1	150.1	30.0	30.0	29.8	150.4	150.0
21	29.9	29.9	30.3	23.0	23.0	23.0	30.6	29.8
22	36.7	36.7	37.2	37.2	37.2	36.9	37.1	36.5
23	28.2	27.8	28.2	28.2	27.9	27.8	26.7	26.6
24	15.5	16.2	16.8	15.5	16.4	16.4	21.0	21.1
25	16.2	16.2	16.5	16.3	16.2	16.0	15.9	16.0
26	16.2	16.2	16.3	16.3	16.4	15.9	16.0	16.0
27	14.9	14.8	15.0	14.9	14.9	14.5	14.7	14.7
28	174.0	174.0	178.4	174.4	174.3	178.1	182.5	174.3
29	109.7	109.7	109.6	22.8	22.8	23.0	109.8	109.8
30	19.6	19.6	19.6	14.9	14.9	14.4	19.6	19.7

Our goal was to develop simple preparative methods for synthesizing glycosides of betulinic (**1**) and dihydrobetulinic (**6**) acids in addition to betulonic (**12**), dihydrobetulonic (**15**), and 3,20-dioxo-30-norlupan-28-oic (**18**) acids for subsequent research on their biological activities.

Monoglucosides at C-28 were prepared in two steps; monoglucosides at C-3 and bisglucosides in three steps from betulinic and dihydrobetulinic acids. Glycosylation of **1** and **6** in Py by tetra-O-acetyl-α-D-glucopyranosylbromide (ABG) with Ag_2O gave monoglucosides 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl-3β-hydroxy-20(29)-lupen-28-oate (**2**) and 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl-3β-hydroxylupan-28-oate (**7**), which were saponified by $NaOCH_3$ in CH_3OH to free 28-O-glucosides **3** and **8**. Repeated glycosylation of **2** and **7** by ABG with Ag_2O in CH_2Cl_2 afforded the corresponding acetates of 3,28-bisglucosides **4** and **9**. Basic hydrolysis of **4** and **9** by heating with KOH in CH_3OH gave the corresponding 3-O-β-D-glucosides of betulinic and dihydrobetulinic acids **5** and **10**. Saponification by $NaOCH_3$ in CH_3OH at room temperature of **9** gave free bisglucoside **11**.

Glycosylation of betulonic **12**, dihydrobetulonic **15**, and 3,20-dioxo-30-norlupan-28-oic **18** acids by ABG both in Py and CH_2Cl_2 gave the corresponding 28-glucosides **13**, **16**, and **19** in high yields with insignificant recovery of the starting acids.

The structures of the products were proved using PMR and ^{13}C NMR spectra (Tables 1-5).

Thus, we proposed a convenient synthesis for glucosides of lupane-type triterpene acids that is suitable on a preparative scale.

Glycoside **5** exhibited stimulatory and glycoside **10** inhibitory activities for growth of root sprouts of *Cucumis sativus* L. [11].

TABLE 2. ^{13}C NMR Chemical Shifts of **15-19**, Platanic Acid (PA), and its 3-Acetate (APA)

C atom	Compound						
	15	**16**	**17**	**18**	**19**	PA	APA
1	39.6	39.6	39.7	39.6	39.4	38.7	38.4
2	34.2	34.2	34.8	34.1	34.0	34.2	34.2
3	218.4	218.0	218.0	218.0	217.8	79.0	80.9
4	47.4	47.4	47.4	47.3	47.2	38.9	49.3
5	54.9	55.0	55.1	54.8	54.7	55.3	55.4
6	19.7	19.7	19.7	19.7	19.6	18.3	18.2
7	33.7	33.8	33.9	33.5	33.5	34.2	34.2
8	40.7	40.7	40.9	40.6	40.5	40.6	40.6
9	49.7	49.7	49.8	49.7	49.7	50.4	50.3
10	36.9	36.9	37.0	36.9	36.8	37.3	37.2
11	21.4	21.4	21.6	21.4	21.4	20.9	21.4
12	26.9	26.9	26.7	27.3	27.2	27.3	28.0
13	38.4	38.2	38.3	37.7	37.3	38.7	37.6
14	42.7	42.7	42.8	42.4	42.3	42.3	42.3
15	32.1	31.7	31.9	31.5	31.0	31.5	31.5
16	22.8	22.6	22.8	28.3	28.0	28.3	28.3
17	56.9	57.2	57.3	56.3	56.6	56.3	56.3
18	48.7	48.6	49.0	49.1	48.6	49.3	50.3
19	44.2	44.1	44.3	51.2	50.5	51.3	51.3
20	29.8	29.8	29.9	212.0	211.6	212.4	212.2
21	29.7	29.7	29.8	29.7	29.6	29.8	29.8
22	37.5	36.9	37.1	36.7	36.1	37.2	36.8
23	26.7	26.7	27.1	26.8	26.6	27.3	27.2
24	21.4	21.1	21.2	21.0	21.0	18.3	20.9
25	16.0	20.2	16.0	16.0	16.0	16.1	16.5
26	16.0	20.2	15.9	16.0	15.6	16.0	16.2
27	14.7	20.2	14.8	16.0	14.6	15.4	16.0
28	182.7	174.5	174.8	182.0	174.1	181.4	182.2
29	14.7	15.0	14.8	30.1	30.1	30.2	30.2
30	14.6	15.1	14.7				

TABLE 3. PMR Chemical Shifts of **2**, **4**, **5**, and **12-14**

Protons	Compound					
	2	**4**	**5**	**12**	**13**	**14**
CH_3	0.75 s	0.72 s	0.75 s	0.93 s	0.93 s	0.81 s
	0.82 s	0.82 s	1.0 s	0.97 s	0.97 s	1.01 s
	0.89 s	0.89 s	1.05 s	0.99 s	1.02 s	1.02 s
	0.96 s	0.95 s	1.10 s	1.02 s	1.06 s	1.12 s
				1.07 s		1.13 s
$= CH_2$	4.60 m	4.61 br.d	4.60 m	4.61 m	4.73 m	4.75 m
	4.74 br.d	4.75 br.d	4.78 br.d	4.74 br.d	4.74 m	4.90 m
H-19	2.94 m	2.95 m	2.7 m	3.02 td	2.9-3.0 t, J = 11.0; 11.0; 4.4	3.36-3.47 td, J = 10.7; 10.7; 4.6
H-3a	3.18 dd	3.05 dd	3.5 m			
H-30	1.68 s	1.68 s	1.8 s	1.7 s	1.7 s	1.7 s

TABLE 3. (Continued)

Protons	Compound					
	2	**4**	**5**	**12**	**13**	**14**
			Carbohydrate part			
H^1	5.69 d, J = 8	5.7 d, J = 8 4.55 d, J = 8	4.37		5.71 d, J = 8	4.21 d, J = 8.2
H^2	5.20 dd	5.05 dd 5.18 dd	4.9-5.0		5.21 dd, J = 8.5; 8.3	4.37 dd, J = 8.7; 8.85
H^3	5.28 t	5.20 t, 5.25 t	4.9-5.0		5.29 t, J = 9.3; 3.0; 9.0	4.,42 t, J = 9.6; 8.7
H^4	5.15 dd	5.00 dd 5.15 dd	4.4-4.45		5.16 dd, J = 5.2; 9.4	4.33 dd, J = 6.1; 8.6
H^5	3.83 m	3.68 m 3.83 m	3.95-4.1		3.84 m	3.83-3.91 m
$2H^6$	4.07 dd 4.31 dd	4.08 dd 4.11 dd 4.25 dd 4.32 dd	4.2-4.3		4.07 dd, J = 12.4; 2.3 4.32 dd, J =12.5; 4.5	4.07 m
OAc	2.02 s 2.04 s 2.08 s	2.01 s 2.02 s 2.03 s 2.08 s			2.02 s 2.04 s 2.08 s	

TABLE 4. PMR Chemical Shifts of **15**-**19**, PA, and APA

Protons	Compound						
	15	**16**	**17**	**18**	**19**	PA	APA
CH_3	0.94 s	0.93 s	0.93 s	0.91 s	0.91 s	0.76 s	0.83 s
	0.97 s	0.94 s	0.96 s	0.95 s	1.00 s	0.82 s	0.85 s
	1.02 s	0.95 s	0.96 s	1.01 s	1.01 s	0.91 s	0.91 s
	1.07 s	0.98 s	1.02 s	1.01 s	1.06 s	0.97 s	1.00 s
		1.02 s	1.07 s	1.07 s		1.01 s	
H-19				3.25 m	3.18 m	3.25 m	3.25 m
H-29	0.76 d	0.75 d	0.76 d				
H-30	0.87 d	0.85 d	0.86 d				
			Carbohydrate part				
H^1		5.69 d; J = 8.1	5.58 d, J = 9		5.7 d, J = 9.3		
H^2		5.15 dd; J = 9.0			5.25 dd, J = 9.3		
H^3		5.23 dt, J = 9.0			5.28		
H4		5.16 dd; J = 9.0			5.15 dd, J = 9.0		
H^5		3.83 m					
$2H^6$		4.07 dd			4.07 d, J = 2.3		
		4.31 dd			4.11 d, J = 2.4		
OAc		2.02 s			2.04 s		
		2.02 s			2.04 s		
		2.03 s			2.08 s		
		2.07 s			2.18 s		

TABLE 5. ^{13}C NMR Spectra of the Carbohydrate Part of **2**, **4**, **5**, **7**, **9**, **10**, **13**, **16**, **17**, **19**

Atom	Compound									
	2	**4**[3], **4**[28]	**5**	**7**	**9**[3], **9**[28]	**10**	**13**	**16**	**17**	**19**
C-1	91.3	102.9	106.5	91.3	103.0	105.8	91.2	91.1	93.6	91.2
		91.3			91.3					
C-2	70.3	72.1	72.0	73.3	72.2	71.3	70.0	70.0	70.3	69.8
		70.3			70.4					
C-3	72.8	71.8	75.7	72.8	71.9	75.0	72.9	72.6	76.1	72.7
		72.8			72.8					
C-4	68.5	69.3	63.2	68.6	69.3	62.4	68.3	68.1		67.8
		68.5			68.6					
C-5	73.2	73.2	77.9	70.3	73.3	77.0	73.2	73.0	73.0	72.5
		73.2			73.3					
C-6	61.8	62.6	63.2	61.9	62.6	62.4	61.8	61.6	67.2	61.4
		61.9			61.9					
OAc	170.2	170.2		170.3	170.3		170.6	170.6		170.4
	169.8	170.2		169.9	170.1		170.2	170.2		170.1
	169.1	169.8		169.2	169.9		169.4	169.5		168.9
	168.7	169.8		168.8	169.9		168.9	169.0		169.3
	20.6	169.1		20.6	169.9		20.7	20.7		20.6
	20.6	169.1		20.6	169.2		20.6	20.6		20.5
	20.6	168.7		20.6	168.8		20.6	20.6		20.5
	20.6	168.7		20.6	168.8		20.6	20.6		20.5
		20.7			20.7					
		20.7			20.7					
		20.6			20.6					
		20.6			20.6					
		20.6			20.6					
		20.6			20.6					
		20.6			20.6					
		20.6			20.6					

[3] - 3-O-Glc(Ac)$_4$; [28] - 28-O-Glc(Ac)$_4$.

EXPERIMENTAL

^{13}C NMR and PMR spectra were recorded on Bruker AVANCE-300 (75 and 300 MHz, respectively) spectrometers in $CDCl_3$ (Me_4Si internal standard). Chemical shifts were calculated for PMR spectra relative to the Me_4Si signal; for ^{13}C spectra, the solvent signal ($CDCl_3$, 77.1 ppm). The multiplicity of the ^{13}C signals was determined from DEPT-135 experiments by the standard method. Homonuclear 2D proton—proton correlation spectra COSY-45 and 2D heteronuclear correlation spectra HSQC and HMBC were also recorded by standard methods. HMBC experiments were optimized for $^nJ_{HC} \approx 10$ Hz. Melting points were determined on a Boetius microstage and are uncorrected. Sorbfil plates (Russia) were used for TLC. Column chromatography was performed over SiO_2 using solvent systems hexane:acetone from 40:1 to 5:1 and C_6H_6:CH_3OH from 15:1 to 5:1. Specific rotation was determined to an accuracy of ±1° on a Perkin—Elmer 141 polarimeter in monochromatic light from a Na lamp (D-line) in 1cm^3 cuvettes (concentration expressed in g/cm^3) and optical pathlength 1.0002 dm in $CHCl_3$ or C_5H_5N solutions. Reaction mixtures for glycosylation were stirred on a magnetic stirrer at room temperature.

Betulin was isolated from the acetone extract of the outer bark of *Betula platyphylla* Sukacz. [*B. mandshurica* (Regel) Nakai] as before [11], mp 247-248°C (EtOH), lit. [21] mp 250-251°C. Betulinic acid (**1**), mp 292°C (EtOH), $[\alpha]_D^{25}$ +9° (*c* 0.004, $CHCl_3$), lit. [12] mp 304-306°C (EtOH), $[\alpha]_D^{20}$ +4 ± 3° (*c* 0.41, $CHCl_3$), was synthesized by oxidation of 3β-acetoxybetulin by *t*-butylchromate prepared by the literature method [22] with subsequent saponification by KOH (10%) in

CH_3OH. Betulin was acetylated with a mixture of Ac_2O and C_5H_5N by the usual method to produce in about 90% yield 3*β*,28-diacetoxybetulin, which was then hydrogenated in AcOH over Pd/C by the literature method [23] to 3*β*,28-diacetoxydihydrobetulin, mp 256-257°C (C_6H_6—EtOH), lit. [23] mp 259°C (CH_2Cl_2—EtOH), and partially saponified by KOH in CH_3OH to 3*β*-acetoxydihydrobetulin, mp 260-262°C (CH_3OH), lit. [24] mp 258-259°C, $[\alpha]_D$ -5.1°, or completely to dihydrobetulin, mp 276-278°C (EtOH), lit. [23] mp 277-278°C (EtOH), $[\alpha]_D$ -20° (*c* 0.9, Py). 3*β*-Acetoxydihydrobetulin was oxidized by $RuO_4/NaIO_4$ with vigorous stirring in the two-phase system EtOAc—H_2O by a method analogous to that in the literature [25] to afford 3*β*-acetoxydihydrobetulinic acid in 83% yield, mp 306-307°C, mass spectrum 500 $[M]^+$; lit. [26] mp 311-312.5°C. Saponification by KOH in CH_3OH of 3*β*-acetoxydihydrobetulinic acid gave dihydrobetulinic acid, mp 305-306°C (EtOH), $[\alpha]_D^{25}$ +4° (*c* 0.0042, $CHCl_3$); lit. [26] mp 323-324.5°C, $[\alpha]_D$ -28.8° (dioxane). Oxidation of betulin by CrO_3 in AcOH according to the literature [27] gave betulonic acid **12**, mp 217-221°C (CH_3CN), $[\alpha]_D^{25}$ +25° (*c* 0.01, $CHCl_3$), lit. [27] mp 245-248°C.

Oxidation of dihydrobetulin by $RuO_4/NaIO_4$ in EtOAc—H_2O [28] by a method analogous to that in the literature [25] afforded dihydrobetulonic acid, mp 261-263°C (EtOH), $[\alpha]_D^{25}$ +19° (*c* 0.01, $CHCl_3$), $[\alpha]_{578}$ +11.7° (*c* 0.027, $CHCl_3$); lit. [23] mp 258-260°, $[\alpha]_D$ +12.3°; [29] mp 250-253°C.

3,20-Dioxo-30-norlupan-28-oic Acid (18). A solution of $Ru(OH)Cl_3$ (103.2 mg, 0.45 mmol) with a suspension of betulin (5.06 g, 11.43 mmol) in EtOAc (200 mL) was vigorously stirred for 9 h, treated dropwise with $NaIO_4$ (15.3 g, 71.5 mmol) in H_2O (150 mL), and left overnight without stirring. The aqueous layer was separated and extracted with EtOAc (3 × 25 mL). The combined EtOAc extracts were treated with stirring with *i*-PrOH (5 mL) to decompose the excess of oxidant and filtered to remove the black precipitate of $RuO_2 \times H_2O$. The filtrate was dried over anhydrous $CaCl_2$ and evaporated to dryness in a rotary evaporator. The resulting colored polycrystalline solid was dissolved in C_6H_6 (200 mL) and filtered from the black precipitate of RuO_2 impurities through a sintered-glass filter (16 pore). Then, impurities of colloidal RuO_2 were removed by filtration through a 1-cm-thick Al_2O_3 layer on another sintered-glass filter. The resulting C_6H_6 filtrate was stirred and treated with KOH solution (10 mL, 10%). The C_6H_6 was decanted from the resinous precipitate of triterpene-acid salts. The solid was dissolved in EtOH (100 mL) and treated with HCl (100 mL, 15%) and H_2O (300 mL). The isolated resinous product was dissolved in EtOH (100 mL), partially decolorized by treatment with activated carbon, filtered, and evaporated to dryness. The resulting solid (2.1 g) was chromatographed over a SiO_2 column with elution by hexane:acetone mixtures [(30:1)→(5:1)] to isolate 3,20-dioxo-30-norlupan-28-oic acid (**18**) (640 mg, 1.4 mmol, 12.3%), mp 223-224°C (EtOH), $[\alpha]_D^{25}$ +31° (*c* 0.01, $CHCl_3$); lit. [30] Me-ester, mp 162-164°, $[\alpha]_D$ +2° (*c* 1.04, $CHCl_3$); and 3*β*-hydroxy-20-oxo-30-norlupan-28-oic (platanic) acid (800 mg, 1.75 mmol, 15%), mp 280-282°C (EtOH), $[\alpha]_D^{25}$ -31° (*c* 0.01, $CHCl_3$); $[\alpha]_{578}$ -29.4° (*c* 0.014, $CHCl_3$); lit. [30] mp 285-287°C, $[\alpha]_D$ -51° (*c* 1, $CHCl_3$).

2,3,4,6-Tetra-O-acetyl-*β*-D-glucopyranosyl-3*β*-hydroxylup-20(29)-en-28-oate (2). A mixture of **1** (182 mg, 0.4 mmol), ABG (328 mg, 0.8 mmol), and Ag_2O (94 mg, 0.4 mmol) in Py (5 mL) was stirred for 3 h, diluted with $CHCl_3$, filtered, and evaporated. The solid was chromatographed over a SiO_2 column using hexane:acetone [(20:1)→(10:1)] to isolate **2** (296 mg, 94.0%), mp 125-130°C (CH_3OH), $[\alpha]_D^{25}$ -10° (*c* 0.0046, $CHCl_3$); lit. [12] mp 124-126°C, $[\alpha]_D$ -3 ± 4° (*c* 0.76, EtOH).

General Method for Deacetylation of 28-(2,3,4,6-Tetra-O-acetyl-*β*-D-glucopyranosyloxy)-derivatives. Approximately 1 mmol of tetraacetate glucoside was dissolved in CH_3OH (30 mL), treated with $NaOCH_3$ in CH_3OH (1 mL, 0.1 N), held for 3-4 h at room temperature (TLC monitoring), neutralized with KU-2-8 H^+ ion-exchange resin, and evaporated to give free glucoside in ~95% yield.

***β*-D-Glucopyranosyl-3*β*-hydroxylup-20(29)-en-28-oate (3).** Saponification of **2** by the usual method gave **3**, mp 229-232°C (EtOH), $[\alpha]_D^{25}$ +5° (*c* 0.005, Py); lit. [3] mp (amorph.), $[\alpha]_D$ 0 ± 2° (*c* 0.16, CH_3OH); lit. [12] mp 213-216°C (CH_3OH), $[\alpha]_D$ -2 ± 4° (*c* 0.43, EtOH).

2,3,4,6-Tetra-O-acetyl-*β*-D-glucopyranosyl-3*β*-(2,3,4,6-tetra-O-acetyl-*β*-D-glucopyranosyloxy)-lup-20(29)-en-28-oate (4). A mixture of **2** (390 mg, 0.5 mmol), ABG (1110 mg, 2.7 mmol), and Ag_2O (632 mg, 2.7 mmol) in CH_2Cl_2 (10 mL) was stirred for 48 h, diluted with $CHCl_3$, filtered, and evaporated. The solid was washed with hot water to remove sugars and chromatographed over SiO_2 using hexane:acetone [(20:1)→(5:1)] to isolate unreacted **2** (83 mg, 21.1%) and **4** (340 mg, 60.8%), mp 225-230°C (EtOH); lit. [3] mp 225-231°C (CH_2Cl_2:Et_2O), $[\alpha]_D$ +1 ± 2° (*c* 0.46, $CHCl_3$).

3*β*-(*β*-D-Glucopyranosyloxy)-lup-20(29)-en-28-oic Acid (5). Compound **4** (80 mg, 0.07 mmol) was dissolved in CH_3OH (10 mL), treated with KOH in CH_3OH (4 mL, 10%), heated on a boiling-water bath for 5 h, neutralized with

KU-2-8 H^+ ion-exchange resin, evaporated, and washed with water to isolate **5** (47 mg, 74.4%), mp amorph., $[\alpha]_D^{25}$ -5° (*c* 0.005, Py).

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl-3β-hydroxylupan-28-oate (7). A mixture of **6** (916 mg, 2 mmol), ABG (1644 mg, 4 mmol), and Ag_2O (936 mg, 4 mmol) in Py (10 mL) was stirred for 6 h, left for 1 d, diluted with $CHCl_3$, filtered to remove AgBr, evaporated, and washed with hot water. The solid was recrystallized from CH_3OH to afford **7** (771 mg, 48.8%). The mother liquor was evaporated and chromatographed over SiO_2 using hexane:acetone [(20:1)→(10:1)]. The overall yield of chromatographically pure **7** was 1051 mg (66.5%), mp 150-153° (EtOH), $[\alpha]_D^{25}$ -13° (*c* 0.01, $CHCl_3$).

β-D-Glucopyranosyl-3β-hydroxylupan-28-oate (8). Saponification of **7** by the usual method gave **8**, mp 294-297°C (EtOH), $[\alpha]_D^{25}$ -3° (*c* 0.01, Py); lit. [3] mp 243-244°C (CH_3OH), $[\alpha]_D$ -21 ± 2° (*c* 0.17, CH_3OH).

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl-3β-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-lupan-28-oate (9). A mixture of **6** (229 mg, 0.5 mmol), ABG (1233 mg, 3 mmol), and Ag_2O (702 mg, 3 mmol) in CH_2Cl_2 (10 mL) was stirred for 2 d and chromatographed over SiO_2 in hexane:acetone [(30:1)→(5:1)] to afford **6** (64 mg, 27.9%), **7** (190 mg, 48.2%), and **9** (80 mg, 14.3%), mp 251-252° (EtOH), $[\alpha]_D^{25}$ -38° (*c* 0.01, $CHCl_3$).

3β-(β-D-Glucopyranosyloxy)-lupan-28-oic Acid (10). Compound **9** (143 mg) was dissolved in CH_3OH (15 mL), treated with KOH in CH_3OH (9 mL, 10%), heated at 50°C for 8 h, neutralized with KU-2-8 H^+, evaporated, and washed with water to remove sugars and isolated **10** (75 mg, 67.2%), mp amorph., $[\alpha]_D^{25}$ +6° (*c* 0.005, Py).

β-D-Glucopyranosyl-3β-(β-D-glucopyranosyloxy)-lupan-28-oate (11). A mixture of **6** (1 mmol), ABG (4 mmol), and Ag_2O (936 mg, 4 mmol) in CH_2Cl_2 (10 mL) was stirred for 3 d and worked up as usual. The solid, which contained a mixture of **7** and **9**, was treated with CH_3OH (30 mL) and KOH in CH_3OH (8 mL, 10%), neutralized by KU-2-8 H^+ ion-exchanger, evaporated, washed with water to remove sugars, and chromatographed over SiO_2 with elution by C_6H_6:CH_3OH [(15:1)→(5:1)] to afford **11** (163 mg, 21%), mp 236-238°C (EtOH), $[\alpha]_D^{25}$ -5° (*c* 0.005, Py) and **8** (389 mg, 63.3%).

β-D-Glucopyranosyl-3-oxolup-20(29)-en-28-oate (13). A mixture of **12** (456 mg, 1 mmol), ABG (822 mg, 2 mmol), and Ag_2O (468 mg, 2 mmol) in Py (10 mL) was stirred for 8 h, diluted with $(CH_3)_2CO$, and poured into a beaker with ice. The precipitate was filtered off, placed on SiO_2, and eluted with $(CH_3)_2CO$ (to remove AgBr). The eluate was evaporated. The solid was dissolved in EtOH (20 mL) containing KOH in EtOH (20 mL, 0.1 N). The saponified product was chromatographed over SiO_2 using C_6H_6:CH_3OH [(100:1)→(25:1)] to afford **13** (454 mg, 73.4%), mp 255° (EtOH), $[\alpha]_D^{25}$, +16° (*c* 0.01, Py) and starting **12** (120 mg, 26.3%). Glycosylation of **12** in CH_2Cl_2 under these same conditions gave 81.6% **13** and 11.2% starting **12** after analogous treatment.

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl-3-oxolupan-28-oate (16). A mixture of **15** (458 mg, 1 mmol), ABG (820 mg, 2 mmol), and Ag_2O (468 mg, 2 mmol) in Py (10 mL) was stirred for 5 h, diluted with $(CH_3)CO$, filtered, and chromatographed over a column of SiO_2 using petroleum ether:acetone [(40:1)→(25:1)] to afford starting **15** (42 mg, 9.2%) and **16** (712 mg, 90.4%), mp 158-160° (EtOH), $[\alpha]_D^{25}$ +4° (*c* 0.01, $CHCl_3$).

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl-3,20-dioxo-30-norlupan-28-oate (19). A mixture of **18** (229 mg, 0.5 mmol), ABG (820 mg, 2 mmol), and Ag_2O (468 mg, 2 mmol) in Py (5 mL) was stirred for 5 h and chromatographed over SiO_2 using petroleum ether:acetone [(40:1)→(10:1)] to afford **19** (290 mg, 73.6%), mp 209-211°C (EtOH), $[\alpha]_D^{25}$ +13° (*c* 0.01, $CHCl_3$).

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