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FURTHER TRITERPENOIDS FROM THE STEMS OF *LITHOCARPUS POLYSTACHYA*

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Key Word Index—*Lithocarpus polystachya*; Fagaceae; triterpenoids; lupeol; taraxerol; 3β-acetoxylupan-29-al; 20-hydroxylupan-3-one; lupane-3β, 29-diol; betulin; morolic and oleanolic acids.

INTRODUCTION

The following compounds have previously been isolated from *Lithocarpus polystachya*: (Wall.) Rhed. friedelin, friedelan-3β-ol, glutinol, β-amyrin, taraxerol, sitosterol and three new cycloartane triterpenes from leaves [1, 2]; friedelin, friedelan-3β-ol, sitosterol and betulinic acid from stems [2, 3]. Neutral and acidic pentacyclic triterpenoids have also been obtained from 9 Hong Kong Lithocarpus species [1–6].

RESULTS

On reinvestigation on a bigger scale, the stems of *L. polystachya* have yielded in addition to those triterpenoids already reported [2, 3], lupeol, taraxerol, betulin, 20-hydroxylupan-3-one (**1**), 3β-acetoxylupan-29-al (**2**), lupane-3β, 29-diol (**3**), morolic acid and oleanolic acid. Compounds **1**–**3** have not previously been isolated from natural sources. They were all saturated compounds (negative tetranitromethane test).

Compounds **1**, $C_{30}H_{50}O_2$, contained a $—CH_2CO$ function [ν_{max} 1700 cm^{-1}, δ 2.40 (2H, *m*)], and an OH group (ν_{max} 3474 cm^{-1}) which could not be acetylated. Reduction of **1** with $NaBH_4$ gave a diol (**4**), which on acetylation yielded a monoacetate (**5**), and on oxidation was converted back to **1**. The presence of a tertiary OH group in these compounds was thus suggested. The NMR spectra of compounds **1**, **4** and **5** all revealed 2 $C\underline{H}_3$ singlets at δ 1.12 and 1.22, showing the existence of a $—C(Me)_2OH$ group, probably belonging to the 20-hydroxylupane and not to the 22-hydroxyhopane series [7], as the latter usually gives two equivalent $C\underline{H}_3$ singlets at δ 1.20 [5]. This was confirmed by the ready dehydration of **1** to give lup-20(29)-en-3-one (lupenone) (**6**), and by $LiAlH_4$ reduction of 20, 29-epoxylupan-3β-yl acetate (**7**) [8] to yield 3β,20-dihydroxylupane, identical with **4**. Compound **1** was thus 20-hydroxylupan-3-one, which has previously been prepared from eisacol (**4**), a natural product [9]. Compound **4** was first isolated in 1954, and named monogynol-A (10], and its structure was confirmed in 1961 [8].

Compound **2**, $C_{32}H_{52}O_3$, contained an equatorial-OCOMe function [ν_{max} 1730, 1250 cm^{-1}, δ 2.02 (3H, *s*), 4.47 (1H, *q*, $J_{ax/ax}$ = 9 Hz, $J_{ax/eq}$ = 7 Hz)] and a —CHO group [ν_{max} 2840, 2720, 1730 cm^{-1}, δ 9.60 (1H, *s*)]. On reduction with $LiAlH_4$ it yielded a diol, $C_{30}H_{52}O_2$, (ν_{max} 3550, 3500 cm^{-1}), identical with compound **3**, and on Wolff–Kishner reduction followed by acetylation it gave 3β-acetoxylupane (**8**). Compound **3** formed a diacetate (**9**), the NMR spectrum of which indicated the presence of a $—\underset{|}{CH}—C\underline{H}_2OAc$ group (δ 3.88, 2H, *d*, J = 8 Hz) probably representing part of the side chain of a lupane derivative. This was confirmed by acid treatment of the epoxide **7** to yield 3β-acetoxylupan-29-al [11], identical with **2**. Hence **3** must be 3β,29-dihydroxylupane. Although **2** and **3** are new natural products, they have previously been synthesised, **2** as described above, and **3** from methyl 3β-acetoxylup-20(29)-en-30-oate (**10**) or 3β-acetoxy-30-oxolup-20(29)-ene (**11**) [12].

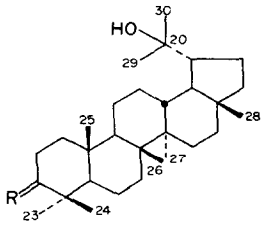
The NMR shifts of the tertiary Me proton signals (δ values) in compounds **1**, **2**, **4**, **5**, **7** and **9** are assigned as shown in Table 1.

In this and previous studies [1–3], it has been shown that a total of 16 triterpenoids have been isolated from

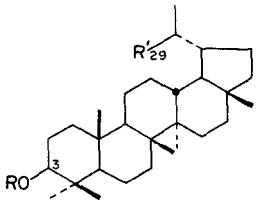
Table 1. NMR shifts of lupane derivatives

Compound	C-23	C-24	C-25	C-26	C-27	C-28	C-29/C-30
1	1.10	1.02	0.93	1.09	0.97	0.80	1.12/1.22
2	0.84	0.84	0.84	1.04	0.89	0.79	—
4	0.96	0.78	0.85	1.07	0.96	0.82	1.12/1.22
5	0.84	0.84	0.86	1.06	0.96	0.81	1.12/1.22
7	0.84	0.84	0.84	1.03	0.93	0.83	1.24
9	0.88	0.88	0.88	1.05	0.94	0.77	—

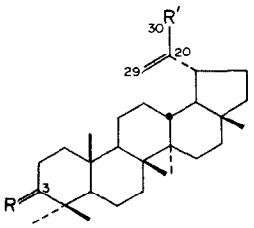
L. polystachya. Compounds **1–3** are examples of rare saturated naturally occurring lupane derivatives, and **2** and **3** are the first two such compounds with oxygen functions at C-29.



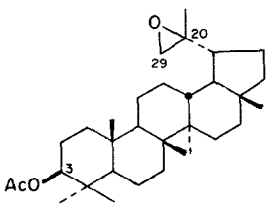
1 R=O
4 R=α-H,β-OH
5 R=α-H,β-OAc



2 R=Ac R'=CHO
3 R=H R'=CH_2OH
8 R=Ac R'=Me
9 R=Ac R'=CH_2OAc



6 R=O, R'=Me
10 R=α-H,β-OAc, R'=COOMe
11 R=α-H,β-OAc, R'=CHO



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EXPERIMENTAL

Optical rotations were recorded in $CHCl_3$ solns, IR spectra for KBr discs, NMR spectra in $CDCl_3$ were determined at 60 MHz using TMS as internal standard. Petrol had bp 60–80°. Known compounds were identified by TLC, mmp, IR and MS comparisons with authentic samples.

Extraction and isolation of compounds. Milled air-dried stems of *L. polystachya* (Wall.) Rhed. (45 kg) were extracted 2 × at room temp with petrol for 10 days. Combined extracts were distilled to give a residue (150 g), which was chromatographed in petrol on alumina (3 kg). Elution with petrol gave friedelin (3.0 g), mp 261–263°, friedelan-3β-ol (1.0 g), mp 285–287°, then lupeol (0.1 g), mp 209–211°; with petrol–C_6H_6 (1:1) yielded taraxerol (1.0 g), mp 287–289°, then sitosterol (0.5 g), mp 139–140°, and finally plates of 3β-acetoxylupan-29-al (**2**) (0.05 g), mp 227–229° (from $CHCl_3$), $[\alpha]_D$ + 10.8° (Lit. [11], mp 223–226°, $[\alpha]_D$ + 14.4°). (Found: M^+ 484. Calc. for $C_{32}H_{52}O_3$: M^+ 484). Further elution with C_6H_6 afforded plates of 20-hydroxylupan-3-one (**1**) (0.04 g), mp 224–225° (from $CHCl_3$), $[\alpha]_D$ + 30.7° (Lit. [9], mp 220–222°, $[\alpha]_D$ + 27.2°). (Found: M^+ 442. Calc. for $C_{30}H_{50}O_2$: M^+ 442); then needles of 3β,29-dihydroxylupane (**3**) (0.05 g), mp 237–239° (from MeOH), $[\alpha]_D$ + 3.0° (Lit. [12], mp 236–238°, $[\alpha]_D$ ± 0°]. (Found: M^+ 444. Calc. for $C_{30}H_{52}O_2$: M^+ 444). Finally elution with C_6H_6–$CHCl_3$ (1:1) gave needles of betulin (0.02 g), mp 254–256°. The residue after extraction with petrol was extracted 2 × at room temperature with ethanol. The acidic solid (7 g) isolated through the sodium salt, was treated with CH_2N_2 in ether, and the product was chromatographed on alumina (150 g). Elution with petrol yielded prisms of methyl betulinate (0.07 g), mp 228–230°, with petrol–C_6H_6 (1:1), needles of methyl morolate (0.01 g), mp 230–232°, IR ν_{max} cm^{-1}: 3580 (OH), 1720, 1225 (COOMe), 1650, 850 (C=CH), then needles of methyl oleanolate (0.02 g), mp 197–200°, IR ν_{max} cm^{-1}: 3380 (OH), 1730, 1160 (COOMe), 3030, 1650, 850 (C=CH).

Attempted acetylation of **1**. **1** (0.02 g) was kept at room temp. in $(MeCO)_2O$ and C_5H_5N for 2 days. The product (0.017 g), mp 222–224°, was identified to be unchanged **1**.

Reduction of **1**. **1** (0.04 g) was stirred with $NaBH_4$ (0.1 g) in $(Me)_2CHOH$ (25 ml) at room temp for 4 hr. The product (**4**) (0.035 g), mp 237–238° (from $CHCl_3$), $[\alpha]_D$ + 27.5°, MS: *m/e* 444 (M^+), $C_{30}H_{52}O_2$. IR ν_{max} cm^{-1}. 3500 (OH). NMR: δ 3.20 (1H, *q*, $J_{ax/ax}$ 9 Hz, $J_{ax/eq}$ 7 Hz, C-3αH). It formed a monoacetate (**5**), mp 253–254° (from $CHCl_3$–MeOH), $[\alpha]_D$ + 21.7°, MS: *m/e* 486 (M^+), $C_{32}H_{54}O_3$, IR ν_{max} cm^{-1}: 3500 (OH), 1720, 1270 (OAc), NMR: δ 4.47 [1H, *q*, $J_{ax/ax}$ 9 Hz, $J_{ax/eq}$ 7 Hz (C-3αH), 2.04, 3H, *s* ($OCOC\underline{H}_3$)].

Oxidation of **4**. **4** (0.025 g) was treated with Jones' reagent. The product (0.02 g), mp 223–225°, was identical with **1**.

Dehydration of **1**. **1** (0.03 g) was refluxed with $POCl_3$ (0.2 ml) and C_5H_5N (25 ml) for 2 hr. The product (0.023 g), mp 169–171° (from petrol), $[\alpha]_D$ + 57.0°, IR ν_{max} cm^{-1}: 1700 (C=O), 3080, 1045, 885 (>C=CH_2), was identical with lupenone (**6**).

Partial synthesis of lupane-3β,20-diol (**4**). Lupenyl acetate (0.05) was treated with *m*-chloroperbenzoic acid (0.2 g) in $CHCl_3$ (150 ml) at 0° for 6 hr to give plates of 20,29-epoxylupan-3β-yl acetate (**7**) (0.04 g), mp 238–240° (from ether), $[\alpha]_D$ + 24.0°, MS: *m/e* 484 (M^+), $C_{32}H_{52}O_3$, IR ν_{max} cm^{-1}. 1730, 1250 (OAc), 880 (epoxy), NMR: δ 2.62 (2H, *s* ), 2.03 (3H, *s*, $OCOCH_{30}$), 4.47 (1H, *q* $J_{ax/ax}$ 9 Hz, $J_{ax/eq}$ 7 Hz, C-3αH). Compound **7** (0.03 g) was then refluxed with $LiAlH_4$ (0.3 g) in dry Et_2O for 18 hr. The product (0.024 g), mp 223–225° (from $CHCl_3$–MeOH), was identical with **4**.

Reduction of **2**. **2** (0.03 g) was refluxed with $LiAlH_4$ (0.5 g) in dry Et_2O (25 ml) for 4 hr. The product (0.025 g), mp 236–238°, IR ν_{max} cm^{-1}: 3500 (OH), was identical with **3**.

Wolff–Kishner reduction of **2**. **2** (0.01 g), NaOH (0.2 g) and hydrazine hydrate (0.2 ml) in diethylene glycol (50 ml) was heated at 120° for 1 hr, then at 210° for 7 hr. The product was treated with $(MeCO)_2O$ (20 ml) and C_5H_5N (1 ml) at room temperature for 3 hr to give plates (0.03 g), mp 247–249°, IR ν_{max} cm^{-1}: 1740, 1255 (OAc), identical with 3β-acetoxylupane (**8**).

Acetylation of **3**. **3** (0.025 g) was acetylated at room temp to give plates of **9** (0.025 g), mp 191–193° (from petrol), $[\alpha]_D$ + 71.1°. (Found: M^+ 528. Calc. for $C_{34}H_{56}O_4$: M^+ 528), IR ν_{max} cm^{-1}: 1730, 1250 (OAc).

Acid isomerization of **7**. The epoxide **7** (0.05 g) in $CHCl_3$–MeOH (1:1) (100 ml) was treated with conc. HCl (1 ml) at room temp for 6 hr. The product (0.04 g), mp 225–228° (from $CHCl_3$), was identical with **2**

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