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TRITERPENOIDS OF *PTEROCARPUS SANTALINUS*: CONSTITUTION OF A NEW LUPENE DIOL

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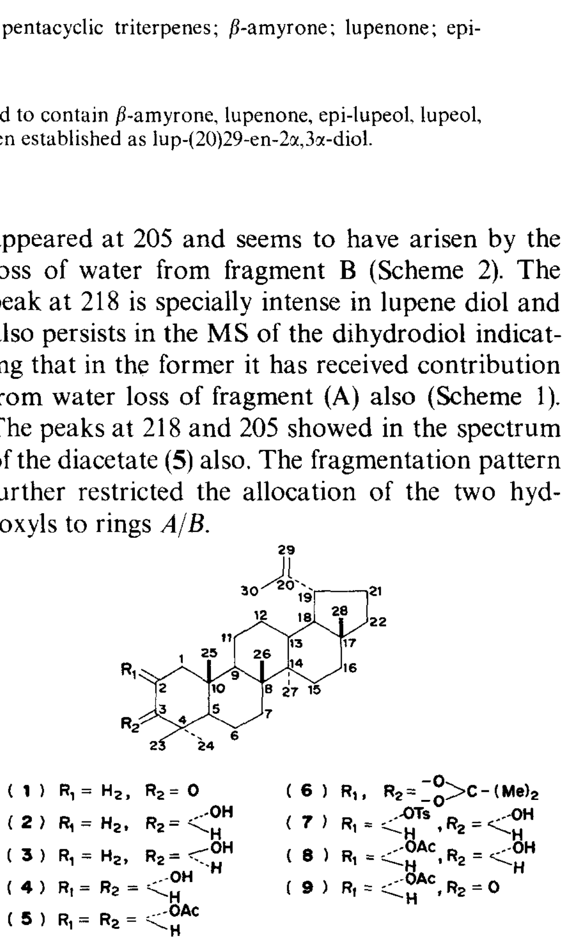
Key Word Index—*Pterocarpus santalinus*; Leguminosae; pentacyclic triterpenes; β-amyrone; lupenone; epi-lupeol; lupeol; lup-(20)29-en-2α,3α-diol.

Abstract—The bark of *Pterocarpus santalinus* has been found to contain β-amyrone, lupenone, epi-lupeol, lupeol, sitosterol and a new lupene diol whose constitution has been established as lup-(20)29-en-2α,3α-diol.

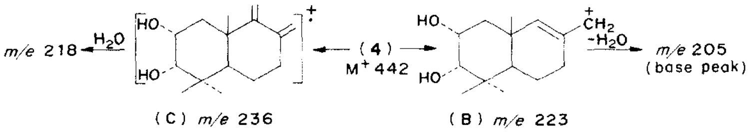
In an earlier publication [1] we described the sesquiterpenoids of *Pterocarpus santalinus* heartwood. Investigation of the bark has now led to the isolation of six triterpenoids.

The light petroleum extract on column chromatography gave β-amyrone, lupenone (**1**), epi-lupeol (**2**), lupeol (**3**) and sitosterol. The chloroform extract on similar treatment gave, as major component, a new triterpene (**4**), m.p. 225–6°, $C_{30}H_{50}O_2$. ν_{max} indicated hydroxyl(s) (3540 cm^{-1}) and exo $=CH_2$ (880, 1640 cm^{-1}). NMR showed six tertiary methyls (δ 0·88, 0·91, 0·93, 1·02, 1·11 and 1·15, 3H each, *s*), a vinylic methyl (δ 1·65, 3H, *s*), two hydroxylic protons (δ 2·30, 2H, *s*), two carbinol methine protons at δ 3·45 (1H, *d*, *J* 2·5 Hz) and 4·05 (1H, m, W/2 21·0 Hz) and exo $=CH_2$ (δ 4·50 and 4·65, 1H each, *d*, *J* 1·5 Hz). Catalytic hydrogenation yielded a dihydro derivative. In its NMR, the exo $=CH_2$ and vinylic methyl signals were replaced by two additional tertiary methyls, indicating an isopropylidine group in the en-diol (**4**). Acetylation of the diol (**4**) and the dihydrodiol gave their corresponding diacetates.

All the above data suggested lup-20(29)-en-diol structure and this was substantiated by the MS of the diol and its derivatives. The former showed diagnostically important peaks at 442 (M^+), 427 (M–Me), 424 (M–H_2O), 409 (M–Me–H_2O), 236 (fragment A), 223 (B), 218 (C), 205 (B–H_2O), and 189 (D). The peaks as 218 and 189 showed that rings *D* and *E* are the same as in lupeol [2]. The base peak for the diol (**4**) and the dihydrodiol appeared at 205 and seems to have arisen by the loss of water from fragment B (Scheme 2). The peak at 218 is specially intense in lupene diol and also persists in the MS of the dihydrodiol indicating that in the former it has received contribution from water loss of fragment (A) also (Scheme 1). The peaks at 218 and 205 showed in the spectrum of the diacetate (**5**) also. The fragmentation pattern further restricted the allocation of the two hydroxyls to rings *A*/*B*.

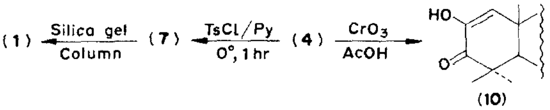


The diol (**4**) was attacked by periodate and formed an acetonide (**6**) indicating the presence of the two hydroxyls on vicinal carbon atoms. This was also supported by the formation of a diosphenol (**10**, Scheme 2) by CrO_3–AcOH oxidation. In its NMR, one olefinic proton at δ 6·32 indicated the presence of –C(OH)–CH_2 group in the diol and thus ruled out the possibility of ring B being hydroxylated. In ring *A*, the choice of C-2 and C-3



Scheme 1.

made from biogenetic considerations was also in agreement with the observed multiplicity of the carbinol methine signals of the diol (**4**) now attributable to the C-3 and C-2 protons respectively. Partial tosylation of the diol gave a monotosylate (**7**). Its NMR had C-3 proton signal of the diol unchanged indicating it to be 2-tosyloxy, 3-hydroxy compound. It was unstable and under the conditions of silica gel column chromatography and prolonged tosylation gave lupenone (**1**). This change involved easy elimination of the tosyloxy group along with C-3 proton followed by ketonization of C-3 hydroxyl (Scheme 2) and thus confirmed the location of the hydroxyls at C-2 and C-3 as well as the lup-(20)29-ene skeleton of the diol. A similar change is probably responsible for the base peak at 205 in the MS of the diol and the dihydrodiol which is the same as in lupenone [2].



Scheme 2.

Partial acetylation of the diol yielded 2-acetoxy, 3-hydroxy compound as shown by its NMR which had only the C-2 protons signal of the diol shifted downfield to δ 5·29 (m). On Jones' oxidation it afforded 2-acetoxy, 3-oxo-lupene (**9**). NMR of the latter displayed C-2 proton as a quartet of equal intensities centered at δ 5·63 and involved in diaxial (J 13·0 Hz) and axial–equatorial (5·9 Hz) coupling with C-1 protons. This showed that the C-2 proton was axial and hence the hydroxyl equatorial (α) [4, 5]. This was also supported by the $J_{\text{vic.}}$ (13 Hz) of C-1 equatorial proton. The axial (α) configuration of C-3 hydroxyl then followed from the small J value of the C-3 proton signal in the NMR of the diol and the diacetate [6].

Thus the full structure of the new diol is lup-(20)29-en-2α, 3α-diol (**4**). Though other epimeric triterpene-2,3 diols are known, α-orientation of both the hydroxyls at C-2 and C-3 is rather uncommon and the only other triterpenes with C-10 methyl and belonging to this class are 12-en-28-oic acids of ursane [7] and oleanane [8] series.

EXPERIMENTAL

All m.ps were recorded on Koffler block. NMR spectra were recorded using TMS as internal reference. Light petrol. refers to fraction, b.p. 60–80°.

Extraction and isolation. The bark (3 kg) was powdered and extracted by boiling successively with (1) light petrol., (2) $CHCl_3$ and (3) EtOH. The light petrol. extract (1) was conc and chromatographed over silica gel. Light petrol. fractions were rechromatographed on Ag^+/SiO_2 (10%) using the same eluent and the two compounds that separated crystallized from MeOH as needles m.p. 179° and 172°. Both gave + ve LB test and were identified as β-amyrone (200 mg) and lupenone (300 mg) respectively by comparison with authentic samples (TLC, m.p., IR). Light petrol. C_6H_6 (1:1) fractions yielded epi-lupeol (500 mg) that crystallized from MeOH as needles m.p. and m.m.p. 210–11°, identical with an authentic sample. Light petrol. C_6H_6 (1:9) eluate yielded lupeol (700 mg) that crystallized from MeOH as needles m.p. and m.m.p. 214–15°, identical with an authentic sample. C_6H_6 eluate gave sitosterol (200 mg) that crystallized from MeOH as needles m.p. 138°, identical with an authentic sample. The $CHCl_3$ extract (2) on chromatography on silica gel yielded small quantities of the above compounds. Further elution with $CHCl_3$ gave lupene diol (**4**, 700 mg); it crystallized from $CHCl_3$–hexane (1 : 3) as long needles, m.p. 225–6°; $[\alpha]_D$ + 25·4 (C 0·23, $CHCl_3$) (Found: C, 81·9; H, 10·9. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%) $\nu_{\max}^{\text{KBr}}$: 880, 1640 (=CH_2), 1356 (gem.-dimethyl), 3540 cm^{-1} (OH). NMR ($CDCl_3$) has fully been described in the text. MS: *m/e* (%) 442 (73), 427 (18), 424 (15), 409 (15), 236 (12), 223 (79), 218 (60), 205 (100), 203 (47), 189 (75). The diacetate crystallized from MeOH as needles, m.p. 180°, $[\alpha]_D$ + 42·0° (C 0·39, $CHCl_3$) (Found: C, 77·7; H, 10·4. $C_{34}H_{54}O_4$ requires: C, 77·5; H, 10·3%) $\nu_{\max}^{\text{nujol}}$: 880, 1648 (=$CH_2$), 1245, 1745 cm^{-1} (–OCOMe). NMR (CCl_4, δ): 8·80, 0·83, 1·00 (9H), 1·25 (*s*, 6 ter. methyls), 1·65 (*s*, 20-Me), 1·85 and 2·09 (3H *s*, each, 2 × –OCOMe), 4·50 and 4·65 (1H each, *d*, J 1·5 Hz, 29-H_2), 4·90 (1H, *d*, J 2·5 Hz, 3β-H) and 5·22 (*m*, $W_{1/2}$ 20·0 Hz, 2β -H). MS: *m/e* (%) 526(35), 466 (12), 423 (8), 391 (10), 320 (20), 307 (8), 218 (20), 205 (30), 189 (33), 43 (100).

Lupane-2α,3α-diol. The diol (**4**, 75 mg) dissolved in EtOAc (8 ml) was hydrogenated over PtO_2 for 6 hr. The dihydrodiol (72 mg), crystallized from MeOH as needles, m.p. 255–6°, $[\alpha]_D$ −14° (C, 0·48, $CHCl_3$) (Found: C, 80·8; H, 12·2. $C_{30}H_{52}O_2$ requires: C, 81·0; H, 11·8%) $\nu_{\max}^{\text{nujol}}$: 3560 cm^{-1} (OH), NMR $CDCl_3$, δ): 0·71, 0·81, 0·90, 0·92, 1·05 and 1·10 (*s*, 6 ter. methyls), 0·75 and 0·85 (3H each, *d*, J 1·2 Hz, 20–Me); 2·00 (2H, *s*, 2-OH, disappeared on D_2O shaking), 3·45 (1H, *d*, J 2·5 Hz, 3β-H) and

4·05 (1H, *m*, W/2 21·0 Hz, 2β -H) MS: *m/e* (%) 426 (M^+-18, 20), 383 (8), 223 (40), 220 (5), 218 (17), 217 (45), 205 (100), 204 (40), 191 (40), 177 (30), 148 (10). The diacetate crystallized from MeOH as needles, m.p. 140°, $[\alpha]_D$ $-32°$ (C 0·25, $CHCl_3$), (Found: C, 76·7; H, 11·1. $C_{34}H_{56}O_4$ requries: 77·2; H, 10·7%) ν_{max}^{nujol}: 1250, 1759 ($-OCOCH_3$). NMR (CCl_4, δ): 0·71, 0·91 (9H), 1·10, 1·30 (*s*, 6 ter. methyls), 0·75 and 0·86 (3H each, *d*, *J* 2·0 Hz, 20-Me), 1·95 and 2·13 (3H each, *s*, 2 × $-OCOCH_3$), 4·95 (1H, *d*, *J*2·5 Hz, 3 β -H) and 5·22 (*m*, W/2 21·0 Hz, 2 β -H).

Lup-20(29)-*en*-2α,3α-*acetonide* (**6**). The diol (50 mg) in dry Me_2CO (1 ml) was added to the solution of *p*-toluenesulphonic acid (18 mg) in Me_2CO (0·5 ml), and kept at room temp. for 1 hr. The acetonide was purified by preparative TLC (neutral Al_2O_3, C_6H_6); it crystallized from MeOH as leaflets (40 mg), m.p. 99°, $[\alpha]_D$ $+49·4°$ (C 0·92, $CHCl_3$) (Found: C, 82·0; H, 11·2. $C_{33}H_{54}O_2$ requires: C, 82·1; H, 11·2%.) ν_{max}^{KBr}: 880 ($=CH_2$), 858, 1057, 1111, 1160, cm^{-1} (acetonide). NMR (CCl_4, δ): 0·75, 8·50, 9·50, 1·00, 1·25 (6H) (*s*, 6 ter. methyls), 1·40 (6H, *s*, methyls of acetonide group), 1·66 (3-H, *s*, 20-Me), 3·58 (1H, *d*, *J* 4·0 Hz, 3β H), 4·00 (m, W/2 15 Hz, 2β-H) and 4·50 and 4·65 signals as described for the diacetate (**5**).

Diosphenol (**10**): The en-diol (**4**, 80 mg) in Me_2CO (5 ml) was treated with CrO_3–AcOH (30 mg of CrO_3 in 1 ml of AcOH, diluted to 4 ml), at 5–10° for $\frac{1}{2}$ hr, diluted with water and extracted with ether, The residue left on removal of ether was purified by column chromatography over silica gel. C_6H_6 eluate gave diosphenol as gummy material (45 mg) which could not be crystallized; it gave +ve ferric reaction; λ_{max}^{EtOH}: 271 nm (ϵ 7590), $\lambda_{max}^{EtOH-KOH}$: 313 nm (ϵ 6000), $\lambda_{max}^{EtOH-HCl}$: 271 nm (ϵ 7600). ν_{max}^{film}: 881, 1652 ($=CH_2$), 3548 cm^{-1} (OH). NMR ($CDCl_3$, δ): 0·80, 0·95 (6H), 1·00 (6H), 1·20 (*s*, 6 ter. methyls), 1·66, 4·50 and 4·65-signals as described for (**5**) and 6·32 (1H, *s*, 1-H).

Lup-(20)29 *en*-2α-*tosyloxy*, 3α-*ol* (**7**). The diol (100 mg) in $CHCl_3$ (1 ml) was treated with a solution of tosyl chloride (70 mg) in pyridine (1 ml) at 0° for 1 hr. The product was first chromatographed over silica gel column. C_6H_6 eluate crystallized from MeOH as rods, m.p. 170°, identical with an authentic sample of lupenone (50 mg) (TLC, m.p., IR). $ChCl_3$ eluate yielded unchanged diol (10 mg) m.p. 224–6°. In another experiment the partial-tosylation product was subjected to TLC (silica gel) for purification. The monotosylate did not crystallize, $[\alpha]_D$ $+22°$ (C 0·8, $CHCl_3$) ν_{max}^{KBr}: 1175, 1190 (tosyl ester), 1360, 3550 cm^{-1} (OH). NMR (CCl_4, δ): 0·80 (6H), 0·82, 0·90, 1·10 (6H) (*s*, 6 ter. methyls), 1·65 (3H, *s*,20-Me), 2·50 (3H, *s*, Me of tosyloxy group), 3·45 (1H, *d*, *J* 2·4 Hz, 3 β -H), 4·50 and 4·65-signals as described for (**5**) and 7·5 (5H, *m*, aromatic protons).

The diol (50 mg) was also treated with tosyl chloride and pyridine at room temp. overnight. Crystallization of the product from MeOH yielded rods (15 mg), m.p. 171–2°, identical with authentic lupenone.

Lup-(20)29-*en*-2α-*acetoxy*, 3α-*ol* (**8**). The diol (100 mg) was treated with Ac_2O/Py at 0° for 1 hr. The monoacetate crystallized from MeOH as colourless needles m.p. 247–8°, $[\alpha]_D$ $+39°$ (C 0·4, $CHCl_3$). (Found: C 79·4; H, 10·6. $C_{32}H_{52}O_3$ requires: C 79·3; H 10·8%.) ν_{max}^{KBr}: 882 ($=CH_2$),1258, 1748 ($-OCOCHMe$), 3548 cm^{-1} (OH). NMR ($CDCl_3$, δ): 0·82, 0·91, 1·00 (6H), 1·05, 1·10 (*s*, 6 ter. methyls) 1·66 (3H, *s*, 20-Me), 2·10 (3H, *s*, $-OCOCH_3$) 3·45 (1H, *d*, 2·5 Hz, 3 β-H), 4·50 and 4·65-signals as described for the acetate (**5**) and 5·29 (1H, *m*, W/2 20 Hz, 2β -H).

Lup-20(29)-*en*-2α-*acetoxy*,3-*one* (**9**): The monoacetate (60 mg) in $MeCO_3$ (2 ml) was treated with excess of Jones' reagent for 1 hr, and the product isolated by extraction with ether. Removal of ether gave ketol acetate (**9**) which crystallized from MeOH as needles, m.p. 255°, $[\alpha]_D$ $+43·3°$ (C 1·2, $CHCl_3$). ν_{max}^{nujol}: 882 ($=CH_2$), 1258, 1748 ($-OCOCMe$), 1725 cm^{-1} (cyclohexanone). NMR ($CDCl_3$, δ): 0·83, 0·98, 1·15 (6H), 1·23, 1·32 (*s*, 6 ter. methyls), 1·67 (3H, *s*, 20-Me), 2·13 (3H, *s*, $-OCOCH_3$), 2·29 (1H, *q*, $J_{1\beta,2\beta}$ 5·9 Hz, $J_{1\beta,1\alpha}$ 12·5 Hz, 1β-H), 4·52 and 4·63 (1H each, *d*, *J* 1·5, 29-H_2) and 5·63 (1H, *q*, $J_{2\beta,1\beta}$ 5·9 Hz, $J_{2\beta,1\alpha}$ 13·0 Hz, 2β-H).

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