

Further C₃₂ Triterpenoids from *Neolitsea pulchella*

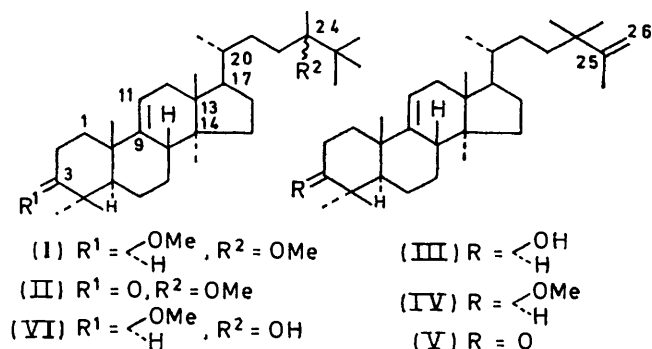
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Three further C₃₂ triterpenoids isolated from the stems of *Neolitsea pulchella*, have been shown to be 3 β ,24 ξ -dimethoxy-24,25-dimethyl-lanost-9(11)-ene (I), 24 ξ -methoxy-24,25-dimethyl-lanost-9(11)-en-3-one (II), and 24,24-dimethyl-lanosta-9(11),25-dien-3 β -ol (III). Compounds (I) and (II) are new.

THE structures of three new C₃₂ triterpenoids isolated by column chromatography of the light petroleum extract of the stems of *Neolitsea pulchella* were found to be 3 β -methoxy-24,24-dimethyl-lanosta-9(11),25-diene (IV), 24,24-dimethyl-lanosta-9(11),25-dien-3-one (V), and 3 β -methoxy-24,25-dimethyl-lanost-9(11)-en-24 ξ -ol (VI).¹ A

¹ W. H. Hui, K. Luk, H. R. Arthur, and S. N. Loo, *J. Chem. Soc. (C)*, 1971, 2826.

further investigation of a larger quantity of a similar extract led to the discovery of three further related minor triterpenoids (I)—(III). The order of elution of the compounds from the column using light petroleum \rightarrow light petroleum-benzene was (IV), (I), (V), (II), (VI), and (III).



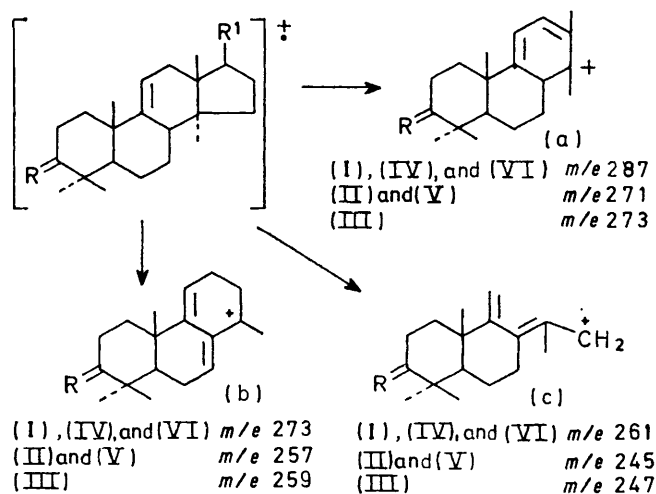
All compounds (I)—(III) gave purple colouration in the Liebermann-Burchardt test. From spectral data a trisubstituted double bond was indicated in each [ν_{\max} , 3050, 862, and 814 cm^{-1} , δ 5.20—5.27 (1H, m)]. Compounds (I) and (II) showed ether linkages at ν_{\max} , 1100 and 1110 cm^{-1} respectively while (II) also revealed a carbonyl group in a six-membered ring (ν_{\max} , 1720 cm^{-1}). In compound (III) a hydroxy (ν_{\max} , 3500 cm^{-1}) and a vinylidene group (ν_{\max} , 3090, 1640, and 890 cm^{-1}) were indicated.

Compound (I), $\text{C}_{34}\text{H}_{60}\text{O}_2$ (M^+ , 500), m.p. 248—250°, [α_D +100.0°, showed ten methyl groups at δ 0.64—1.05, and two methoxy-groups, one of which (at C-3) was probably equatorial [δ 3.40 (3H, s) and 2.60—2.80 (1H, ca. q)] [cf. signals for (IV) and (VI)]¹ and the other [δ 3.30 (3H, s)] was presumably tertiary, since there was no evidence of another methine proton. The latter was proved to be neither in the rings nor at C-20 by mass spectral fragments at m/e 327 (M^+ — side chain — 2H), 287, 273, and 261 [species (a), (b), and (c) in Scheme 1] which also indicated a $\Delta^{9(11)}$ double bond.¹ Further peaks at m/e 255, 241, and 229 showed loss of MeOH from (a), (b), and (c) respectively. These fragments were identical with those from (IV) and (VI) (Scheme 1). Thus a 3-methoxy-group was indicated. A *t*-butyl group at the end of the side chain in compound (I) was indicated by ions at m/e 443 (M^+ — C_4H_9) and 411 (M^+ — C_4H_9 — MeOH) (cf. peaks for (VI) at m/e 429 and 397¹). Thus compound (I) was probably related to (VI) with a methoxy- instead of a hydroxy-group at C-24. Methylation of compound (VI), gave a small yield (due to steric hindrance) of a compound which was identical with (I). Compound (I) is thus 3 β ,24 ξ -dimethoxy-24,25-dimethyl-lanost-9(11)-ene.

Compound (II), $\text{C}_{33}\text{H}_{56}\text{O}_2$ (M^+ , 484), m.p. 178—181°, [α_D +89.1° had signals at δ 3.30 (3H, s) with no signal at δ 2—3 (tertiary methoxy-group) and 0.69—1.22 (10 \times

Me); m/e 311, 271, 257, and 245 [(M^+ — side chain — 2H), (a), (b), and (c) respectively (see Scheme 1)] which indicated the identity of the ring system with that of compound (V).¹ Thus the carbonyl function was presumably at C-3 and the methoxy-group in the side chain. Fragments at m/e 427 (M^+ — C_4H_9) and 395 (M^+ — C_4H_9 — MeOH) again indicated a terminal *t*-butyl group in the side chain. Compound (II) was thus postulated to be 24 ξ -methoxy-24,25-dimethyl-lanost-9(11)-en-3-one, and this was confirmed by reducing it with sodium borohydride to give the 3 β -alcohol as the main product, which was then methylated to give a compound identical with (I).

Compound (III), $\text{C}_{32}\text{H}_{54}\text{O}$ (M^+ , 454), m.p. 219—221°, [α_D +70.0°, had an isopropenyl group giving signals at δ 4.70 (2H, m) and 1.65 (3H, s), probably a C-3 equatorial hydroxy-group [δ 1.56 (1H, s, exchangeable) and 3.00—3.34 (1H, ca. q)], and eight methyl groups (δ 0.62—1.02). The mass spectrum of compound (III) had peaks at m/e 421 (M^+ — Me — H_2O), 313 (M^+ — side chain — 2H), 273 (a), 259 (b), 247 (c), 255 [(a) — H_2O], 241 [(b) — H_2O], and 229 [(c) — H_2O]. All the above data



SCHEME 1

agreed well with those for 3 β -hydroxy-24,24-dimethyl-lanost-9(11),25-diene prepared by sodium borohydride reduction of compound (V);¹ mixed m.p.s of the two compounds and of their acetates showed no depression. The product of methylation of (III) was identical with 3 β -methoxy-24,24-dimethyl-lanosta-9(11),25-diene (IV).¹

Since the first report² of a C_{32} triterpenoid six such related compounds have now been obtained, all from *Neolitsea pulchella*. Only two other naturally occurring C_{32} triterpenoids have been reported; namely cyclo-neolitsin [3 β -methoxy-24,24-dimethyl-9(19)-cyclo-lanost-25-ene] from *Neolitsea dealbata*³ and cyclobalanone [24,24-dimethyl-9(19)-cyclo-lanost-25-en-3-one] from *Quercus glauca*.⁴ It is noteworthy that compounds with an additional C-25 methyl group such as (I), (II), and

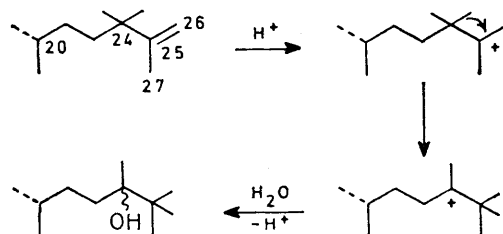
² H. R. Arthur and S. N. Loo, *Tetrahedron Letters*, 1967, 3767.

³ R. Ritchie, R. G. Senior, and W. C. Taylor, *Austral. J. Chem.*, 1969, 22, 2371.

⁴ Y. Tachi, S. Taga, Y. Kamano, and M. Komatsu, *Chem. and Pharm. Bull. Japan*, 1971, 19, 2193.

(VI) have never been reported elsewhere, and that friedelin and friedelan-3 β -ol were the only triterpenoid constituents found in the local species of *Quercus glauca*.⁵

The biosynthesis of dimethyl triterpenoids has not been studied, although pathways for monoalkylation at C-24 and formation of the Δ^{25} double bond have been extensively investigated.⁶ It could be postulated that simple extensions of such pathways might lead to the formation of the 24,24-dimethyl-25-ene side chain. Protonation of the terminal double bond at C-26 followed by migration of one of the methyl groups at C-24 to C-25, and finally addition of water to C-24 with loss of a proton would lead to the 24-hydroxy-24,25-dimethyl derivative (Scheme 2).



SCHEME 2

EXPERIMENTAL

N.m.r. spectra were recorded for solutions in deuteriochloroform with a Hitachi model R-20 (60 MHz) instrument, i.r. spectra for Nujol mulls with a Perkin-Elmer 337 spectrophotometer and mass spectra with a Hitachi-Perkin-Elmer RMS-4 spectrometer with a direct inlet. Optical rotations were taken for solutions in chloroform. Alumina (B.D.H. analytical grade; activity II) was used for column chromatography. Light petroleum had b.p. 60–80°. Identities of all compounds were proved by mixed m.p., i.r., and n.m.r. spectral comparisons with authentic samples.

Isolation of Compounds.—Milled air-dried stems (30 kg) of *Neolitsea pulchella* were extracted twice with light petroleum at room temperature for one week and the combined concentrated extracts were chromatographed on alumina (3 kg). Elution with light petroleum yielded prisms of 3 β -methoxy-24,24-dimethyl-lanosta-9(11),25-diene (IV) (6.1 g), m.p. 215–217°, $[\alpha]_D^{25} +90.0^\circ$ (*c* 1.0). Continued elution with light petroleum gave a solid which after several recrystallizations from chloroform–methanol afforded prisms of 3 β ,24 ξ -dimethoxy-24,25-dimethyl-lanost-9(11)-ene (I) (0.15 g), m.p. 248–250°, $[\alpha]_D^{25} +100.0^\circ$ (*c* 1.1) (Found: C, 81.4; H, 11.9. $C_{34}H_{60}O_2$ requires C, 81.5; H, 12.1%), ν_{max} 3050, 1640, 1100, 862, and 814 cm^{-1} . Further elution with the same solvent yielded 24,24-dimethyl-lanosta-9(11),25-dien-3-one (V) (3.2 g), m.p. 170–172°, $[\alpha]_D^{25} +60.2^\circ$ (*c* 1.0). Elution with light petroleum–benzene (4:1) gave a solid, which after several recrystallizations from chloroform–methanol yielded plates of 24 ξ -methoxy-24,25-dimethyl-lanost-9(11)-en-3-one (II) (0.07 g), m.p. 178–181°, $[\alpha]_D^{25} +89.1^\circ$ (*c* 0.7) (Found: C, 81.9; H, 11.8. $C_{33}H_{56}O_2$ requires C, 81.8; H, 11.6%), ν_{max} 3050, 1720, 1110, 862, and 814 cm^{-1} . Elution with light petroleum–benzene

(7:3) afforded 3 β -methoxy-24,25-dimethyl-lanost-9(11)-en-24 ξ -ol (VI) (0.21 g), m.p. 275–177°, $[\alpha]_D^{25} +51.0^\circ$ (*c* 1.0). Further elution with light petroleum–benzene (7:3) gave needles which on repeated recrystallization from chloroform–methanol yielded 24,24-dimethyl-lanosta-9(11),25-dien-3 β -ol (III) (0.25 g), m.p. 219–221°, $[\alpha]_D^{25} +70.0^\circ$ (*c* 1.0) (Found: C, 84.5; H, 11.8. Calc. for $C_{32}H_{54}O$: C, 84.5; H, 12.0%), ν_{max} 3500, 3090, 3050, 1640, 1040, 890, 862, and 814 cm^{-1} , identical with the product from the reduction of 24,24-dimethyl-lanosta-9(11),25-dien-3-one (V).¹

Methylation of Compound (VI).—Potassium (0.10 g), compound (VI) (0.05 g), and methyl iodide (2 ml) in benzene were boiled under reflux for several hours under nitrogen.¹ The solid isolated was chromatographed on a column of silica gel (5 g). Elution with light petroleum–benzene (9:1) gave a small quantity of a solid which was recrystallized twice from chloroform–methanol to give prisms of 3 β ,24 ξ -dimethoxy-24,25-dimethyl-lanost-9(11)-ene (2 mg), m.p. 247–250°, ν_{max} 3050, 1640, 1100, 862, and 814 cm^{-1} , identical with compound (I). Further elution of the column with light petroleum–benzene (4:1) yielded unchanged (VI) (0.035 g), which was then used to obtain a further supply of compound (I).

Reactions of Compound (II).—To a solution of compound (II) (0.04 g) in dioxan (20 ml) was added a solution of sodium borohydride (0.02 g) in aqueous dioxan (1:1; 10 ml). The mixture was kept at 20° for 1 h. The dried product was chromatographed on alumina (5 g). Elution with light petroleum–benzene (9:1) gave unchanged compound (II) (0.01 g). Elution with light petroleum–benzene (3:2) yielded a crystalline solid (0.02 g) which was crystallized from chloroform–methanol, then dissolved in benzene, and methylated with methyl iodide and potassium in benzene.¹ The product was chromatographed on silica gel (3 g) to give in the earlier fractions prisms (0.004 g), m.p. 247–250°, ν_{max} 3050, 1640, 1100, 862, and 814 cm^{-1} , identical with compound (I). The later fractions gave unchanged material (0.006 g).

Reactions of Compound (III).—(a) *Acetylation.* Compound (III) (0.05 g) was refluxed with acetic anhydride and pyridine for 3 h. The product in light petroleum was filtered through a column of silica gel, and recrystallized from light petroleum–acetone to give plates of the acetate (0.03 g), m.p. 236–239°, ν_{max} 3090, 3050, 1740, 1640, 1250, 890, 862, and 817 cm^{-1} , δ 1.67 (s, C=CMe), 4.67 (m, C=CH₂), 5.20 (m, C=CH), 4.30–4.48 (*ca.* q, 3-H), 2.02 (OAc), and 0.62–1.05 (9 \times Me), identical with 24,24-dimethyl-lanost-9(11),25-dien-3 β -yl acetate.¹

(b) *Methylation.* Compound (III) (0.05 g) was methylated and the product was purified in the usual manner to yield prisms (0.02 g), m.p. 215–217°, ν_{max} 3090, 3050, 1640, 1100, 890, 862, and 814 cm^{-1} , identical with compound (IV).

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⁵ W. H. Hui, C. T. Ho, and C. W. Yee, *Austral. J. Chem.*, 1965, **18**, 2043.

⁶ T. W. Goodwin, *Biochem. J.*, 1971, **123**, 29²