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STUDIES ON INDIAN MEDICINAL PLANTS. PART XXXVI[1]: NEW D:E-CIS NEOHOPANE DERIVATIVES FROM ALANGIUM LAMARCKII

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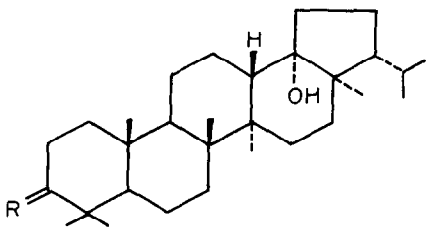
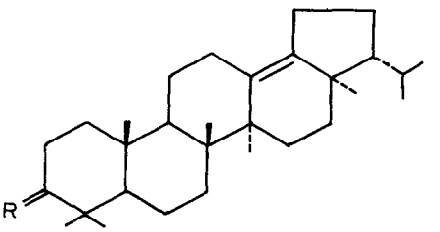
We earlier reported[2] the isolation of three uncharacterised minor triterpene alcohols from the leaves of Alangium lamarckii Thw. (Alangiaceae). The present communication deals with the structure elucidation of triterpenes B and C, now redesignated as isoalangidiol (I) and alangidiol (II) respectively.





I R = βH, αOH
II R = αH, βOH
III R = βH, αOAc
IV R = αH, βOAc
V R = O

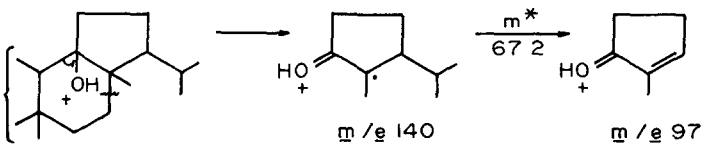
VI R = βH, αOAc
VII R = αH, βOAc
VIII R = O
IX R = βH, αOH
X R = αH, βOH

Both the compounds, molecular formula $C_{30}H_{52}O_2$ (M^+ 444), showed negative TNM test and with acetic anhydride-pyridine at 100° formed the respective mono-acetates ($C_{32}H_{54}O_3$; M^+ 486) III and IV which still exhibited the hydroxyl band in the IR spectrum. The NMR spectra (100 MHz; $CDCl_3$) revealed the acetoxy function in III to be axial, adjacent to a methylene

(C_3-H at δ 4.63, t, $\underline{W}_{1/2}$ = 6 Hz), while that in IV to be equatorial in a similar environment (C_3-H at δ 4.48, q, $\underline{W}_{1/2}$ = 16 Hz). No signal for C$\underline{H}$OH was however observed. Therefore the second hydroxy group, resistant to acetylation, was inferred to be tertiary in nature in both the triterpenes.

Jones oxidation of I formed the hydroxy-ketone V, $C_{30}H_{50}O_2$ (M^+ 442), ν_{max}^{Nujol} 3500, 3450-3200 (br), 1710 cm^{-1}. The presence of a 3-keto group in it was indicated by a positive Zimmermann test and supported by an M-86 peak in the mass spectrum analogous to some 4,4-dimethyl-3-keto steroids[3]. The smooth reduction of V with KBH_4 in ethanol at room temperature to a mixture of II (88%) and I (12%) confirmed the triterpene alcohols to be epimeric at C-3 with the more stable equatorial hydroxyl in II.

The presence of an isopropyl group in I-V was indicated by the prominent loss of 43 mass units from the molecular ion, M-18 or M-60 in the mass spectra of the compounds. The peaks at $\underline{m}/\underline{e}$ 207 and 189 in the spectrum of I or at $\underline{m}/\underline{e}$ 205 in that of V, known to involve A/B rings, however ruled out the migrated hopane systems like arborane. Again base peak(s) at $\underline{m}/\underline{e}$ 140 and/or 97 with respective compositions of $C_9H_{16}O$ and C_6H_9O (high resolution) which characterised all the spectra indicated the most probable location of the hydroxy group to be at C-18 in a lupane/neohopane or at C-17 in a hopane/isohopane skeleton. The genesis of the two ions could be rationalised as follows (for neohopane system):



$\underline{m}/\underline{e}$ 140 $\underline{m}/\underline{e}$ 97

Phosphorus oxychloride-pyridine (at 100° for 3 hr) smoothly dehydrated III, IV and V to two products each, resolved by chromatography over argentised silica gel. Only the major components (90%) were obtained in sufficient quantities and characterised respectively as VI, VII and VIII. Hydrolysis of VI and VII yielded the corresponding alcohols IX and X. Physical constants of

all the compounds are given in Table 1. The mass spectrum of the major product (VI) from III showed prominent peaks at m/e 205 and 218 indicative of a 13(18) double bond[4], while the dehydroketone was proved to be identical with hopenone-II (VIII)[5] containing ca. 2% of hopenone-I[6]. These results evidently locate the tertiary hydroxy group in the triterpenes at C-18 in the neohopane system, the small amount of hopenone-I being conceivably formed by isomerisation. The α configuration of the hydroxy group could be deduced from the ease of dehydration and the 1:3 diaxial relationship between this function and the 14-methyl group was revealed by the pyridine induced downfield shift[7] (at least 0.27 ppm) of a methyl signal in the NMR spectrum[8] of III.

Table 1: Physical constants of the triterpenes and their derivatives

Str.no.	I	II	III	IV	V	VI[b]	VII[b]	VIII[6]	IX[b]	X[b]
M.p.(°C)	226	228	215	262	216	176	231	170	224	220
$[\alpha]_D$(deg.)[a]	+36.5	+49.6	±0	+39.4	+65.6	-	+27.9	+48.1	-16.3	-

[a]In $CHCl_3$. [b]Perhaps containing ca. 2% of an isomer[6].

Alangidiol and isoalangidiol were therefore concluded to be the hitherto unreported 18α-B':A'-neogammacerane-3β,18-diol (II) and its 3α-epimer (I) respectively. They thus appear to represent the first examples of the naturally occurring D:E-cis neohopane derivatives and belong to the rare group of pentacyclic triterpenes with a free hydroxyl group at the ring juncture. They could conceivably arise through hydroxylation at the C-18 carbonium ion of the biogenetic intermediate from which neomotiol (B':A'-neogammacer-12-en-3β-ol) and other migrated hopanes may also be derived.

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References and Notes

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5. H.Fazakerley, T.G.Halsall and E.R.H.Jones, J.Chem.Soc., 1877 (1959).
6. From the VPC data, the IR (CS_2), NMR ($CDCl_3$ at 60 MHz), ORD and mass spectra, the dehydroketone was indistinguishable from hopenone-II (VIII). On the other hand, its considerable higher melting point (170°) than that of the latter (lit[5] m.p. 152-154°) and the distinct IR spectra of the two samples in KBr were difficult to explain. These discrepancies however disappeared when 2% of the higher melting hopenone-I, the most probable impurity, was added to hopenone-II. It is remarkable that such a small amount of contaminant would result in elevation of melting point and quite different IR spectrum in crystalline state. We are greatly indebted to Prof.H.Ageta of Shōwa College of Pharmaceutical Sciences, Tokyo, Japan for the detailed comparison.
7. P.V.Demarco, D.Doddrell, E.Farkas, B.L.Mylari and E.Wenkert, J.Am.Chem.Soc. 90, 5180 (1968).
8. The 60 MHz NMR spectrum of III in $CDCl_3$ showed the lowest field methyl signal at δ 1.18. The spectrum in pyridine exhibited signals for seven methyl groups between δ 0.88-1.10 besides two sharp signals at δ 1.40 and 1.45. We prefer to ascribe the latter chemical shift to the deshielded methyl since in the comparable system of lupan-3α-yl acetate a broad signal centred at δ 1.37 ppm in the NMR spectrum in $CDCl_3$ sharpened to a peak at δ 1.40 when the spectrum was run in pyridine.