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TERPENE ALCOHOLS OF HELICHRYSUM DENDROIDEUM

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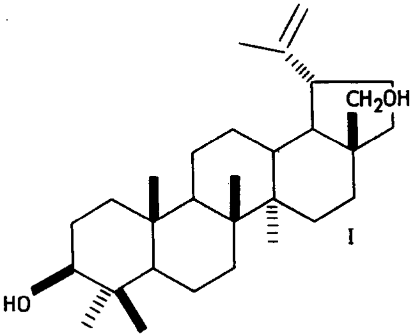
The Australian Compositae, Helichrysum dendroideum N. H. Wakefield is a shrub common to the Eastern coast of Australia and characterized by an especially heavy coating of leaf wax (ca. 9%). A chloroform extract of leaves was saponified and the neutral fraction chromatographed over alumina; all the isolations were followed by gas chromatography on a 3% OV-17 column. The first eluates yielded a series of straight chain hydrocarbons identified by GLC (mainly the C_{27}, C_{29} and C_{31} homologs) and compound A which was identified as the triterpene diol, betulin (I), by comparison with an authentical sample (1). Repeated chromatography over alumina and over silica gel impregnated with silver nitrate afforded a series of diterpene alcohols consisting of five isomeric diols, $C_{20}H_{32}O_2$, a triol, $C_{20}H_{32}O_3$, and a tetrol, $C_{20}H_{34}O_4$. The molecular formulas were established by high resolution mass spectrometry (2) of the alcohols and of their trimethylsilyl derivatives. The formulas, melting points and rotations of the terpenes are recorded in Table I. Two of the compounds (B and D) were identified as known tetracyclic diterpenes; the structure of the three other diterpene diols is the subject of this communication.

The IR spectrum of diterpene B showed an absorption band at 875 cm^{-1} characteristic of a vinylidene group. The presence of this function was confirmed in the NMR (2) by a broad singlet at 4.76 ppm (2H). In addition the NMR revealed two quaternary methyl groups (0.99, 1.21 ppm) and an axial hydroxymethyl (3) AB quartet at 3.28, 4.18 ppm (J = 11 cps). The physical characteristics of this diol (Table I) and of its diacetate correspond to those of (-)kaur-16-ene-3α,19-diol (II) and its diacetate previously isolated from a Beyeria species (4).

TABLE I

Compound	Formula		m.p.°C	$[\alpha]_D^{\circ}$	Diacetate m.p.°C
A	$C_{30}H_{50}O_2$	(I)	259-260	+17 (pyrid)	221-222
B	$C_{20}H_{32}O_2$	(II)	183-184	-73 (EtOH)	112-113
C	$C_{20}H_{32}O_2$	(III)	149-150	+39 (EtOH)	103-104 ($[\alpha]_D$ + 30° (EtOH))
D	$C_{20}H_{32}O_2$	(IV)	179-180	+52 ($CHCl_3$)	
E	$C_{20}H_{32}O_2$	(V)	168-170	+36 (EtOH)	
F	$C_{20}H_{32}O_2$	(VI)	193-195	-37 (EtOH)	
G	$C_{20}H_{32}O_3$		216-217	-32 (EtOH)	
H	$C_{20}H_{34}O_4$		279-280	-40 (EtOH)	



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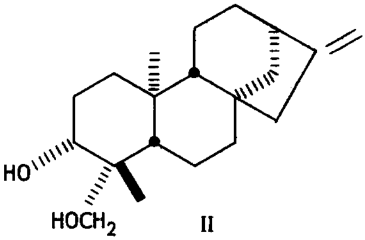

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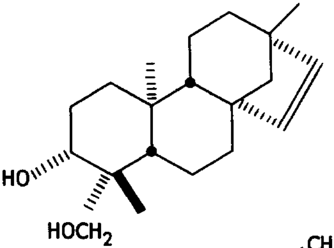

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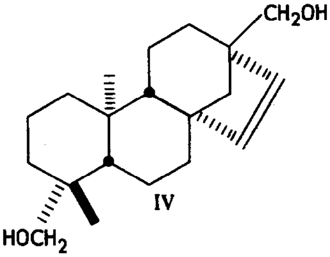

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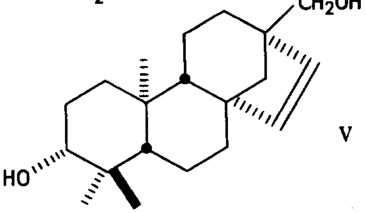

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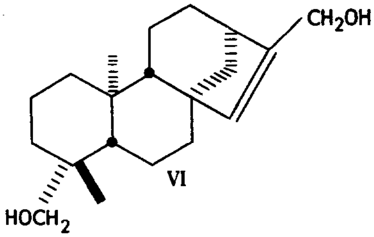

VI

Although a direct comparison of II and B was not possible their NMR spectra were found to be identical.

The NMR of C and of its diacetate suggested a stachene skeleton. An AB quartet characteristic of a cis-disubstituted double bond appeared at 5.45, 5.65 ppm (J = 5.5 cps) in the diol and 5.48, 5.68 (J = 5.5) for the diacetate. The spectrum of the diol displayed three quaternary methyls at 0.70, 1.00 and 1.23 ppm which shifted in the diacetate to 0.77 and 1.01 (6H). By analogy with diol B an axial 4-hydroxymethyl group was suspected: a typical AB quartet appeared at 3.22, 4.20 ppm (J = 11 cps) and in the diacetate the corresponding methylene quartet was at 4.10, 4.43 (J = 12). In the spectrum of the diacetate a one proton multiplet at 4.58 ppm (W1/2 15 cps) can be attributed to an axial proton geminal to a secondary acetoxy group (4,5).

The stachene nucleus was demonstrated by conversion of the diol to isostevane (8) (stachane, beyerane) through reduction of its benzylthioether. As in the case of diol B (4) the presence of a 1,3-glycol system was indicated by formation of an ethylidene derivative (m.p. 120-121°) and by oxidation by Jones reagent to a ketoaldehyde (m.p. 109-110°, NMR signal at 9.67 ppm characteristic of an axial (6) aldehyde group) which was converted to a norketone (m.p. 78-79°) in alkali. Ghisalberti and Jefferies (7) had obtained 3α,19-ethylidenedioxystach-15-ene from beyerol (8) [(+)stach-15-ene-3α,17,19-triol]. This compound proved identical (mixed m.p., NMR, GLC) with the ethylidene derivative of C and therefore established the structure of C as (+)stach-15-ene-3α,19-diol (III).

The NMR of diol D had features characteristic of a stachene derivative: an AB quartet corresponding to a cis-disubstituted double bond (5.55, 5.85 ppm, J = 6 cps) and two quaternary methyls (0.73, 0.97 ppm). It also revealed an AB quartet (3.42, 3.78 ppm, J = 10.5 cps) that could be assigned to an axial hydroxymethyl group (3) and a two proton singlet at 3.48 ppm attributed to the methylene of another primary alcohol group. Catalytic hydrogenation furnished a dihydro derivative m.p. 205-206°. At this point a direct comparison confirmed that D was IV: (+)stach-15-ene-17,19-diol (17-hydroxymonogynol). This diol had previously been isolated from Erythroxylon monogynum by two independent groups (9) and its structure is well established.

The few milligrams of pure diols E and F obtained by preparative gas chromatography precluded a chemical proof of structure at this time. However, the NMR spectra resulting from the summation of 25 scans (CAT) were sufficiently informative to assign tentative structures to both compounds: that of a stachene derivative (V) for E and of an isokaurene (VI) for F.

The spectrum of E exhibited a typical AB quartet for a cis-disubstituted double bond (5.60, 5.83 ppm, J = 5.5 cps), a two proton singlet at 3.50 ppm which can be attributed to the 17-hydroxymethyl group and sharp signals for three quaternary methyls (0.76, 0.80, 0.99 ppm). The higher field signal is assigned to the C_{10} stachene-type methyl while the two other absorptions are consistent with a 4,4-gem dimethyl group adjacent to a 3-equatorial hydroxyl group (10).

The NMR spectrum of F is in good agreement with structure VI for this diol. The two quaternary methyls appeared at 0.96 and 1.03 ppm and an AB quartet at 3.52, 3.84 ppm (J = 10.5 cps) is characteristic of an axial hydroxymethyl group. In addition the spectrum displayed a two proton doublet at 4.27 ppm (J = 1 cps) and a broad one proton signal at 5.40 ppm. These signals are consistent with the 17-allylic hydroxymethyl group and the 15-vinyl proton respectively. The presence of an allylic alcohol function was confirmed by manganese dioxide oxidation of a milligram of F in chloroform at room temperature to a compound of molecular formula $C_{20}H_{30}O_2$ (mass spectrometry).

This plant is noteworthy in producing a triterpene of one enantiomeric series and diterpenes of the opposite configuration. The diterpenes III, IV and V constitute hydroxylation patterns of the (+)stach-15-ene nucleus while II and VI reflect analogous oxidations of the (-)kaur-16-ene system. This appears to be the first time that kaurene and stachene derivatives have been found in the same plant and their coexistence strongly supports the common pimaradiene intermediate postulated by Wenkert in his theory on the biogenesis of tetracyclic diterpenes (11).

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