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BIOGENETICALLY SIGNIFICANT SESQUITERPENOIDS FROM *RUBUS ROSIFOLIUS* OIL[1]

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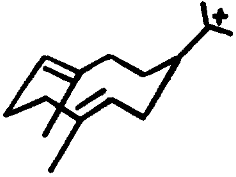
The importance of cyclodecadienes (1) and 4,10-*epi*-eudesmanes (2) as precursors in the biogenesis of the nootkatane (3) and spirovetivane (4) sesquiterpenoids has been stressed in recent literature[2-9]. Moreover, the isolation of increasing numbers of *epi*-eudesmanes from natural sources[5-19] has established this "unusual"[10] configuration as a naturally occurring structural group. This communication reports the isolation of the desisopropyl sesquiterpene pregeijerene (5) and novel isomers of eudesmol and bicyclogermacrene from the steam-volatile leaf oil of the Australian native raspberry *Rubus rosifolius* (Rosaceae). Chemical, spectroscopic and biogenetic evidence suggest that the eudesmol, rosifoliol, has structure (6) and that the bicyclogermacrene is (7). Structure (6) has previously been proposed[2] as a possible precursor of the nootkatones α-vetivone (8) and calarene (9).



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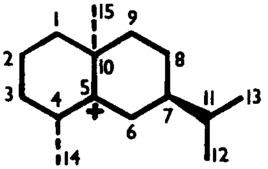

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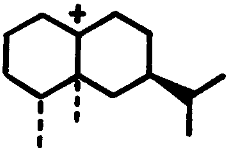

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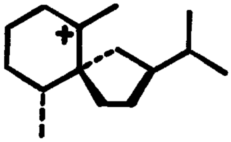

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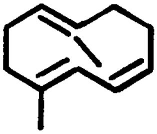

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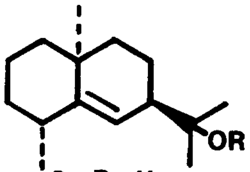
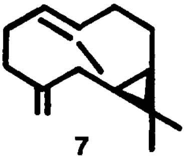


6 R = H
10 R = $CONHC_{10}H_7$



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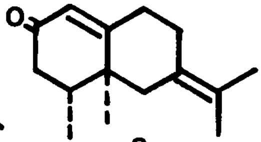

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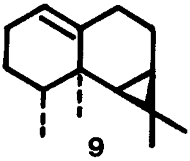

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Rosifoliol, the major component (41%) was filtered from the oil of several shrubs collected in the Royal National Park near Sydney. Recrystallisation yielded needles m 84°, $[\alpha]_D$ + 105°, $C_{15}H_{24}$ (M^+ 204.1876). The presence of OH in the ir (3300 cm^{-1}) and pmr (δ1.36) spectra indicated a tertiary alcohol where the molecular ion was not detected[20]. This was confirmed by the formation of a naphthylurethane derivative (10) m 158°, $[\alpha]_D$ + 155°, $C_{26}H_{33}NO_2$ (M^+391.249) indicating a $C_{15}H_{26}O$ formula for rosifoliol.

Dehydrogenation of rosifoliol yielded eudalene (11), hydrogenation yielded a dihydroderivative not identical to dihydroeudesmol (12)[21] and dehydration yielded (-)-δ-selinene (13) ($[\alpha]_D$ -212^0)[11], thus establishing rosifoliol as a 10-*epi*-eudesmol. Pmr studies with double irradiation and europium shift experiments indicated a selin-5-en-11-ol structure. The spectrum contained one unresolved vinylic doublet at δ5.44 (ΔEu 10.0 ppm/mol.equiv.) showing coupling (J 3.2 Hz) to the proton resonating at δ2.03 (ΔEu 14.8). As the latter signal experienced $Eu(dpm)_3$ shifts similar in magnitude to the *gem*-dimethyl signal at δ1.26 (ΔEu 13.7) the vinylic proton can be assigned to the C6 position as in (6). The ^{13}C nmr proton decoupled and off-resonance spectra supported this structure and shifts (Table 1) were assigned using chemical shift theory and published shifts of similar compounds.

Table 1. ^{13}C Chemical Shifts of Rosifoliol (6).

Carbon position	1*	2	3	4	5	6	7	8	9*	10	11	12†	13†	14†	15
Off-reson. mult.	t	t	t	d	s	d	d	t	t	s	s	q	q	q	q
δ	39.6	17.7	33.6	38.8	133.2	121.0	45.4	20.3	41.3	34.4	73.5	27.2	27.4	27.8	22.4

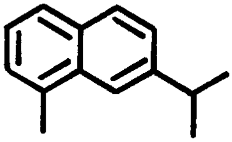
*† cannot distinguish between these resonances.

The low $J_{4,6}$ values obtained for rosifoliol (6) and its naphthylurethane (10) (≈0.0 and 0.5 Hz respectively), indicate, when compared with the analagous Δ^4-3-oxo-steriod series (14)[22], a near planar relationship for H4-C4-C5-C6-H6. The W $h/_2$ value of 7 Hz for the C4 proton when the C14 protons are irradiated suggests that the C4 proton lies *gauche* to both of the C3 protons. These conditions are satisfied by two conformers: the C14β methyl boat form (15) and the C14α methyl chain form (16). As the cyclohexane boat conformer is less stable except when favoured for steric reasons[23] and as the 4β,10α combination is rare in nature, (16) is favoured.

Some authors[2] would assume a 7β configuration despite the existence of 7α-substitution (e.g. laevojuneol, (17)[17,18]). The $J_{6,7}$ values of 3.2 for rosifoliol (6) and 3.0 Hz for the α-naphthylurethane (10) indicate a typical cyclohexene system with a dihedral angle of approximately 43^0[24]. $J_{7,8e}$ and $J_{7,8a}$ (4.7 and 6.5 Hz) for (10) indicate that the C7 proton lies *gauche* to both the C8 protons suggesting that the isopropanol group is either *pseudo*-axial α (18) or *pseudo*-axial β (19). The former is eliminated on the grounds that the bulky α-substituent is sterically incompatible with the C10 α methyl group (this is not the case with (17) where the substituent group would be equatorial to the fully saturated ring). With rosifoliol, the steric interactions of the saturated system have been relieved[9] by unsaturation at C5.

Thus the structure and absolute configuration of rosifoliol can be represented as 4R, 7R, 10S-selin-5-en-11-ol (6) pending confirmation by synthesis.

Pregeijerene (5) constituting 20% of the oil was removed by extraction with aqueous $AgNO_3$[25]. The remaining fraction contained a $C_{15}H_{24}$(M^+ 204.1870) hydrocarbon (12% of the oil) $[\alpha]_D$ -13^0(crude) showing the presence of a terminal methylene group (887, 3070 cm^{-1}, δ4.76,4.88), a trisubstituted double bond (δ5.25 1Hbm) with one methyl substituent (δ1.57 3Hd J 1Hz), a cyclopropane ring (δ0.8-0.9) and a *gem*-dimethyl group (δ0.97 3Hs, 0.99 3Hs). These results suggest a bicyclogermacra-1(10),4(14)-diene structure (7) which in view of the epimeric nature of rosifoliol (6) and the conformation of bicyclogermacra-1(10),4(5)-diene(20)[26] is most likely to have conformation (21).



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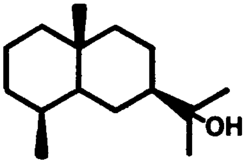

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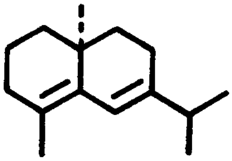

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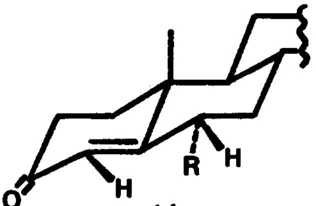

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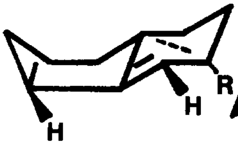

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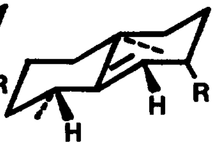

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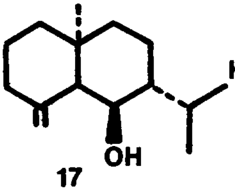

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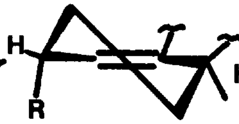

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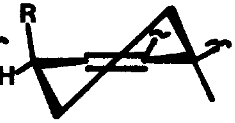

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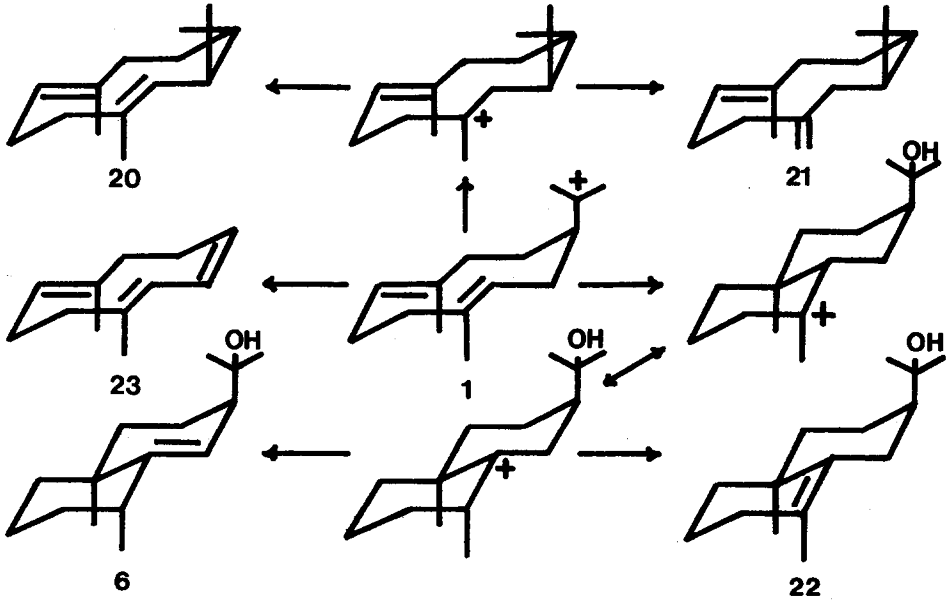
The formation of these three *R. rosifolius* constituents and the related bicyclogermacra-1(10),4(5)-diene (20) and 10-*epi*-γ-eudesmol (22)[19] can be accounted for with currently accepted biogenetic theory from carbocation (1) as shown in Scheme 1. Such a pathway would imply a different conformer (23) for pregeijerene than that obtained from *Geijera parviflora*[27].



Scheme 1

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