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STUDIES OF AUSTRALIAN SOFT CORALS. XXIII
THE CO-OCCURRENCE OF BICYCLOGERMACRENE AND LEMNACARNOL DERIVATIVES IN *PARERYTHROPODIUM FULVUM*.

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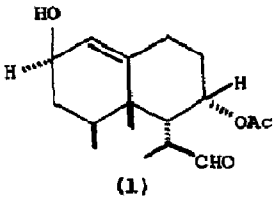
Abstract: The isolation of oxygenated bicyclogermacrenes, likely precursors of several classes of sesquiterpenes, is reported from the soft coral *Parerythropodium fulvum*.

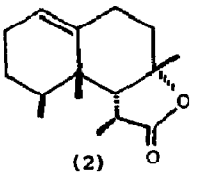
We have recently reported a number of new sesquiterpenes containing the nardosinane (e.g. 1)[1], lemnalan (e.g. 2)[2] and aristolane (e.g. 3)[3] skeletons derived from the genera *Lemnalia* and *Paralemnalia* (family Nephtheidae). In several instances, these compounds have been accompanied by the hydrocarbon germacrene C (4), although one might have expected a bicyclogermacrene (5) to be the more immediate precursor.[4] We now report the isolation of such a precursor.

Dichloromethane extraction of the yellow encrusting soft coral, *Parerythropodium fulvum* (Forskal 1775) (family Alcyoniidae)[5], collected on Holbourne Island off Bowen, North Queensland, afforded a 0.5% extract. Rapid silica gel chromatography afforded four sesquiterpenes (6), (7), (8), and (9). The least polar component, whose structure we show to be the bicyclogermacrene acetate (6)[6], could be converted to the related alcohol (7)[7] by hydrolysis or prolonged chromatography on silica gel. However, the less abundant alcohol (7) was present in the extract and was not an artifact of isolation. The other naturally occurring components were lemnacarnol (8)[8], and its 2-keto derivative (9)[9] as deduced spectroscopically and confirmed by comparison with authentic samples. Considerable amounts of 7-methoxylemnacarnol (10)[10] arose from methanolysis of lemnacarnol during its purification, while 2-*epi* lemnacarnol (11)[11] was the quantitative product from sodium borohydride reduction of the 2-keto compound (9).

The structure of the bicyclogermacrenes (6) and (7) remained to be elucidated. The acetate (6) (0.001%)[6] could be hydrolysed to the alcohol (7) which was reacetylated to give (6) without rearrangement. Proof of structure was obtained using the crystalline alcohol (7)[7], $C_{15}H_{24}O$, which contained two double bonds by ^{13}C n.m.r. and was thus bicyclic. The presence of a cyclopropane ring bearing two methyl groups also followed from the ^{13}C n.m.r. Two doublet signals at 30.5, 29.2 ppm collapsed to singlets on selective irradiation of proton resonances near δ1. Cyclopropyl methines are the only CH resonances to occur in this region. The presence of a high field carbon *singlet* at 20.7 ppm and two sharp methyl resonances at δ1.04 (15.4 ppm) and δ1.12 (26.1 ppm) confirmed the nature of the remaining substitution on the cyclopropane ring in (7) [and (6)][12]. Careful proton double resonance experiments at 100 MHz enabled a chain of coupling to be established between the cyclopropyl methines and the other ring protons (Table 1). This tabulation shows the direct interrelation, by means of coupling constants, between signals attributed to the chain of atoms H10(1) to H3 and from H4 to H8 (including attached methyl



(1)



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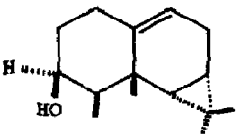
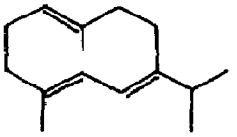
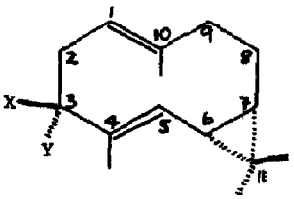


(3)



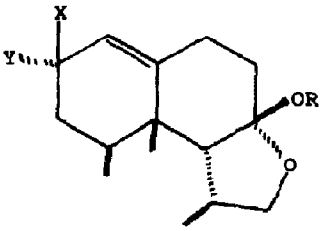
(4)



(5) X = Y = H

(6) X = OAc; Y = H

(7) X = OH; Y = H



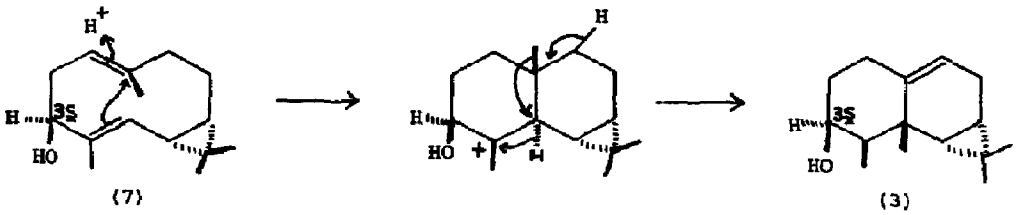
(8) X = H, Y = OH
R = H

(9) X , Y = O

(10) X = H, Y = OH
R = CH_3

(11) X = OH, Y = H
R = H

Scheme 1



(7) (3)

TABLE 1: ^{1}H and ^{13}C n.m.r. values for (7) including shift reagent data.

Atom	^{13}C, ppm (m)	^{1}H, δ, m, J Hz	Δν Eu(fod)$_3$ Hz
C10	141.8 (s)	-	
10-CH_3	21.1 (q)	1.52 d, 1.5	28
C1	122.3 (d)	4.90, m, 8.5, 8.5, 1.5	28
C2	37.2, 34.7, 27.0 (t)	2.28, m, 8.5, 8.5, 6.7, 8.5	112
C3	79.7 (d)	4.06, dd, 6.7, 8.5	139
C4	152.9 (s)		
4 - CH_3	10.9 (q)	1.67, d, 1.5	75
C5	124.0 (d)	4.46, m, 11.4, 1.5	28
C6	30.5 (d)	1.32, dd, 11.4, 8.7	33
C7	29.2 (d)	0.63, m, 8.7	
C8	37.2, 34.7, 27.0 (t)	1.84, m	
C9	37.2, 34.7, 27.0 (t)	2.4, m	
C11	20.7 (s)		
11 -CH_3	15.4 (q)	1.04	3
11 -CH_3	26.1 (q)	1.12	6

groups). Micro-ozonolysis[13] afforded 3-hydroxy-4-oxopentanal identical by g.c.m.s. with an authentic sample[14] enabling the two fragments to be joined at the C3 - C4 bond. Since the molecule was bicyclic, the ring must be a germacrene ring and structure (7) follows.

The relative stereochemistry about the cyclopropane ring could be inferred from the magnitude of the appropriate coupling constants. Thus the observed $J_{6,7}$ = 8.7 Hz implies a *cis* stereochemistry[15], and the large $J_{5,6}$ = 11.4 Hz value implies a *trans* periplanar relationship between these protons . Evidence derived from ^{13}C n.m.r. chemical shifts of vinyl methyl groups leading to the double bond geometry in (7) is consistent with the E-4,5 double bond (4-methyl, 10.9 ppm), the shielding being caused by an adjacent oxygen substituent (see refs. 3 and 14), and the chemical shift of the 10-methyl resonance (21.1 ppm) compares with the value found in germacrene C (20 ppm)[15] which contains E double bonds[16]. Information on the relative configuration of (7) was available from the shift reagent studies reported in Table 1. Considering the secondary alcohol group as the site of complexation with $Eu(fod)_3$, one observes a neglegible shift in the cyclopropyl *gem* dimethyl resonances whereas the methine proton H6 is relatively strongly shifted. If the cyclopropane ring was on the same side of the germacrene ring as the alcohol group, *one* of the methyl resonances would be expected to be shifted quite strongly. The presence of a significant shift in H6 and near zero shifts in the *gem*-dimethyl groups are taken as evidence for the *trans* relationship of the alcohol group to the cyclopropane ring. The secondary alcohol carbon was shown to have the 3S absolute configuration as determined by the Horeau procedure[17]. The absolute stereochemistry of (7) is as represented, (3S)-*trans* 3-hydroxybicyclogermacrene.

When one examines the absolute configuration of the further cyclised aristolane derivative (3), isolated from *Lemnalia humesi*[3], it is obvious that cyclisation of the bicyclogermacrene (7) and methyl migration will yield the aristolane (3) with the correct absolute stereochemistry (Scheme 1). Allylic oxidation at the alternative C2 position, followed by cyclisation and methyl migration, could afford 2-hydroxyaristolane derivatives, the cyclopropane ring of which could be oxidatively opened to give the lemnacarnol derivatives present in this coral.

While the isolation of lemnacarnol from this coral is unexpected on taxonomic grounds, it is not particularly surprising in the light of the ubiquity of symbiotic zooxanthellae in most soft corals.

ACKNOWLEDGEMENTS: We thank the Australian Research Grants Committee for financial support.

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2. B.F. Bowden, J.C. Coll, and S.J. Mitchell, *Aust.J.Chem.*, in press (Part XIX).
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4. T.K. Devon and A.I. Scott, "Handbook of Naturally Occurring Compounds, Vol II", (Academic Press, New York, 1972) p.56.

5. Tentative classification: Registered sample number G12639. Queensland Museum, Gregory Terrace, Brisbane 4000, Australia.

6. *(3S)-trans 3-acetoxybicyclogermacrene* (6): oil, $[\alpha]_D$ -25.1° (c, 0.2), νmax 1725 cm^{-1}; ^1H n.m.r: (CCl_4) δ0.59 (m, 1H), 1.04 (s, 3H), 1.11 (s, 3H), 1.48 (s, 3H), 1.58 (s, 3H), 2.00 (s, 3H), 4.45 (d, J 11 Hz, 1H), 4.85 (m, 2H). ^{13}C n.m.r: 169.9 (s), 142.5 (s), 126.1 (s), 125.4 (d), 121.2 (d), 80.7 (d), 37.1 (t), 31.4 (t) 30.5 (d), 29.1 (d), 27.0 (t), 26.1 (q), 21.1 (q,q), 20.8 (s), 15.4 (q), 11.4 (q); mass spectrum: $^m/_e$ $M^{\cdot+}$ 262 (42%).

7. *(3S)-trans 3-hydroxybicyclogermacrene* (7): m.p. 116-117°C; $[\alpha]_D$ -49.5° (c, 0.11); Found: C, 81.7; H, 11.2. $C_{15}H_{24}O$ requires C, 81.8; H, 11.0%; νmax3300-3200 cm^{-1}; ^1H + ^{13}C n.m.r. see Table 1: mass spectrum $M^{\cdot+}$ 220 (55%), 202 (15), 187 (17), 161 (36), 149 (23), 147 (30), 137 (32), 123 (33), 121 (43), 119 (30), 110 (36), 109 (100). Horeau determination rotation - 0.083°.

8. We thank Professor B. Tursch for an authentic sample of lemnacarnol. By t.l.c. it was identical with our sample but more than 50% decomposed. Lemnacarnol (8) m.p. 160-164° (lit 160-163°), $[\alpha]_D$ -123.8° (C, 0.1); value for partially decomposed standard: $[\alpha]_D$ -50° (C, 0.05).

9. D. Daloze, J.C. Braekman, P. Georget, and B. Tursch, *Bull.Soc.Chim.Belg.*, 86, 47 (1977). This component was only partially described: *2-oxolemnacarnol* (9): λmax (EtOH) 241.5 nm (ε 12,300); ^1H n.m.r: ($CDCl_3$) δ1.03 (m, 3H), 1.11 (d, J 6 Hz, 3H), 1.29 (s, 3H), 3.52 (t, J 8 Hz, 1H), 3.90 (t, J 8 Hz, 1H), 4.64 (bs, 1H), 5.95 (s, 1H); ^{13}C n.m.r: 198.0 (s), 169.2 (s), 126.3 (d), 107.2 (s), 71.9 (t), 58.2 (d), 41.8 (s), 41.3 (t), 38.4 (d), 35.4 (d), 32.5 (t), 28.2 (t), 18.7 (q), 17.3 (q), 15.7 (q).

10. *7-methoxylemnacarnol*: oil, $[\alpha]_D$ -34° (c, 0.16), νmax 3240 (br) cm^{-1}; ^1H n.m.r. (CCl_4): δ0.85 (d, J 6 Hz, 3H), 0.99 (s, 3H), 1.07 (s, 3H), 3.18 (3H, s), 3.24 (t, J 8 Hz, 1H), 3.73 (t, J 8 Hz, 1H), 3.91 (m, 1H), 5.46 (d, J 4Hz, 1H); ^{13}C n.m.r. ($CDCl_3$): 145.1 (s), 123.8 (d), 110.4 (s), 72.5 (t), 63.6 (d), 57.8 (d), 48.5 (q), 40.7 (s), 37.4 (d), 35.9 (t), 29.2 (t), 29.0 (d), 26.7 (t), 19.7 (q), 17.8 (q), 16.0 (q), mass spectrum. $^m/_e$ $M^{\cdot+}$ 266 (21%).

11. *2-epi-lemnacarnol*, m.p. 128-130°C $[\alpha]_D$ -19.2° (C, 0.07); νmax (nujol) 3320 cm^{-1}; ^1H n.m.r. ($CDCl_3$): δ0.88 (d, J 6Hz, 3H), 1.07 (d, J 6 Hz, 3H), 1.16 (s, 3H), 3.46 (t, J 7 Hz, 1H), 3.85 (t, J 7 Hz, 1H), 4.22 (bt, J 6 Hz, 1H), 5.50 (s, 1H) mass spectrum $^m/_e$ 252 (15%), 234 (24), 219 (26), 192 (25), 190 (33), 175 (42), 161 (35), 137 (58), 136 (100). Horeau determination: rotation + 0.007°; 2R configuration.

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14. B.F. Bowden, J.C. Coll, S.J. Mitchell, G.J. Stokie, and J.F. Blount, *Aust.J.Chem.*, 31, 2035 (1978).

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16. K. Morikawa and Y. Hirose, *Tetrahedron Lett.*, 1799 (1969).

17. A. Horeau, *Tetrahedron Lett.*, 506 (1961).

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