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A SERIES OF NOVEL BICYCLIC DITERPENES FROM Dilophus prolificans (BROWN ALGA, DICTYOTACEAE)

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Metabolites from marine species have increased the number of basic diterpene carbon skeletons to such an extent that they now rival their more ubiquitous sesquiterpene relatives in both number and diversity[1,2]. Many of the more recent examples have been isolated from brown algae of the order Dictyotales and can be regarded as examples of known sesquiterpene carbocyclic skeletons with an additional *iso*-pentenyl 'starting' unit. Thus pachydictyol 'A' (1),[3] which incorporates the sesquiterpene guaiane skeleton, and dilophol (2)[4], an extension of the germacrene skeleton, are examples of an increasing number of diterpenes of which this generalisation is valid.

We now describe the isolation of four new diterpenes from the brown alga *Dilophus prolificans*** which are analogues of the sesquiterpene skeleton bicyclogermacrene of which the only reported example is the hydrocarbon (3)[5].

Extraction of various samples of the freeze-dried alga, collected on the New South Wales coast near Sydney gave a 3% dry weight extract in which the diterpene constituents (*ca*. 50%) usually consisted of varying ratios of compounds (4), (5) and (6), isolated by column and HPLC chromatography on silica gel. A single collection of the alga contained, in addition to (4), (5) and (6), the compound (7) which was readily crystallised from diethyl ether or methanol.

Certain structural features of (5) - (7) were common to each compound. Thus the ^{1}H n.m.r. (Table 1), ^{13}C n.m.r., m.s., i.r. and u.v. spectra indicated common structural units (8), (9) and (10). The functionality (10) was also supported by the addition of methanol across the Δ^5 double bond when (5) was allowed to stand in slightly basic methanolic solution. Although ^{1}H and ^{13}C n.m.r. spectroscopy indicated the units (8) and (9) to be present in (4) the -enone system (10) was absent and spectral data suggested the presence of a β-epoxyketone function from which (5) might be generated by ring opening followed by dehydration. Treatment of (4) in d_5 pyridine with a trace of sodium methoxide indeed gave (5) and the partial structure (10) could be expanded to (11) for compounds (5) to (7).

The structure of (7) was determined by single crystal X-ray analysis of a sample crystallised from diethyl ether in the space group $P\ 2_1$ with a 9.649(6) Å, b 9.230(7) Å, c 12.910(6) Å, β 107.66(4)°, Z = 2, d_{calcd} 1.092 g. cm^{-3} and μ(Cu Kα) 5.96 cm^{-1}. The intensity data were measured on a Hilger-Watts diffractometer (Ni filtered Cu Kα radiation, θ-2θ scans, pulse height discrimination). The size of the crystal used for data collection was approximately 0.18 x 0.25 x 0.53 mm; the data were not corrected for absorption. Of the 1591 accessible reflections for θ < 57°, 1467 were considered to be observed [I > 2.5σ(I)]. The structure was solved by a multiple solution procedure[6] and was refined by full matrix least squares. In the final refinement, anisotropic thermal parameters were used for the heavier atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations but their parameters were not refined. The final discrepancy indices are R = 0.055 and wR = 0.062 for the 1467 observed reflections. The final difference map has no peaks greater than $\pm$ 0.3 e A^{-3}. A stereoprojection of the molecule is shown in Figure 1. It was not possible to determine the absolute stereochemistry from X-ray data, thus all formulae represent only relative stereochemistry.

The complete structure of (4), (5) and (6) followed from a comparison of their spectral data and that of (7). ^{1}H n.m.r. data is shown in Table 1 and other relevant data is listed below.

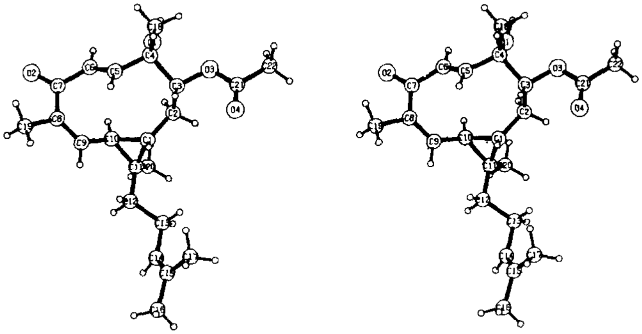
Epoxydilophone (4), $C_{20}H_{30}O_2$, was isolated as an oil; $[\alpha]_D^{20}$ + 167° (c = 0.95, $CHCl_3$). I.r., ν_{max} (film) 3400 (b), 1690 cm^{-1}. U.v., λ_{max} (MeOH) 254 (log ϵ2.91). ^{13}C n.m.r. δ($CDCl_3$) 208.3 (s), 137.4 (s), 130.9 (s), 125.6 (d), 124.3 (d), 60.5 (s), 58.2 (d), 43.6 (t), 36.7, 36.1, 33.0, 29.7, 26.4, 25.6, 25.3, 24.9, 19.7 (2C), 18.1, 17.5. Mass spectrum (70 eV) 302 (20, M^+), 287 (5), 259 (9), 233 (26), 175 (23), 135 (40), 109 (48), 107 (51), 105 (30), 84 (85) and 69 (100%).

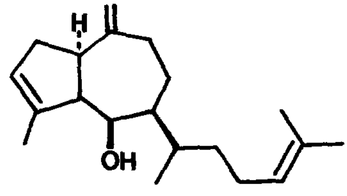
Dilopholone (5), $C_{20}H_{30}O_2$, was isolated as an oil by silica gel chromatography; $[\alpha]_D^{20}$ + 172° (c = 0.3, $CHCl_3$). I.r., ν_{max} (film) 3400 (b), 1650 cm^{-1}. U.v., λ_{max} (MeOH) 212, 240 (sh), 282 nm (log ϵ, 3.73, 3.57, 3.00). ^{13}C n.m.r. δ($CDCl_3$) 202.8 (s), 159.5 (d), 141.6 (s), 131.0 (s), 130.8 (d), 125.3 (d), 124.4 (d), 71.7 (s), 47.9 (t), 42.3 (t), 36.5 (d), 28.4, 26.9, 25.6, 25.1, 24.5, 20.4, 19.6, 17.6, 13.3. Mass spectrum (70 eV) 302 (41 M^+), 287 (3), 284 (5), 259 (13), 161 (35), 135 (45), 122 (30), 84 (42), 69 (94), 43 (100%).

epi-Acetoxydilopholone (6), $C_{22}H_{32}O_4$, was isolated as colourless needles; mp. 104-105°; $[\alpha]_D^{20}$ + 162° (c = 0.32, $CHCl_3$). I.r., ν_{max} (film) 3450 (b), 1725, 1650, 1370, 1230 cm^{-1}. U.v., λ_{max} (MeOH) 218, 242, 285 nm (log ϵ, 3.90, 3.80, 3.20). ^{13}C n.m.r. δ($CDCl_3$) 201.9 (s), 169.6 (s), 155.6 (d), 142.5 (s), 131.2 (s), 130.1 (d), 128.7 (d), 124.1 (d), 82.1 (d), 73.1 (s), 42.1 (t), 35.4 (d), 28.4, 26.6, 25.6, 25.1 (2C), 23.8, 21.0, 20.5, 17.7, 13.4. Mass spectrum (12 eV) 360 (13, M^+), 345 (8), 342 (8), 317 (22), 300 (18), 282 (15), 257 (22), 239 (20), 189 (55), 161 (80), 151 (100).

Acetoxydilopholone (7) $C_{22}H_{32}O_4$; mp. 179°; $[\alpha]_D^{20}$ - 58° (c = 0.47, $CHCl_3$). I.r., ν_{max} (KBr) 3380, 1720, 1643, 1617, 1250 cm^{-1}. U.v., λ_{max} (MeOH) 248, 299 (log ϵ, 3.54, 3.38). ^{13}C n.m.r. δ($CDCl_3$) 200.0 (s), 169.7 (s), 150.0 (d), 138.3 (d), 135.8 (s), 131.4 (s), 126.0 (d), 123.9 (d), 79.9 (d), 73.4 (s), 39.9 (d), 35.7, 33.9, 31.4, 31.0, 25.7, 25.6, 24.9, 21.0, 19.7, 18.1, 17.5. Mass spectrum (12 eV) 360 (1), 300 (1.5), 293 (2.5), 282 (1.5), 277 (3), 257 (2.5), 231 (5), 189 (30), 161 (35), 69 (100).

**R.R.I.M.P. Museum number FN 1359/000.





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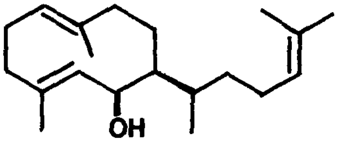

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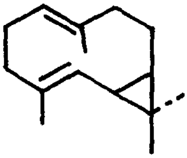

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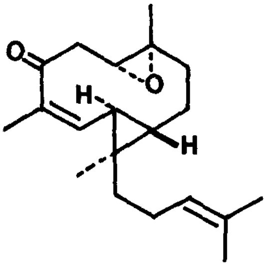

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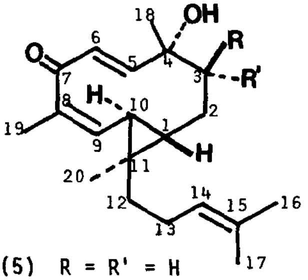
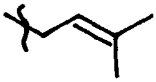


(5) R = R' = H

(6) R = OAc, R' = H

(7) R = H, R' = OAc



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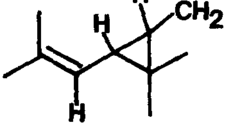

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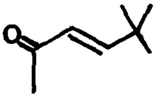

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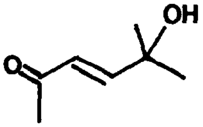

(11)

TABLE 1.

^{1}H n.m.r. spectral data of compounds (4) - (7) in $CDCl_3$ (δ values relative to TMS)

C-H	(4)	(5)	(6)	(7)
C 1-H	0.55, m	0.42, m		0.38, m
C 2-H				1.92 (1H)*, 1.56 (1H)*
C 3-H			4.50, dd, J 4, 4Hz	4.80, dd, J 10, 2Hz
C 5-H	2.48,dd,J 12,12Hz	7.20, d, J 16Hz	6.92, d, J 16Hz	6.44, d, J 16Hz
C 6-H	3.02, m	5.92, d, J 16Hz	5.98, d, J 16Hz	6.18, d, J 16Hz
C 9-H	5.18, bd, J 9Hz	5.68, bd, J 6Hz	5.60, bs, W 1/2 8Hz	5.88, bd, J 9Hz
C10-H	0.88, dd, J 9, 4Hz	0.94*	0.82*	0.90*
C14-H	5.00, bt, J 7Hz	4.96, bt, J 7Hz	4.95, bt, J 7Hz	5.06, bt, J 7Hz
C16-H	1.60, bs	1.56, bs	1.56, bs	1.60, bs
C17-H	1.68, bs	1.62, bs	1.65, bs	1.68, bs
C18-H	1.44, s	1.44, s	1.39, s	1.32, s
C19-H	1.84, bs	1.90, bs	1.90, bs	1.90, bs
C20-H	1.04, s	0.94, s	0.92, s	1.03, s
OAc			2.09, s	2.14, s

*approximate position established by double resonance experiments.

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