Dilophol, a New Ten-membered-ring Diterpene Alcohol from the Brown Alga *Dilophus ligulatus*

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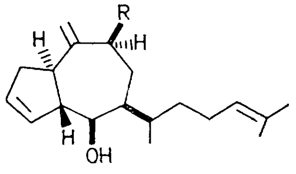
Summary From the brown alga *Dilophus ligulatus* a diterpene alcohol with a novel ten-membered-ring skeleton, dilophol (**4**), has been isolated and its structure determined by chemical and spectroscopic methods.

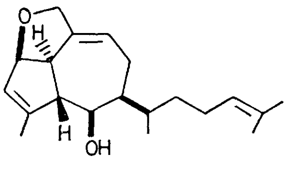
Recently some diterpenes [pachydictyol A (**1**), and dictyols A (**2**) and B (**3**)] possessing an unusual perhydroazulene skeleton have been isolated from brown seaweeds of the family Dictyotaceae.[1,2] From the alga, *Dilophus ligulatus* (Kütz.) Feldm., belonging to the same family we have now isolated a ten-membered-ring diterpene alcohol, dilophol (**4**), possibly related biogenetically to pachydictyol A and dictyols.

Chloroform extraction of freeze-dried alga, harvested from the littoral zone of the east coast of Sicily (Porto Palo), followed by repeated column chromatography of the extract allowed the isolation, in addition to pachydictyol A, of dilophol, $C_{20}H_{34}O$ (precision mass spectrometry), $[\alpha]_D$ −4·3, n_D 1·5187. The presence of the oxygen atom in a secondary hydroxy-group is inferred from an i.r. band at 3300—3100 cm^{-1}, an ion at *m/e* 272 ($M^+ - H_2O$) in the mass spectrum, and the formation of a monoacetate (**5**) [M^+, *m/e* 332; $[\alpha]_D$ −18·7; ν_{max} 1740 and 1240 cm^{-1}; δ (CCl_4) 1·93 (3H, s, AcO) and 5·52 br (1H, d, *J* 9 Hz, CHOAc)]. This hydroxyl-group must be allylic, since in the n.m.r. spectrum of (**4**) recorded in C_6D_6 (in CCl_4 the lower field region is poorly resolved), the signal of the CHOH proton, centred at δ 4·55 (*J* 9 Hz) appears as the B part (further split by coupling with 7-H, *J* 2 Hz) of an AB system, while the pertinent A part is centred in the olefinic region at δ 5·02. Other n.m.r. signals are seen at δ (CCl_4) 0·98 (3H, d, *J* 6 Hz, 11-Me), 1·46 (3H, s, 10-Me), 1·60 (6H, s, 4-Me and *trans*-15-Me), and 1·70 (3H, s, *cis*-15-Me), and δ (C_6D_6) 4·87 br (1H, 1-H) and 5·25 br (1H, t, *J* 7 Hz, 14-H).

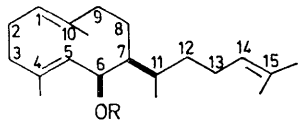
These data indicate that at least three double bonds must be present in the molecule. That the additional degree of unsaturation implied by the formula of dilophol is due to a ten-membered ring has been established by its aromatization (Se at 300 °C) to 1,4-dimethyl-7-(1,5-dimethylhex-5-enyl)-azulene. Indeed, other ten-membered-ring compounds (germacrane derivatives) are known to give by aromatization azulenes and naphthalenes.[3] The formation of the aforementioned azulene, which is identical with that obtained from pachydictyol A under the same conditions, reveals in addition the identity of the side chain and the position of the annular methyl groups. All the above data and the formation of laevulinic acid by oxidation with $KMnO_4$–$NaIO_4$ in Bu^tOH–H_2O permits the formulation of dilophol as (**4**) (without stereochemistry of the nucleus).



(1) R = H
(3) R = OH



(2)



(4) R = H
(5) R = Ac

The unusually high field of the 10-Me resonance (δ 1·46) has been attributed to transannular shielding by the 4,5-double bond. This requires a *trans* configuration of both double bonds.[4] The intramolecular nuclear Overhauser effects between 4-Me and 5-H, and 10-Me and 1-H, which were much smaller than expected for *cis* relationships,[5] accord with this postulation. On the other hand, a 12—13% enhancement of the integrated absorption of the C*H*OH signal by irradiation at the frequency of the 4-Me or 10-Me resonance indicates that the CHOH methine proton is near to these groups. These results provide evidence that the preferred conformation of the ten-membered ring matches that reported for comparable substances of established structure,[4] with the planes of both double bonds approximately perpendicular to that of the ring and a *syn* relationship between the methyl groups.

The magnitude of the coupling (*J* 2 Hz) between 6-H and 7-H reveals that the OH group and the side chain are *cis* related. This also agrees with the observation that the 11-Me experiences a rather large chemical shift (25·5% of that of the CHOH methine proton) on complexation with $Eu(fod)_3$. Accumulated results suggest that dilophol possesses the stereochemistry indicated in structure (**4**), since the alternative structure with the opposite stereochemistry at C-6 and C-7 appears unlikely considering the stereochemistry of the co-occurring and probably biogenetically related pachydictyol A.

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