DITERPENES FROM DICTYOTA DICHOTOMA

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Abstract—Two new and two known diterpenes were isolated from *Dictyota dichotoma*. The structures of the new diterpenes were elucidated from spectral and X-ray crystallographic evidence. The structures of the new compounds are related to the metabolites of *D. dichotoma* var. *implexa*.

INTRODUCTION

A number of diterpenes have been isolated from brown algae of the family Dictyotaceae [1-6]. Hirschfeld *et al.* [1] determined the structure of pachydictyol A (1), isolated from *Pachydictyon coriaceum*, by X-ray analysis. Fattorusso *et al.* [2] have subsequently described four guiane-diterpenes (2-5) from *Dictyota dichotoma* var. *implexa* and have related each of these compounds to pachydictyol A. Some of these compounds were also found in the sea hare *Aplysia depilans*, which was known to feed upon *D. dichotoma* [3]. Other diterpenes have been isolated from *Dichyota crenulata* [4], *D. flabellata* [4], *D. acutiloba* [5] and *Dilophus ligulatus* [6]. We wish to describe the isolation of two known and two new diterpenes from a sample of *D. dichotoma* collected intertidally at Overton on the Bristol Channel, U.K.

RESULTS AND DISCUSSION

The ether-soluble material from ethanol extracts of D. dichotoma (Huds.) Lamouroux was chromatographed on florisil. Selected fractions were further purified by rechromatography on silica gel to obtain four diterpenes. In order of polarity, these were pachydictyol A (1) (0.064% dry wt), dictyol B acetate (6) (0.05%), dictyotadiol (7) (0.026%) and dictyol C (4) (0.039%).

Dictyol B acetate (6), obtained as an oil, $[\alpha]_D = +59^{\circ}$ (c = 1.27), had the molecular formula $C_{22}H_{34}O_3$. The IR spectrum contained bands at 3500 (-OH) and 1740 cm⁻¹ (acetate). The PMR spectrum of 6 had an acetate singlet at δ 2.16, suggesting that 6 was a monoacetate of a diterpene diol. The PMR spectrum contained a doublet at δ 1.03 (J = 7 Hz) assigned to a secondary methyl group, singlets at 1.63, 1.71 and 1.81 assigned to vinyl methyl groups, and signals due to an α -hydroxy proton at 3.95 (m), an α -acetoxy proton at 5.16 (t, J = 7 Hz) and vinyl protons at δ 4.94 (bs), 5.00 (bs), 5.12 (t, J = 7 H) and 5.34 (bs). Reduction of the acetate 6 with lithium aluminium hydride in ether gave dictyol B (2), which was identical in all respects to an authentic sample. determined by single crystal X-ray analysis. Preliminary X-ray photographs revealed monoclinic

symmetry for dictyotadiol (7). Accurate lattice constants, determined from a least-square fit of fifteen 2θ values, were a = 12.969 (1), b = 5.784 (1), c = 13.349 (2) Å and $\beta = 110.87$ (1)°. The extinction condition (OkO, missing if k = 2n + 1) conformed to the common chiral space group P₂₁. A measured and calculated density of 1.1 g/cc indicated two molecules of composition C₂₀H₃₂O₂ in the unit cell or one per asymmetric unit.

Comparison of the PMR spectra of 2 and 6 indicated

Dityotadiol (7), mp 150–1°C, $[\alpha]_D = +1.3^\circ (c = 0.15)$, had the molecular formula $C_{20}H_{32}O_2$. The diol did not

show a molecular ion in the MS, the highest peak being

at m/e 286 (M⁺-H₂O). Since the diol was insoluble in

most solvents, the PMR spectrum was recorded in acetone-d₆. The PMR spectrum was difficult to inter-

pret, since many signals coincided or overlapped. The

vinyl protons at C-2 and C-3 gave rise to a sharp singlet

at δ 5.71, indicating that the C-2 proton was not coupled

to the proton at C-1, which appeared as a sharp doublet

at 3.20 ppm. A broad singlet at δ 4.54 was assigned to the

protons of the exocyclic methylene group. This singlet

overlapped a multiplet at δ 4.48, which was assigned to

the α -hydroxy proton. The signals at δ 1.01 (d, J = 7 Hz),

1.60 and 1.66 were assigned to the methyl groups in the side chain, while the singlet at 1.42 ppm was assigned to the methyl at C-4. The structure of dictyotadiol (7) was

that 6 must be the allylic acetate of 2.

All unique reflections with $2\theta \le 114^\circ$ were collected using monochromated CuK_x (1.54178 Å) radiation and a computer-controlled four-circle diffractometer operating in the ω -scan mode. A total of 1473 diffraction maxima were investigated in this fashion, and after correction for Lorentz, polarization, and background effects, 1278 (87 %) were judged observed ($F_0^2 \ge 3\sigma(F_0^2)$).

The angular dependence of the diffraction maxima were suppressed as they were converted to normalized structure factors. An initial set of 100 phases was obtained via a multisolution weighted tangent formula approach [7]. A substantial molecular fragment was revealed, and the remaining nonhydrogen atoms were located in a subsequent electron density synthesis [8, 9]. Full-matrix least-squares refinements with isotropic temperature factors for hydrogen atoms and anisotropic temperature

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factors for nonhydrogen atoms converged to a conventional discrepancy index of 0.039 for the observed reflections. No attempt was made to determine the absolute configuration of dictyotadiol, and the drawing of the final X-ray model shown in Figure 1 represents an arbitrary choice of enantiomers.*

In addition to the four products described, the sample of D. dichotoma also contained some minor constituents, which were isolated in insufficient quantities for structural elucidation. The MS data indicated that these minor constituents were also diterpenes. The diterpenes found in this sample of D. dichotoma are not substantially different from those found in D. dichotoma var. implexa, suggesting that the two varieties are closely related from the chemosystematic as well as the systematic viewpoint.

EXPERIMENTAL

Mp's are reported uncor. NMR spectra were recorded at 100 and 220 MHz; chemical shifts are expressed as values in ppm relative to tetramethylsilane (0). MS were measured at 70 eV.

Extraction and isolation procedures. Dictyota dichotoma was collected at Overton (Gower Peninsula, S. Wales, U.K.) in July 1975. The wet algae was immersed in EtOH (21.) for 2 weeks and the EtOH decanted. The dried alga (210 g) was powdered and continuously extracted with EtOH until the extracts were clear. The combined EtOH extracts were concn in vacuo and the resulting aq. suspension (~250 ml) extracted with Et₂O. The Et₂O extracts were dried and concn to give a dark brown gum (~5 g), which was chromatographed on florisil using the eluant sequence hexane, Et₂O, EtAC. Fractions

* Fractional coordinates, bond distances, bond angles and observed and calculated structure factors may be obtained from Dr. J. Clardy. 4-6 (hexane-Et₂O (9:1) eluant) were combined and rechromatographed to obtain pachydictyol A (135 mg, 0.064% dry wt), identical in all respects to an authentic sample. Fractions 8-10 (hexane-Et₂O (4:1) eluant) were combined and rechromatographed on Sil gel plates (1.5 mm thick) to obtain dictyol B acetate (6) as an oil (10.5 mg, 0.05% dry wt): $[\alpha]_{D}^{25} = +59^{\circ}$ (c = 1.27, MeOH); IR (film) cm⁻¹: 3500, 1740; NMR (CDCl₃): δ 1.03 (3H, d, J = 7 Hz), 1.63 (3H, s), 1.71 (3H, s), 1.81 (3H, s), 2.16 (3H, s), 3.95 (1H, m), 4.94 (1H, bs), 5.00 (1H, bs); m/e, (re. int.): 346 (5), 328 (21), 286 (52) ,268 (40), 225 (12), 201 (12), 197 (21),



Fig. 1. A computer-generated perspective drawing of dictyotadiol (7). Hydrogen atoms are omitted for clarity, and no absolute configuration is implied.

186 (38), 157 (100); high resolution mass measurement, observed 346.2497, $C_{22}H_{34}O_3$ requires 346.2508. Fractions 12-14 (Et₂O eluant) were combined and concn to obtain a crystalline material which was recrystallised from Me₂CO-hexane to obtain dictyotadiol (7) (55 mg, 0.026 %): mp 150-1°, $[\alpha]_{6}^{25} = +1.3°$ (c = 0.15, MeOH), IR (nujol) cm⁻¹: 3500; NMR (acctone-d₆) 1.00 (3H, d, J = 7 Hz), 1.44 (3H, s), 1.60 (3H, s), 1.68 (3H, s), 3.20 (1H, d, J = 8 Hz), 4.48 (1H, m), 4.54 (2H, bs), 5.15 (1H, t, J = 7 Hz), 5.74 (2H, s); m/e, (rel. int.): 287 (21), 286 (100), 271 (10), 268 (20), 253 (9), 225 (7), 201 (63); high resolution mass measurements, observed 286.2292, $C_{20}H_{30}O$ (M-H₂O) requires 286.2297. The mother liquors from fractions 12-14 were rechromatographed to obtain dictyol C (4) (81 mg, 0.039%) which had spectral properties which were identical to those quoted for authentic material [6].

Dictyol B (2). A soln of the acetate 6 (18 mg, 0.052 mmol) in dry Et₂O (1 ml) was added dropwise to a stirred suspension of Li AlH₄ (50 mg) in dry Et₂O (10 ml). The reaction mixture was boiled under reflux for 2 hr and allowed to cool. Excess reagent was destroyed by dropwise addition of EtAc, then 1% KOH soln (10 drops). The soln was filtered and dried over dry Na₂SO₄. Evap. of the solvent gave an oil which solidified on addition of one drop of hexane. The diol 2 (14 mg, 89% yield), mp 015–110° (Lit. [6] 110–114%), $[\alpha]_D^{25} = 70^\circ$ [Lit. +73.5°], was identical in all respects to an authentic sample.

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