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DICTYOL H, A NEW TRICYCLIC DITERPENOID FROM THE BROWN SEAWEED *DICTYOTA DENTATA*

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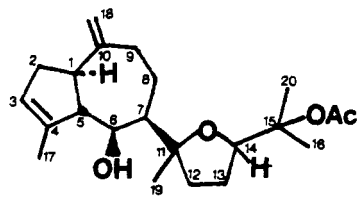
Brown seaweeds of the family Dictyotaceae are a rich source of new and structurally unique natural products. The type genus of this family, *Dictyota*, is a recognized source of a number of new diterpene ring systems (1). Our investigations of a previously unstudied species of this genus, *Dictyota dentata* Lamouroux, has revealed the presence of a complex mixture of known and unknown diterpenoids. In this paper, we report the structure of one of these new diterpenoids (**1**) which, in accord with established although trivial nomenclature, we have named dictyol H (2-5).

D. dentata was found in abundance in 3-5 m of water at Boomers Beach on the southwest coast of Barbados during a December 1982, collecting expedition. The alcohol-preserved alga was homogenized in a 2:1 mixture of $CHCl_3$-MeOH and the lipid extract handled in a standard manner to yield 9.8 g of a dark green tar. Chromatography over tlc grade silica gel in the vacuum mode sequentially yielded the known compound pachydictyol A (**2**) (6), dictyol H (**1**), two unidentified diterpenoids, and the known compound dictyol C (**3**) (7). The known compounds (**2,3**) were identified by comparison of their spectral features with published data (6,7).

Final purification of **1** employed hplc to yield 42 mg of dictyol H (0.43% of extract). Pure **1** showed $[\alpha]^{32}D$ +7.1, (c=1.70, $CHCl_3$) and analyzed for $C_{22}H_{34}O_4$ by hrms (362.2467, 1.0 mamu error). The two carbon atoms in addition to the diterpene portion were clearly present as an acetate group [ir



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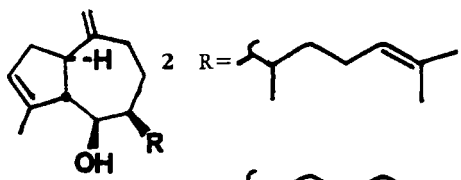

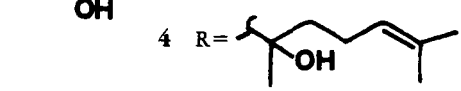

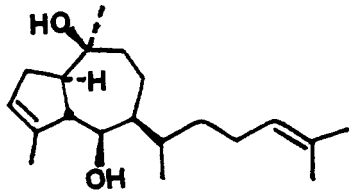

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(CCl_4) $\nu_{C=O}$ 1750 cm^{-1}; ^1H nmr (C_6D_6) δ 1.82 (3H, s); ^{13}C nmr ($CDCl_3$) δ 170.51 (s), 22.55]. Three of the six degrees of unsaturation inherent in this molecular formula were accountable by two olefins [^{13}C nmr δ 152.19 (s), 142.01 (s), 123.64 (d), 107.28 (t)] and the acetate carbonyl. The remaining three degrees were thus due to a tricyclic skeleton.

Comparison of the ^{13}C-nmr spectrum obtained for **1** with those of the series of known compounds from this genus, the dictyols (8), indicated **1** possessed a carbobicyclic portion identical with pachydictyol A (**2**) and dictyol E (**4**) (carbons 1 to 10, 17 and 18, Table 1), including the secondary alcohol at C-6 (^1H nmr δ 4.01, dd, J=2.7, 7.9). The re-

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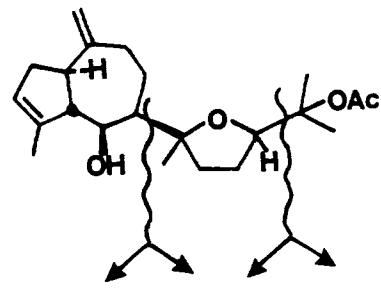
TABLE 1. ^{13}C-nmr Data of Dictyol H Compared to the Known Compound Dictyol E (7)

Carbon	Dictyol H (**1**) ($CDCl_3$)	Dictyol E (**4**) ($CDCl_3$)
1	46.07 (d)	46.2
2	33.99 (t)	33.8
3	123.64 (d)	124.4[a]
4	142.01 (s)	140.9
5	59.45 (d)	60.3
6	73.37 (d)	74.4
7	50.13 (d)	48.7
8	22.18[a]	21.7
9	40.43 (t)	40.5[b]
10	152.19 (s)	155.9
11	86.91 (s)	76.2
12	35.07 (t)	41.0[b]
13	25.97 (t)	23.3
14	83.50 (d)	124.2[a]
15	82.15 (s)	131.7
16	24.51 (q)	25.7
17	15.84 (q)	15.8
18	107.28 (t)	107.1
19	22.55[a]	25.4
20	22.55[a]	17.4
OAc	22.55[a]	
	170.50 (s)	

[a,b]Signals within a column may be interchanged.

mainder of the molecule ($C_{10}H_{17}O_3$) was thus envisioned as a modified side chain of **2** or **4** and contained a tertiary acetate (^{13}C nmr δ 82.15, s)[2] located at C-15 by hrms ($C_5H_9O_2$, 101.0610, 0.7 mamu error, 10.4%) and an additional oxygen atom present as an ether [^{13}C nmr δ 86.91 (s), 83.50 (d)]. To account for the final degree of unsaturation, the ether must be cyclic, and due to the presence of only two protons adjacent to the ether methine proton (H at C-14: δ 3.55, dd, J=7.5), must bridge C-11 and C-14 or C-12 and C-15. This latter alternative (C-12 to C-15) was discounted on the basis of the hrms (see Scheme 1) and calculations of carbon atoms C-11 through C-16 for both possibilities (9). The above carbon shifts for the tetrahydrofuran are in good agreement with several model tetrahydrofurans (10,11) and rule out the alternative tetrasubstituted tetrahydropyran with secondary acetate. By this reasoning, the structure of dictyol H is as given in formula **1**.



176 185 261 101
159 143 243
157 125

SCHEME 1. Observed high resolution eims cleavages for dictyol H (**1**).

Dictyol H was found to be weakly active in the KB9 antitumor assay (IC_{50}=22 μg/ml) and inactive in antimicrobial assays against *Pseudomonas aeruginosa* (100 μg/dose) and *Escherichia coli* (100 μg/dose).

EXPERIMENTAL

GENERAL.—Ir spectra were obtained on a Perkin-Elmer 283 spectrometer, optical rotations on a Perkin-Elmer Model 141 polarimeter using a 10-cm microcell, and nmr spectra recorded on Varian T-60, JEOL FX 90Q and Bruker HX 500 spectrometers. All chemical shifts are relative to TMS (δ=O). Low resolution mass spectra were obtained on a Hewlett Packard 5995 A mass spectrometer. All solvents were distilled from glass prior to use.

COLLECTION, EXTRACTION, CHROMATOGRAPHY.—*D. dentata* was collected in 3-5 m of water at Boomers Beach, Barbados, in December 1982 and immediately stored in i-PrOH. Plant pressings made at the time of collection were identified by Dr. David Ballantine, Department of Marine Science, University of Puerto Rico, Mayaguez, and voucher material is deposited in the herbarium of the University of Puerto Rico Marine Laboratory at La Parguera.

The algae (dry wt., 174.6 g) were homogenized and repeatedly extracted with $CHCl_3$-MeOH (2:1) to yield 9.8 g of a dark green tar (5.60% of dry wt). This extract was

[2]This shift of δ 82.15 favorably compares with other tertiary acetates; for example, see F.W. Wehrli and T. Nishida, *Fortschritte der Chemie*, **36**, 27 (1979).

chromatographed in the vacuum mode over tlc grade silica gel (pentane-CH_2Cl_2-EtOAc-MeOH). Compound **2** eluted with 45% CH_2Cl_2-pentane, **1** with 10% EtOAc-CH_2Cl_2, the two unidentified diterpenoids with 15% EtOAc-CH_2Cl_2, and **3** with 20% EtOAc-CH_2Cl_2. Metabolite **1** was further purified by hplc employing a 25 cm×3.9 mm column of μ-Porisil (15% Et_2O-hexane) to give pure dictyol H as an oil (42 mg, 0.43% of extract).

Dictyol H (**1**).—The colorless oil showed $[\alpha]^{32}D$ +7.1 (c=1.70, $CHCl_3$); ir (CCl_4) 3450, 2910, 1750, 1641, 1460, 1381, 1250, 1180, 1100, 1040, 1010, 960, 920, 910 cm^{-1}; ^1H nmr (500 MHz, C_6D_6) δ 5.21 (1H, bs), 4.70 (2H, s), 4.01 (1H, dd, *J*=2.7, 7.9 Hz), 3.55 (1H, dd, *J*=7.5, 7.5 Hz), 2.56 (1H, ddd, *J*=3, 5, 15 Hz), 2.47 (2H, m), 2.37 (1H, bt, *J*=7 Hz), 2.15 (1H, m), 2.00 (1H, bddd, *J*=5, 10, 15 Hz), 1.88 (1H, m), 1.81 (3H, s), 1.77 (3H, bs), 1.5-1.8 (5H, m), 1.46 (3H, s), 1.37 (1H, ddd, *J*=5.8, 8.6, 12.2 Hz), 1.32 (3H, s), 1.09 (3H, s); ^{13}C nmr (22.5 MHz, $CDCl_3$) δ 170.51 (s), 152.19 (s), 142.01 (s), 123.64 (d), 107.28 (t), 86.91 (s), 83.50 (d), 82.15 (s), 73.37 (d), 59.45 (d), 50.13 (d), 46.07 (d), 40.43 (t), 35.07 (t), 33.99, 25.97, 24.51, 22.55 (3C), 22.18, 15.84 (q); hrms obs M^+ *m/z* 362.2467 ($C_{22}H_{34}O_4$, 1.0 mamu dev., 3.4%), 302.2245 ($C_{20}H_{30}O_2$, 0.1 mamu dev., 41.1%), 284.2141 ($C_{20}H_{28}O$, 0.1 mamu dev., 35.0%), 261.1855 ($C_{17}H_{25}O_2$, 0.0 mamu dev., 6.6%), 243.1763 ($C_{17}H_{23}O$, 1.4 mamu dev., 7.7%), 241.1602 ($C_{17}H_{21}O$, 0.9 mamu dev., 35%), 221.1543 ($C_{14}H_{21}O_2$, 0.7 mamu dev., 11.7%), 198.1416 ($C_{15}H_{18}$, 0.7 mamu dev., 24.6%), 185.1179 ($C_{10}H_{17}O_3$, 0.1 mamu dev., 58.2%, 176.1184 ($C_{12}H_{16}O_1$, 1.7 mamu dev., 3.8%), 159.1155 ($C_{12}H_{15}$, 1.9 mamu dev., 14%), 157.1002 ($C_{12}H_{13}$, 1.5 mamu dev., 23.8%), 145.1021 ($C_{11}H_{13}$, 0.4 mamu dev., 24.7%), 143.1079 ($C_8H_{15}O_2$, 0.7 mamu dev., 50.9%), 134.1101 ($C_{10}H_{14}$, 0.6 mamu dev., 34.5%), 127.1126 ($C_8H_{15}O$, 0.3 mamu dev., 67.2%), 125.0969 ($C_8H_{13}O$, 0.3 mamu dev., 100.0%), 121.1020 (C_9H_{13}, 0.3 mamu dev., 36.4%), 109.1033 (C_8H_{13}, 1.5 mamu dev., 30.2%), 107.0873 (C_8H_{11}, 1.2 mamu dev., 43.3%), 105.0717 (C_8H_9, 1.2 mamu dev., 30.3%), 101.0610 ($C_5H_9O_2$, 0.7 mamu dev., 10.4%), lrms (70eV, 90°C) 362(1.1), 302(38), 284(21), 261(5.5), 243(6.5), 212(7.7), 198(15), 185(55), 173(10), 159(15), 157(24), 143(64), 133(26), 127(55), 125(100), 121(36), 107(45), 101(11), 91(32), 81(33), 71(45), 55(46).

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