i.V. abgedampft. Dem gewogenen Extrakt wurde eine definierte Menge Phenyläthylalkohol als innerer Standard zugemischt und I gaschromatographisch bestimmt [10]. GC-Bedingungen; Siemens L 350 Allglassystem, 3,8 m Säule, 0,15 mm i. d., Dexsil 2% auf Chromosorb G-AW DMCS, N_2 25 ml/min, FID, Injektor/Detektor-temperatur 220°. Ofentemperatur linear steigend von 80° auf 190°. Anstiegsrate 3°/min. Der experimentell ermittelte Korrekturfaktor Valeranon-Phenyläthylalkohol betrug 1.07 bei einer Standardabweichung von 0,10 ($n = 47$ Messungen). Er wurde nach jeweils drei Analysen überprüft,

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PACHYDICTYOL-A EPOXIDE, A NEW DITERPENE FROM THE BROWN SEAWEED *DICTYOTA FLABELLATA*

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Key Word Index—*Dictyota flabellata*; Dictyotaceae; marine diterpene; perhydroazulene.

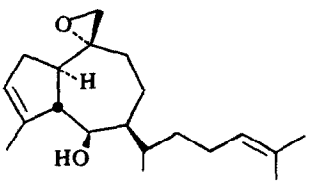
INTRODUCTION

Brown seaweeds (Phaeophyta) of the genus *Dictyota* (family Dictyotaceae) are common inhabitants of the shallow water and intertidal communities, particularly in subtropical and tropical areas. Extracts of a variety of *Dictyota* species have been shown to exhibit cytotoxic [1], antibacterial [2–4], and antiviral [5] activities, and herbivores appear to avoid these delicate plants. In initial attempts to isolate the active secondary metabolites from this group, we described the structure of pachydictyol-A, a weakly antibiotic diterpene from the related alga *Pachydictyon coriaceum* [6]. We wish to report here that the exomethylene epoxide isomer of pachydictyol-A occurs naturally in the brown alga *Dictyota flabellata* (Collins) Setchell et Gardner from the Gulf of California.

RESULTS AND DISCUSSION

Silica gel column chromatography of the crude chloroform extract of *D. flabellata* did not separate pachydictyol-A epoxide (**1**) and fucosterol, which were eluted in equal amounts. Acetylation (25°) of the mixture, however, and subsequent chromatography gave pure samples of unchanged **1**, $[\alpha]_D$, + 28.6°, (*c*, 3.1, $CHCl_3$), and fucosterol acetate. MS established compound **1** as a diterpene alcohol of the composition $C_{20}H_{32}O_2$, $M^+ = 304$, $M^+-H_2O = 286$. Its IR absorptions confirmed the presence of hydroxyl (3450 cm^{-1}) and discounted the existence of carbonyl functionality. Proton and carbon NMR data were in close agreement with pachydictyol-A (**5**), [6]. ^1H NMR (CCl_4, 220 MHz): δ 0.98 (3H, *d*, $J = 7$ Hz), 1.36–1.91 (multiple bands, 9H), 1.20 (2H, *m*), 1.57 (3H, *s*), 1.66 (3H, *s*), 1.74 (3H, *s*), 2.34 (1H, *d*, $J = 5$ Hz), 2.48 (2H, *m*), 2.62 (1H, *d*, $J = 5$ Hz), 3.84 (1H, *dd*, $J = 8$, 3 Hz), 5.07 (1H, *dd*, $J = 7, 7$ Hz), 5.18 (1H, *bs*). ^{13}C NMR ($CDCl_3$, 20 MHz): δ 15.7, 17.5, 17.7, 20.6, 25.9, 25.9, 31.2, 34.9, 35.4, 39.7, 43.9, 48.8, 50.6, 58.0 (*t*), 62.2 (*s*), 74.6 (*d*) 124.2 (*d*), 125.0 (*d*), 131.3 (*s*), 141.2 (*s*).

The nature of the second oxygen atom in compound **1** was not readily assigned from spectral data. However, the clear absence of the exocyclic methylene function (proton resonance at δ 4.68 in **6**; IR bands at 884 and 1600 cm^{-1}), which was not replaced by an additional methyl group,



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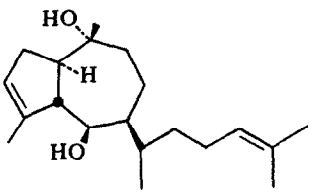

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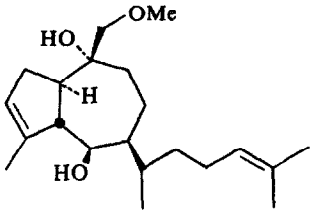

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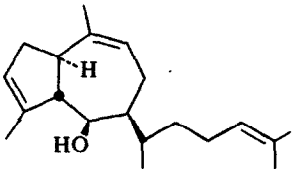

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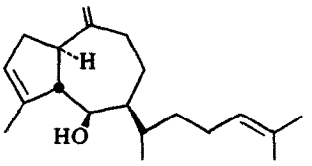

5

suggested that epoxidation had occurred. The ^{13}C NMR resonance at 58.0 (*t*) and 62.2 (*s*) also suggested epoxidation at the exomethylene position. This functionality was confirmed by its facile addition of methanol to yield compound **2**. The most significant spectra features of **2** were proton resonances for methoxyl at δ 3.33 (3H) and a geminal AB double doublet at δ 3.23 and 3.89, respectively, for the non-equivalent methoxy methylene protons. Further, **1** reacted smoothly with LAH to yield a single diol **3**, with the simultaneous generation of a new methyl group at δ 1.18 in the NMR spectrum. Diol **3** is the tertiary alcohol epimer of the natural product dictyol C, recently isolated from *Dictyota dichotoma* [7], and, accordingly, is physically and spectrally highly comparable but not identical.

In a low-yielding reaction, diol **3** was converted to a mixture of alcohols **4** and **5** with $POCl_3$–Py at 0°. The minor product, pachydictyol-A (**5**) was identical in all respects to an authentic sample from *P. coriaceum*. In this dehydration, tetrasubstituted olefins from bridgehead elimination were not produced. Assuming a *trans*-diaxial conformation for elimination under these reaction conditions [8], compound **3** must have its tertiary hydroxyl *cis* in relation to the adjacent bridgehead proton. Molecular models suggest that **4** and **5** would be the exclusive products of this epimer. Since LAH reduction of **1** does not influence the quaternary epoxide carbon, the stereochemistry at this center in **1** and **3** must be identical.

EXPERIMENTAL

NMR spectra were recorded at 220 MHz and are reported in δ units relative to internal TMS. IR data were recorded as soln spectra or thin films. *D. flabellata* was collected at Sandy Beach, Puerto Peñasco, Sonora, Mexico, during June and October 1975.

Isolation of pachydictyol-A epoxide (**1**). The air-dried and finely milled (1 mm) plants of *D. flabellata*, (1 kg) were exhaustively extracted with MeOH–$CHCl_3$ in (1:4) in a Soxhlet extractor. A voucher specimen of this alga has been deposited in the National Herbarium of the Smithsonian Institution, Washington, D.C. The extract was concnd, and the residue (32 g) was chromatographed on a column (5 × 100 cm) of Davison, Grade 62 Si gel. Elution with Et_2O–C_6H_6 (1:49) gave semisolid fractions shown by TLC on Si gel to be 2 compounds in equal amounts. All fractions which contained the epoxide **1** were combined (**1** stains bright blue with H_2SO_4 spray at 100°) and acetylated with Ac_2O–Py at room temp. for 24 hr. After typical work-up and column chromatography on Si gel, 1.3 g of **1** and 0.9 g of fucosterol acetate were obtained. Pachydictyol-A epoxide remained an oil, despite numerous purifications by HPLC on μ-porasil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 830, 900, 1000, 1050, 1380, 1460, 2950, 3450. High resolution MS: $C_{20}H_{32}O_2$, M^+ *m/e* observed 304.2403, required 304.2402.

MeOH addition to epoxide **1**. 50 mg **1** and 20 ml 10% KOH–MeOH were combined and warmed to 50° for 48 hr. The loss of **1** and formation of a more polar product was monitored by Si gel TLC. The reaction mixture was diluted to 75 ml with H_2O and the products extracted with Et_2O (3 × 50 ml). Removal of solvent, followed by PLC on Si gel (Et_2O–C_6H_6, 7:3), gave pure methoxyalcohol **2** as a viscous oil. IR, $\nu_{max}^{CCl_4}$ cm^{-1}: 875, 890, 1050, 1120, 1200, 1340, 1385, 1460, 2950, 3550. NMR (CCl_4, 220 MHz): δ 5.14 (1H, *bs*), 5.05 (1H, *dd*, J = 7,7 Hz), 3.81 (1H, *dd*, J = 8,3 Hz), 3.89 (1H, *d*, J = 9 Hz), 3.33 (3H, *s*), 3.23 (1H, *d*, J = 9 Hz), 1.02–2.48 (~11H, *m*), 1.74 (3H, *s*), 1.66 (3H, *s*), 1.57 (3H, *s*), 0.95 (3H, *d*, J = 7 Hz).

LAH reduction of **1**. 25 mg **1** was treated with an excess of LAH (20 mg) in dry Et_2O at room temp. Aq. hydrolysis and EtO_2 extraction followed by purification by HPLC on μ-porasil, gave crystalline **3** (20 mg) mp 91–92° (petrol). NMR ($CDCl_3$, 220 MHz): δ 5.32 (1H, *bs*), 5.15 (1H, *dd*, J = 7,7 Hz),

3.91 (1H, *m*), 2.32 (4H, *m*), 2.00 (2H, *m*), 1.3–1.9 (~10H, *m*), 1.80 (3H, *s*), 1.68 (3H, *s*), 1.59 (3H, *s*), 1.18 (3H, *s*), 1.0 (3H, *d*, $J = 7$ Hz).

Dehydration of 3. 100 mg diol **3** were dissolved in 20 ml purified Py and cooled to 0° under N_2. 2 ml $POCl_3$ was slowly added to maintain 0°, and the mixture was stirred for 2 hr. The mixture was allowed to warm to ambient and was hydrolyzed with ice, neutralized with $NaHCO_3$, and extracted with Et_2O (3 × 75 ml). TLC on Si gel showed two products, R_f 0.80 and 0.52 (Et_2O–C_6H_6, 7:3). The upper product stained blue and the lower red upon H_2SO_4 spraying and warming. The lower spot was isolated by PLC and further purified by HPLC on μ-porasil, which indicated a 7:3 ratio of **4** to **5**. Pachydictyol-A (**5**) was isolated in poor recovery (15 mg) and was identical in all respects to an authentic sample. The less polar products from this reaction are apparently ethers and were not further investigated.

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NEUE DITERPENE AUS *DIMORPHOTHECA*- UND *VIGUIERA*-ARTEN*

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Key Word Index—*Dimorphotheca aurantiaca*; *Viguiera grammatoglossa*; Compositae; new cupressene derivatives; diterpenes.

Die bisher untersuchten Vertreter aus der Tribus Calenduleae haben gezeigt, daß hier Diterpene sehr häufig vorkommen. Auch *Dimorphotheca aurantiaca* enthält neben geringen Mengen der weitverbreiteten Polyine **1** und **2** [1] sowie Caryophyllen (**3**) ein Gemisch von drei Diterpensäuren, das erst nach Veresterung mit Diazomethan trennbar ist. Den unpolareren Ester **5** haben wir bereits aus *D. pluvialis* isoliert [2]. Bei den beiden anderen Estern handelt es sich nach dem NMR- und MS offenbar um die Tiglinsäureester **7** und **9**, deren Stereochemie jedoch aus Substanzmangel nicht völlig sichergestellt werden konnte. Auch *D. pseudoaurantiaca* enthält **4** und **6** und den Alkohol **11**, der nach den NMR-Daten mit Erythroxylol A identisch ist [3].

* 105. Mitt. in der Serie 'Natürlich vorkommende Terpen-Derivate', 104. Mitt. Bohlmann, F., Zdero, C. (1977) *Phytochemistry*, in press.

Tabelle 1. ^{1}H-NMR-Signale von **7**, **9** und **10** (δ-Werte, $CDCl_3$, TMS als innerer Standard)

	7	**9**	**10**
3-H	*dd* 4.54	*dd* 4.62	
11-H		*t*(*br*) 5.15	
15-H	*d* 5.46	*d* 5.26	*d* 5.48
16-H	*d* 5.67	*d* 6.12	*d* 5.70
17-H	*s* 1.00	*s* 1.00	*s* 1.00
18-H	*s* 0.65	*s* 0.85	*s* 0.61
19-H	*s* 1.23	*s* 1.15	*s* 1.00
20-H	—	—	*s*(*br*)9.75
23-H	*qq* 6.84	*qq* 6.85	—
24-H	*d*(*br*) 1.77	*d*(*br*) 1.77	—
25-H	*s*(*br*) 1.80	*s*(*br*) 1.80	—
OMe	*s* 3.71	*s* 3.71	—

J(Hz): 15, 16 = 5.5; **7** und **9**: 2, 3 = 11; 2′, 3 = 4; 23, 24 = 7; 23, 25 = 1;