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TWO MINOR DOLABELLANE DITERPENOID CONSTITUENTS FROM A *DICTYOTA* SPECIES

CORRADO TRINGALI, GIOVANNA ORIENTE, MARIO PIATTELLI,

Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria 6, 95125 Catania, Italy

and GIOVANNI NICOLOSI,

Istituto del CNR per lo Studio delle Sostanze Naturali di Interesse Alimentare e Chimico-Farmaceutico, Viale A. Doria 6, 95125 Catania, Italy

In recent years, a number of diterpenoids based on the dolabellane skeleton have been isolated from marine sources (1-11), many of them possessing remarkable biological properties (4,8,9,11).

In a continuation of our search for bioactive dolabellane compounds from brown algae, we have now isolated two minor constituents (**1** and **2**) from the $CHCl_3$ extract of a previously investigated *Dictyota* sp. (8-10). Comparison of the pertinent spectral data (ms, ir, ^1H nmr, and ^{13}C nmr) with those of the co-occurring known alcohols **3** and **4** clearly indicated that the new compounds were the corresponding acetates. Conclusive identification was achieved by alkaline hydrolysis which afforded the free alcohols identical in all respects, including optical rotation, with authentic samples of **3** and **4**. Conversely, acetylation of the latter compounds afforded products indistinguishable from **1** and **2**, respectively.

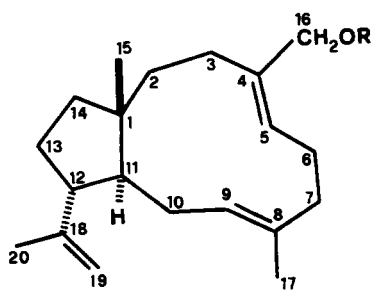
The new compounds are currently under investigation, together with a number of already known dolabellane compounds, for antimicrobial and molluscicidal activity.

EXPERIMENTAL

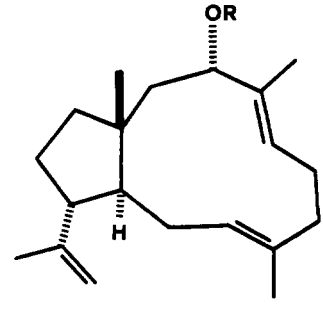
GENERAL EXPERIMENTAL PROCEDURES.—Spectra were recorded using the following instruments: ms, AEI MS 902 at 70 eV (direct introduction); ir, Perkin-Elmer 684; ^1H nmr, Bruker WP 250 (250 MHz); ^{13}C nmr, Bruker WP 250 (62.9 MHz, DEPT sequence). Optical rotations were determined with a Perkin-Elmer 141 instrument. Preparative liquid chromatography (plc) was effected on a Jobin-Yvon Miniprep liquid chromatograph; hplc was carried out on a Varian 5000 instrument. Whatman Partisil PXS 10/25 Si gel and M9 10/25 Si gel columns were used respectively for analytical and preparative hplc. Tlc plates and adsorbents for plc were from E. Merck. 10% $Ce(SO_4)_2$ in 2N H_2SO_4 was used as the spray detection reagent.

PLANT MATERIAL.—*Dictyota* sp. was collected by SCUBA near Portopalo (southeast Sicily) in July 1983. A specimen was deposited in the Herbarium of the Institute of Botany, University of Catania, Catania, Italy.

ISOLATION.—Air-dried alga (600 g) was ground and extracted with $CHCl_3$ (3×2 liters) under stirring. After solvent removal, the residue (12 g) was taken up in 80% Et_2O in hexane and passed through a column of Florisil. The eluate was evaporated and chromatographed on Si gel, using 25% Et_2O in hexane as the eluent. Frac-



1 R=Ac
3 R=H



2 R=Ac
4 R=H

tions exhibiting similar tlc profiles were pooled, and those containing a mixture of **1** and **2** were subjected to careful plc (LiChroprep Si 60, 25% CH_2Cl_2 in hexane). Complete purification of the two compounds was achieved by hplc (Partisil M9 10/25 Si, 4% Et_2O in hexane) which gave 30 mg of **1** and 100 mg of **2**.

16-ACETOXY-1(*R*), 11(*S*), 12(*R*)-DOLABELLA-4(*E*),8(*E*),18-TRIENE (**1**).—The less polar diterpenoid **1** was obtained as a colorless oil, $[\alpha]^{25}D = +52.2°$ (c=1 in EtOH); ms *m/z* 330 (M^+, $C_{22}H_{34}O_2$), 315 (M^+-Me), 270 (M^+-AcOH), 255 (M^+-AcOH-Me); ir ($CHCl_3$) ν max 1728, 1240 cm^{-1} (acetoxy); ^1H nmr ($CDCl_3$) δ 5.24 (dd, J=10.5 and 3 Hz, 1H, H-5), 5.16 (dd, J=10.5 and 4 Hz, 1H, H-9), 4.82 and 4.66 (bs, 1H each, 2×H-19), 4.52 (AB system, J=11.5 Hz, 2×H-16), 2.71 (ddd, J=8, 7.5 and 7.5 Hz, 1H, H-12), 2.05 (s, 3H, CH_3COO-), 1.72 (s, 3H, 20-Me), 1.49 (s, 3H, 17-Me), 1.04 (s, 3H, 15-Me); ^{13}C nmr ($CDCl_3$) ppm 15.4 (q), 20.9 (q), 23.5 (q), 23.8 (q), 24.3 (t), 26.2 (t), 29.0 (t), 32.8 (t), 39.9 (t), 42.7 (t), 43.4 (d), 43.8 (t), 45.6 (s), 50.8 (d), 62.9 (t), 112.0 (t), 125.6 (d), 133.0 (d), 132.2 (s), 134.0 (s), 146.8 (s), 170.8 (s).

3(*S*)-ACETOXY-1(*R*), 11(*S*), 12(*R*)-DOLABELLA-4(*E*),8(*E*),18-TRIENE (**2**).—Compound **2** was a white crystalline solid, mp 115-117°; $[\alpha]^{25}D = -31.1°$ (c=1 in EtOH); ms *m/z* 330 (M^+, $C_{22}H_{34}O_2$), 315 (M^+-Me), 270 (M^+-AcOH), 255 (M^+-AcOH-Me); ir ($CHCl_3$) ν max 1715, 1250 cm^{-1} (acetoxy); ^1H nmr ($CDCl_3$) δ 5.41 (dd, J=12 and 6 Hz, 1H, H-3), 5.20 (dd, J=12 and 4 Hz, 1H, H-9), 5.16 (dd, J=12 and 2 Hz, 1H, H-5), 4.91 and 4.68 (bs, 1H each, 2×H-19), 2.59 (ddd, J=12, 6 and 6 Hz, 1H, H-12), 1.98 (s, 3H, CH_3COO-), 1.72 (s, 3H, 16-Me), 1.55 (s, 3H, 17-Me), 1.51 (s, 3H, 20-Me), 1.21 (s, 3H, 15-Me); ^{13}C nmr ($CDCl_3$) ppm 10.7 (q), 15.5 (q), 21.3 (q), 23.2 (q), 24.3 (t), 24.8 (q), 28.0 (t), 28.5 (t), 39.7 (t), 41.7 (t), 41.9 (d), 42.6 (t), 47.2 (s), 51.3 (d), 81.0 (d), 111.4 (d), 126.4 (d), 131.1 (s), 132.5 (d), 134.7 (s), 145.7 (s), 170.1 (s).

ALKALINE HYDROLYSIS OF **1** AND **2**.—A solution of **1** (10 mg) in MeOH (3 ml) was stirred for 3 h with 0.5 ml aqueous NaOH (30%) at room temperature. After neutralization with 1% HCl, the mixture was extracted with Et_2O. The organic phase was taken to dryness and the residue subjected to hplc (10% Et_2O in hexane) to give a compound identified as **3** ($[\alpha]^{25}D$, ms, ir, ^1H nmr).

When **2** (15 mg) was subjected to analogous treatment it gave a product identical with **4** ($[\alpha]^{25}D$, ms, ir, ^1H nmr).

ACETYLATION OF **3** AND **4**.—A thin film of **3** (10 mg) in a round bottomed flask was exposed to vapors of Ac_2O/pyridine in a sealed system for 30 min. The product was taken up with Et_2O and purified by hplc (Partisil M9 10/25 Si, 4% Et_2O in hexane) to give an acetate identical with **1**.

The same treatment was applied to **4** (10 mg) and gave a product identified as **2**.

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