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TWO NEW FARNESYLACETONE DERIVATIVES FROM THE BROWN ALGA *SARGASSUM MICRACANTHUM*

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Key Word Index—*Sargassum micracanthum*; Phaeophyceae; brown alga; bisnorditerpenes; farnesylacetone derivatives.

Abstract—From the brown alga, *Sargassum micracanthum*, two new farnesylacetone derivatives were isolated and their structures elucidated from spectral analyses and chemical correlation to a known farnesylacetone derivative.

INTRODUCTION

Several species of *Sargassum* are known to contain farnesylacetone derivatives [1] and geranylgeranylphenyl derivatives [2–5].

The present paper describes the isolation and structure determination of the two new farnesylacetone derivatives **4** and **5**, as well as the chemical correlation between **4**, **5** and the known **2**.

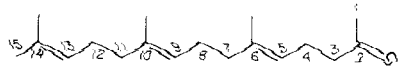
RESULTS AND DISCUSSION

Acetone extracts of fresh *S. micracanthum* (Kützing) Yendo were partitioned between water and hexane. The hexane-soluble compounds were then fractionated (see Experimental) to yield five bisnorditerpenes. Three of these terpenes were identified as farnesylacetone (**1**), and the diketones **2** and **3** by direct comparison with authentic samples [1]. The spectral data of the two remaining terpenes (**4** and **5**) suggested that they were related to farnesylacetone.

Compound **4**, colourless liquid, had the same molecular formula ($C_{18}H_{30}O_2$; $[M]^+ = 278.2237$) as **2**, which indicated that **4** was an isomer of **2**. Its IR spectrum (1705 cm^{-1}) showed that **4**, unlike **2**, contained no α,β-unsaturated carbonyl group, whilst its ^1H NMR spectrum revealed the presence of an acetyl (δ 2.11, 3H, *s*), an isopropyl (δ 0.91, 6H, *d*, $J = 7$ Hz), and two trisubstituted olefinic groups (δ 5.18, 2H, *m*) together with a methylene group flanked by a carbonyl group and a double bond (δ 3.02, 2H, *s*). Comparison of these spectral data with those of **2** indicated that the double bond was located at C-9 in **4** rather than at C-10 as in **2**. The proposed structure (**4**) was confirmed by chemical transformation of **4** to **2** (*vide post*).

Compound **5**, colourless liquid, had a molecular formula ($C_{18}H_{30}O_2$; $[M]^+$ 278.2237) which indicated that it was also an isomer of **2**. Its IR spectrum (1672 and 1610 cm^{-1}) and UV spectrum [244 nm (log ε 4.07)] suggested the presence of an α,β-unsaturated carbonyl group in **5**. Its ^1H NMR spectrum was almost identical with that of **2** except for the chemical shift of the methyl group at C-10 (δ 2.11 in **5**: δ 1.87 in **2** assigned to the *Z*-configuration [1]). This shift showed that **5** was a stereoisomer of **2** in which the configuration of the double bond at C-10 was E.

To confirm structures **4** and **5**, the isomer (**4**) with β,γ-unsaturated ketone group was isomerized by the action of NaOMe to afford a stereoisomeric mixture of two conjugated ketones, **2** and **5**. Separation of the mixture by prep. HPLC gave **2** and **5**, which were identical with those isolated from the alga.



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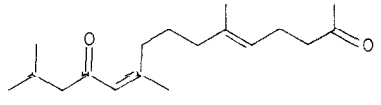

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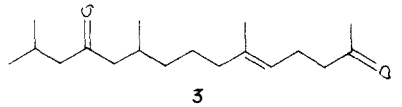

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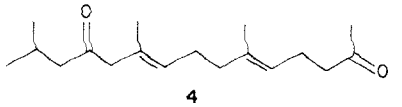

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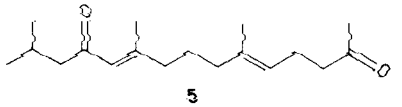

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EXPERIMENTAL

UV: MeOH; IR: $CHCl_3$; ^1H NMR [Varian HA-100D, Varian NV-21 (90 MHz) and Varian CFT-20]; $CDCl_3$, TMS as int. standard. MS: heated inlet system or direct inlet system, 70 eV; TLC, Si gel 60 PF_{254} (No. 7747) (E. Merck, A. G., W. Germany), prep. TLC 1.5 mm; CC: Si gel 60 (E. Merck, A. G., W. Germany); prep. HPLC (Jasco Tri Rotar-II): Zorbax ODS and Cosmosil 5 C_{18} with CH_3CN–H_2O (3:1).

Extraction and isolation. The wet alga (*S. micracanthum* 4.1 kg; collected in July off the coast of Gosa, Mie Prefecture, Japan) was extracted with Me_2CO (26 l.). The extract was concd to 2.4 l., then partitioned between hexane and H_2O. The hexane layer was dried over Na_2SO_4 and concd to give 55.3 g of an oil, a part of which (9.8 g) was subjected to CC on Si gel (29 × 4.5 cm; 200 g) developed successively with $CHCl_3$ and $CHCl_3$–EtOAc. The early fractions (503 mg) eluted with $CHCl_3$ were further separated by prep. TLC on Si gel with C_6H_6–EtOAc (10:1) to give pure farnesylacetone (1) (395 mg): IR 1702 cm^{-1}; MS *m/z* 262 $[M]^+$; ^1H NMR: δ 1.60 (9H, *s*), 1.67 (3H, *s*). 2.10 (3H, *s*), 5.11 [3H, *t*, (*br*), J = 6 Hz].

The later fractions (910 mg) eluted with $CHCl_3$ were further separated by prep. TLC on Si gel with C_6H_6–Me_2CO (10:1) affording an oil (632 mg), which was chromatographed over Si gel (50 × 2 cm; 60 g) with hexane–EtOAc (20:1) to give two fractions, A (155 mg) and B (224 mg). Prep. HPLC of the fraction A (105 mg) afforded **2** (60.5 mg) and **3** (9.5 mg).

Compound **2**: IR 1705, 1670, 1610 cm^{-1}; UV λ_{max}^{MeOH} 242 nm (log ϵ 4.07); MS *m/z* 278 $[M]^+$; ^1H NMR: δ 0.91 (6H, *d*, J = 7 Hz), 1.62 (3H, *s*), 1.87 (3H, *d*, J = 1.5 Hz), 2.14 (3H, *s*), 5.09 [1H, *t* (*br*), J = 7 Hz], 6.04 (1H, *s*, *br*).

Compound **3**: IR 1705 cm^{-1}; MS *m/z* 280 $[M]^+$; ^1H NMR: δ 0.87 (3H, *d*, J = 7 Hz), 0.93 (6H, *d*, J = 7 Hz), 1.64 (3H, *s*), 2.14 (3H, *s*), 5.08 [1H, *t*(*br*), J = 7 Hz].

Prep. HPLC of the fraction B (61 mg) gave pure samples of **4** (14.3 mg) and **5** (21.9 mg).

Compound **4**: colourless liquid; IR 1705 cm^{-1}; MS *m/z* 278 $[M]^+$. (Found 278.2237: Calcd for $C_{18}H_{30}O_2$, 278.2245.) ^1H NMR δ 0.91 (6H, *d*, J = 7 Hz), 1.62 (6H, *s*), 2.11 (3H, *s*), 3.02 (2H, *s*), 5.18 (2H, *m*).

Compound **5**: colourless liquid; IR 1705, 1672, 1610 cm^{-1}; UV λ_{max}^{MeOH} 244 nm (log ϵ 4.07); MS *m/z* 278 $[M]^+$. (Found 278.2237: Calcd for $C_{18}H_{30}O_2$, 278.2245.) ^1H NMR: δ 0.93 (6H, *d*, J = 7 Hz), 1.62 (3H, *s*), 2.11 (3H, *d*, J = 1.5 Hz), 2.14 (3H, *s*), 5.10 [1H, *t* (*br*) J = 7 Hz], 6.04 [1H, *s*(*br*)].

Transformation of **4** *to* **2** *and* **5**. **4** was dissolved in a 0.024 M NaOMe soln in dry MeOH and the soln was stirred at 50° for 1 hr under N_2, and then diluted with H_2O. The mixture was extracted with Et_2O (2 × 5 ml). The combined organic extracts were dried over Na_2SO_4, and concd to give an oily product (2.5 mg). Prep. HPLC of the oily product gave **2** (0.5 mg) and **5** (1.0 mg), which were identical with natural **2** and **5**, respectively, in all respects (IR, ^1H NMR, MS, HPLC retention times and TLC mobility).

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