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A QUINONE–HYDROQUINONE COUPLE FROM THE BROWN ALGA *CYSTOSEIRA STRICTA*

VINCENZO AMICO, GIOVANNA ORIENTE, MARIO PIATTELLI, GIUSEPPE RUBERTO and CORRADO TRINGALI

Istituto Dipartimentale di Chimica dell'Università di Catania, V. le A. Doria, Catania, Italy

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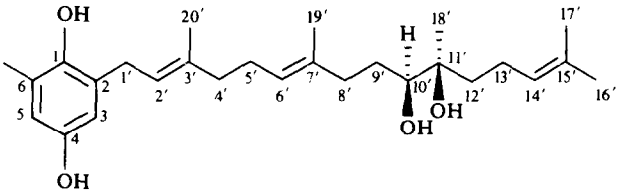
Key Word Index—*Cystoseira stricta*; Cystoseiraceae; brown algae; (2′*E*,6′*E*)-2-(10′,11′-dihydroxygeranyl-geranyl)-6-methylquinol; (2′*E*,6′*E*)-2-(10′,11′-dihydroxygeranylgeranyl)-6-methyl-1,4-benzoquinone.

Abstract—(2′*E*,6′*E*)-2-(10′,11′-Dihydroxygeranylgeranyl)-6-methylquinol and (2′*E*,6′*E*)-2-(10′,11′-dihydroxy-geranylgeranyl)-6-methyl-1,4-benzoquinone have been isolated from the brown alga *Cystoseira stricta*. The structures of the new algal metabolites have been elucidated by spectral analysis and chemical degradation.

In the course of our investigation on the constituents of the brown algae belonging to the family Cystoseiraceae [1–3], we have now found that chromatographic separation of the chloroform extract of *Cystoseira stricta* (Montagne) Sauvageau var. *spicata* (Ercegovic) Giaccone yields two new compounds, **1** and **2**.

Compound **1** was obtained as an oil, $[\alpha]_D^{CHCl_3} + 7°$. The MW and formula, $C_{27}H_{42}O_4$, were established by mass spectroscopy. The IR spectrum showed absorptions for hydroxyl (3340 cm^{-1}) and olefin (1610 cm^{-1}) functions, and UV spectrum (λ_{max}^{EtOH} 292 nm, $\epsilon = 2300$) was indicative of a quinol. The ^{13}C NMR exhibited signals for a dialkylated quinol ring (δ



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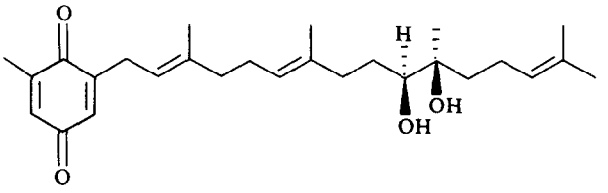

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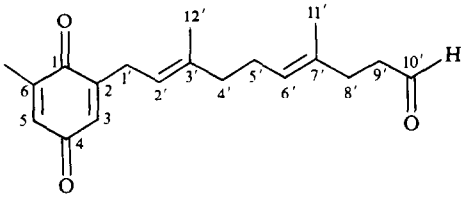

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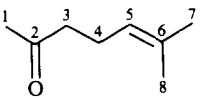

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149.0 *s*, 135.1 *s*, 115.7 *d*, 145.9 *s*, 114.1 *d*, 128.0 *s*), a secondary alcohol (*δ* 76.4 *d*), a tertiary alcohol (*δ* 74.6 *s*), and three non-conjugated olefin groups (*δ* 137.5 *s*, 131.9 *s*, 125.6 *s*, 124.9 *d*, 124.6 *d*, 122.3 *d*). In addition, seven methylene carbons (*δ* 39.5 *t*, 38.8 *t*, 36.7 *t*, 29.5 *t*, 29.3 *t*, 25.8 *t*, 22.0 *t*) and six methyl groups (*δ* 25.7 *q*, 21.0 *q*, 17.7 *q*, 16.0 *q*, 16.0 *q*, 16.0 *q*) were observed. The 270-MHz ^{1}H NMR spectrum allowed us to deduce, by the presence of two *meta*-coupled ($J = 2$ Hz) protons at *δ* 6.35 and 6.37, the substitution pattern on the aromatic ring. The Me-6 signal was observed at *δ* 2.15 and the benzylic methylene as a doublet at *δ* 3.22 ($J = 7$ Hz) coupled to an adjacent olefin proton at *δ* 5.18. Two additional vinyl proton signals (H-6′, 14′) were seen at *δ* 5.09 and 5.01. The proton at C-10′ was discerned as a double doublet ($J = 9$ and 3 Hz) at *δ* 3.38 which was simplified to a doublet ($J = 9$ Hz) by irradiation at *δ* 1.60 (H-9′$_a$) or to a doublet ($J = 3$ Hz) by irradiation at *δ* 1.46 (H-9′$_b$). The protons of the allylic methylenes at C-4′, 5′, 8′, 13′ were observed as a complex signal centered at *δ* 2.08. Other bands in the ^{1}H NMR spectrum were a multiplet at *δ* 1.5, overlapped with other signals, due to the methylene protons of C-12′, and the methyl singlets at *δ* 1.65 (H-20′), 1.69 (H-16′), 1.58 (H-19′), 1.58 (H-17′) and 1.10 (H-18′). That the two alcoholic groups deduced from the ^{13}C NMR spectrum were embodied in an *α*-glycol moiety was confirmed by the formation of an acetonide, while their location in the C_{20}-side chain was shown by periodic acid oxidation, which yielded aldehyde (**3**), $C_{19}H_{24}O_3$, and 6-methylhept-5-en-2-one (**4**), $C_8H_{14}O$. The assignment of the NMR signals of both degradation products (see Experimental) was straightforward. The configuration of the C-2′ and C-6′ double bonds in **1** was determined to be *E* from the upfield chemical shifts of the signals (*δ* 16.0, 16.0) due to the 19′ and 20′-Me groups. ^{1}H NMR analysis of the acetonide of **1** established a *cis* relationship between the Me-11′ group and the H-10′ proton; indeed, irradiation of the Me-11′ signal caused an 11% NOE enhancement [4]. Therefore, the new algal quinol must be an *erythro*-isomer represented by stereostructure **1** (or its enantiomer).

Silver oxide oxidation of **1** gave the *p*-benzoquinone **2**, $C_{27}H_{40}O_4$, $[\alpha]_D^{CHCl_3} + 15°$, m.p. 43–44°, which was also isolated from the alga. Conversely, the quinone **2** was smoothly reduced by $NaBH_4$ to the hydroquinone **1**. Compound **1** was quite resistant to air oxidation (when a dilute ethanolic solution was left at room temperature for a week, **2** was barely detectable by TLC), but was partly converted into the corresponding quinone during open column chromatography. Therefore, the possibility was considered that **2** was an artefact of the isolation process. However, when a small sample of the alga was rapidly extracted in the field and the extract immediately examined by TLC, quinone **2** was found in appreciable amounts.

Algal plastoquinones, plastohydroquinones and related compounds have been previously isolated from members of the Sargassaceae [5, 6] and Dictyotaceae [7, 8] and some of them found to possess ichthyotoxic, cytotoxic and antimicrobial activity [7, 8].

EXPERIMENTAL

General procedures. Preparative liquid chromatography (PLC) was carried out on a Jobin–Yvon Miniprep LC.

Extraction and isolation. The air-dried and ground alga (1.2 kg), collected in Oct. 1980 near Cava d'Aliga, Sicily, was

Table 1. ^{1}H NMR spectral data of compounds **1** and **2** (270 MHz, $CDCl_3$, TMS as internal standard)

Assignment*	1	2
H-3	6.35 *d* ($J = 2$ Hz)	6.34 *m(br)*
H-5	6.37 *d* ($J = 2$ Hz)	6.43 *m(br)*
H-1′	3.22 *d* ($J = 7$ Hz)	3.07 *d* ($J = 7$ Hz)
H-2′	5.18 *m*	5.06 *m*
H-4′	2.08	2.06
H-5′	2.08	2.06
H-6′	5.09 *m*‡	5.06 *m*
H-8′	2.08	2.06
H-9′$_a$	1.60†	1.60†
H-9′$_b$	1.46†	1.46†
H-10′	3.38 *dd* ($J = 9$ and 3 Hz)	3.35 *dd* ($J = 9$ and 3 Hz)
H-12′	1.50†	1.50†
H-13′	2.08	2.06
H-14′	5.01 *m*‡	5.06 *m*
H-16′	1.69 *s*	1.65 *s*
H-17′	1.58 *s*	1.61 *s*
H-18′	1.10 *s*	1.12 *s*
H-19′	1.58 *s*	1.61 *s*
H-20′	1.65 *s*	1.61 *s*
Me-6	2.15 *s*	2.03 *d* ($J = 2$ Hz)

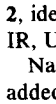
*Assignments confirmed by decoupling.
†Overlapped with other signals.
‡Interchangeable.

extracted with $CHCl_3$ (×3) at room temp. Evaporation of the $CHCl_3$ left a dark green oil (55 g) which was treated with Et_2O (100 ml). The ethereal soln was taken to dryness and the residue (45 g) subjected to chromatography on a Si gel column (4 × 120 cm), using increasing concns of Et_2O in petrol as the eluant. Fractions of 200 ml were collected and those exhibiting similar TLC profiles were combined. Fractions 75–83 were pooled and subjected to PLC (Lichroprep, 3% *iso*-PrOH in petrol) to give a yellow oil which slowly crystallized on standing in the refrigerator. Recrystallization from EtOH-hexane gave 150 mg (0.0125% dry wt) of 2 - (10′,11′ - dihydroxygeranylgeranyl) - 6 - methyl - 1,4 - benzoquinone, m.p. 43–44°; $[\alpha]_D + 15°$ (*c* 1.38, $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3450, 1655, 1645, 1610; UV λ_{max}^{EtOH} nm: 254 (ϵ = 17200); MS *m/z*: 428.2901 $[M]^+$ (calc. for $C_{27}H_{40}O_4$, 428.2926), 410 $[M - H_2O]^+$, 392 $[M - 2H_2O]^+$, 302, 173 (base), 127, 69; ^1H and ^{13}C NMR: see Tables 1 and 2 respectively. Prep. TLC (Lichroprep, 55% Et_2O in petrol) of fractions 95–100 gave 2-(10′,11′-dihydroxygeranylgeranyl)-6-methylquinol (1.2 g; 0.17% dry wt); $[\alpha]_D + 7°$ (*c* 2, $CHCl_3$); IR ν_{max}^{film} cm^{-1}: 3350, 1610: UV λ_{max}^{EtOH} nm: 292 (ϵ = 2300); MS *m/z*: 430.3057 $[M]^+$ (calc. for $C_{27}H_{42}O_4$, 430.3083), 412 $[M - H_2O]^+$, 394 $[M - 2H_2O]^+$, 304, 302, 175 (base), 127, 69; ^1H and ^{13}C NMR: see Tables 1 and 2 respectively. In a separate experiment, a small collection of *C. stricta* was extracted in the field with $CHCl_3$–MeOH (1 : 1). After addition of H_2O the organic layer was concd and examined by TLC Si gel, petrol–Et_2O, 1 : 1; 1% $Ce(SO_4)_2$ in 2 N H_2SO_4 as spray reagent]. Compounds **1** and **2** were present in a ratio *ca* 10 : 1, as judged from visual comparison with standard mixtures.

Table 2. ^{13}C NMR spectral data of compounds **1** and **2** (20.1 MHz, $CDCl_3$, TMS as internal standard)

	1	2
C-1	149.0 *s*	188.1 *s*
C-2	135.1 *s*	148.5 *s*
C-3	115.7 *d*	133.2 *d*
C-4	145.9 *s*	188.1 *s*
C-5	114.1 *d*	132.3 *d*
C-6	128.0 *s*	145.9 *s*
C-1′	29.5 *t*	27.2 *t*
C-2′	122.3 *d*	118.5 *d*
C-3′	125.6 *s*	135.4 *s*
C-4′	39.5 *t*	39.1 *t*
C-5′	25.8 *t*	26.1 *t*
C-6′	124.9 *d**	124.6 *d**
C-7′	137.5 *s*	139.6 *s*
C-8′	36.7 *t*	36.4 *t*
C-9′	29.3 *t*	29.3 *t*
C-10′	76.4 *d*	77.1 *d*
C-11′	74.6 *s*	75.0 *s*
C-12′	38.8 *t*	38.5 *t*
C-13′	22.0 *t*	22.0 *t*
C-14′	124.6 *d**	124.5 *d**
C-15′	131.9 *s*	131.8 *s*
C-16′	25.7 *q*	25.5 *q*
C-17′	17.7 *q*	17.6 *q*
C-18′	21.0 *q*	21.0 *q*
C-19′	16.0 *q*	16.0 *q*
C-20′	16.0 *q*	16.0 *q*
Me-6	16.0 *q*	16.0 *q*

Multiplicities were obtained by off-resonance decoupling experiments.
*Interchangeable.

Isopropylidene acetal of **1**. Compound **1** (30 mg) dissolved in Me_2CO (5 ml) was stirred in the presence of Dowex 50 (H^+ form) resin for 15 min. Filtration and evaporation of the Me_2CO gave an oil which was subjected to prep. TLC (Si gel, petrol–Et_2O, 1 : 1) to yield the pure acetal (20 mg). MS *m/z* 470 $[M]^+$; ^1N NMR (80 MHz, $CDCl_3$, TMS): δ 3.71 (1H, *dd*, *J* = 8 and 4 Hz, H-10′), 1.07 (3H, *s*, Me-11′), 1.3 and 1.4 (3H each, *s*, $(Me)_2C$ ).

Periodic acid oxidation of **1**. To **1** (100 mg) in Et_2O (2 ml) was added 4 ml of a satd soln of H_5IO_6 [9]. A ppt. of HIO_3 was immediately formed and was filtered off. Evaporation of the solvent gave a residue which was subjected to Si gel chromatography (Et_2O–C_5H_{12}, 1 : 4) to give aldehyde **3** (45 mg) and ketone **4** (15 mg).

Aldehyde **3**: Oily, MS *m/z*: 300.1763 $[M]^+$ (calc. for $C_{19}H_{24}O_3$, 300.1725), 243, 175 (base), 137; ^1H NMR (80 MHz, $CDCl_3$, TMS): δ 9.64 (1H, *s*, H-10′), 6.47 [1H, (*br*), H-5], 6.39 [1H, *m*(*br*), H-3], 5.08 (2H, *m*, H-2′ and H-6′), 3.07 (2H, *d*, *J* = 7.5 Hz, H-1′), 2.38 (4H, *m*, 2H-8′ and 2H-9′), (3H, *s*, Me-6), 2.02 (4H, *m*, 2H-4′ and 2H-5′), 1.60 (6H, *s*, 3H-11′ and 3H-12′); ^{13}C NMR (20.1 MHz, $CDCl_3$, TMS): δ 200.1 (*s*), 188.8 (2C, *s*), 146.9 (*s*), 144.3 (*s*), 138.0 (*s*), 132.0 (*s*), 131.4 (*d*), 130.5 (*d*), 123.4 (*d*), 116.8 (*d*), 41.2 (*t*), 38.8 (*t*), 31.3 (*t*), 27.2 (*t*), 25.7 (*t*), 15.8 (*q*), 15.7 (*q*), 15.5 (*q*).

6-*Methylhept-5-en-2-one* (**4**): MS *m/z* 126.1012 $[M]^+$ (calc. for $C_8H_{14}O$, 126.1044); ^1H NMR (80 MHz, $CDCl_3$, TMS): δ 5.04 (1H, *m*, H-5), 2.20–2.42 (4H, *m*, 2H-3 and 2H-4), 2.11 (3H, *s*, H-1), 1.66 (3H, *s*, H-7), 1.60 (3H, *s*, H-8).

Ag_2O *oxidation of* **1** *to produce* **2**. Ag_2O (70 mg) and Na_2SO_4 (60 mg) were added to a soln of **1** (50 mg) in Et_2O (3 ml) and the suspension was stirred for 20 min [10]. The ppt. was filtered off and the soln was evapd to give 43 mg of **2**, identified by comparison of the physical properties ($[\alpha]_D$, IR, UV, MS, NMR) with those of the natural product.

$NaBH_4$ *reduction of* **2** *to produce* **1**. $NaBH_4$ (10 mg) was added to a soln of **2** (50 mg) in EtOH (3 ml) and the mixture was kept at room temp. for 15 min. After addition of H_2O (10 ml), excess reagent was destroyed by addition of dil. HCl and the organic material was extracted with Et_2O (×3). The combined extracts were dried (Na_2SO_4) and evaporated *in vacuo* to yield 45 mg of an oil, homogeneous by TLC, whose physical properties ($[\alpha]_D$, IR, UV, MS, NMR) were identical with those of **1**.

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