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ISOPRENOID DIHYDROQUINONES FROM A BROWN ALGA, *CYSTOPHORA* SP.

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Key Word Index—*Cystophora* sp.; Sargassaceae; geranyltoluquinol; geranyltoluquinone; methyl ethers.

Abstract—The lipid-soluble extract of the brown alga *Cystophora* sp. has yielded three new derivatives of geranyltoluquinol.

Apart from the family Dictyotaceae, brown algae (Fucales) have not been examined chemically to the same extent as red algae. Of the Australian species of the former, a number of the genus *Cystophora* have been investigated [1] and in general, they are a rich source of catecholamines. In addition, derivatives of farnesyl acetone are found in *C. moniliformis*, whereas *C. expansa* and *C. platylobium* contain δ-tocotrienol as the major lipid-soluble metabolite [1]. *C. torlosa* yields a complex mixture of polyenes, alkenyl resorcinols and a phloroglucinol derivative which is also the major metabolite of *C. congesta* [1]. We have now examined the lipid-soluble extract of an unclassified *Cystophora* sp., collected from the wave-swept rock platforms near Hamelin Bay, Western Australia. Three new derivatives of geranyl toluquinol have been isolated and their structural elucidation is presented in this report.

Chromatography of the CH_2Cl_2 extract of the alga resulted in the isolation of three new compounds. The least polar compound (**1**) (0.03% dry wt of alga), $C_{17}H_{22}O_{21}$, was obtained as an unstable yellow oil. Absorption bands in the UV spectrum, λ_{max} 250 nm (ε, 22900), and IR spectrum, 1660 and 1620 cm^{-1}, were indicative of a 1,4-benzoquinone moiety [2]. The ^1H NMR spectrum contained a multiplet which was shown by decoupling experiments to consist of a *d* × *t* ($J_d = 2.5$, $J_t = 1.8$ Hz) at δ 6.48 and a *d* × *q* ($J_d = 2.5$, $J_q = 1.5$ Hz) at δ 6.55 with long-range coupling to a doubly allylic methylene group (δ 3.13) and to a vinyl methyl (δ 2.05) and was assigned to vinylic protons α- to a carbonyl group. The NMR spectrum also revealed the presence of a 3,7-dimethylocta-2,6-dienyl chain which in the MS gave rise to significant ions at *m/z* 69 and 137. From this evidence the compound could be formulated as a 2,6-disubstituted-1,4-benzoquinone. The *E*-configuration of the internal double bond of the geranyl side-chain follows from the chemical shift of the signal for the 3′-methyl carbon (~16 ppm) [3] in the ^{13}C NMR spectrum of **1** (Table 1). Thus, the compound is shown to be (2′*E*)-2-(3′,7′-dimethylocta-2′,6′-dienyl)-6-methyl-2,5-cyclohexadiene-1,4-dione (**1**).

Examination of a portion of the crude extract after acetylation led to the isolation of the diacetate (**9**) but no benzoquinone (**1**) could be detected, suggesting that the hydroquinone (**8**) is in fact the natural product.

The second compound isolated (**2**) (0.03%), $C_{19}H_{28}O_2$, was obtained as a clear oil. The ^1H NMR spectrum showed, in addition to resonances attributable to a geranyl side-chain, signals due to two aromatic protons (δ 6.56), singlets at δ 3.68 and 3.74 for two methoxyl groups and at δ 2.28 for an aromatic methyl group. The predicted structure for this compound (2′*E*)-1,4-dimethoxy-2-(3′,7′-dimethylocta-2′,6′-dienyl)-6-methylbenzene (**2**) was confirmed by interrelation with **1**. Thus hydrogenation of **3** afforded 1,4-dimethoxy-2-(3′,7′-dimethyloctyl)-6-methylbenzene (**3**) identical with a sample obtained by hydrogenation and methylation of **1**. The configuration of the 2′,3′-double bond follows from the chemical shift of the 3′-methyl carbon (~16 ppm) [3] in the ^{13}C NMR spectrum of **2** (Table 1).

The major component **4** (0.08%), $C_{18}H_{26}O_2$, appeared, from spectroscopic characteristics, to be a demethylated analogue of **2** and this was confirmed when methylation yielded **2**. Evidence for the position of the hydroxyl group at C-4 came from the NMR spectrum of the acetate of **2** (**5**) which showed a down-field shift (0.25 ppm) of the *ortho*-protons compared to their chemical shift in the phenol **4**. Furthermore, attempts to cyclize **4** to the corresponding chromane or chromene were unsuccessful. In contrast, the isomer **6**, which was readily prepared by condensation of 1-hydroxy-4-methoxy-6-methylbenzene with geranyl chloride [4] cyclized to the corresponding chromene **7** on treatment with DDQ [4].

Isoprenylated dihydroquinones and benzoquinones have been encountered recently in sponges [5], algae [5–7] and tunicates [8]. In cases where these contain a toluquinol moiety, the 2,6-disubstitution pattern, as found for δ-tocotrienol and δ-tocopherol [9], is observed whereas simple prenylated dihydroquinones or benzoquinones from terrestrial plants show 2,5-disubstitution [10–12].

EXPERIMENTAL

General experimental details have been described [13].

Extraction and isolation of components of Cystophora *sp.* Samples of the alga [specimen (Accession No. UWS 2978) deposited in the Herbarium, Botany Department, University of Western Australia], collected from the wave-swept rock

Table 1. ^{13}C NMR data of **1**, **2**, **4–6** and **9** (20.1 MHz, $CDCl_3$, TMS as internal standard)

Carbon	**1**	**2**	**4**	**5**	**6**	**9**
1	188.1	150.8^a	150.5^a	154.5	147.0^a	145.6^a
2	146.0^a	135.6^b	135.9^b	136.0^a	125.6^b	135.1^b
3	132.5^b	113.0^c	114.1^c	120.3^b	113.3^c	120.3^c
4	188.1	155.8^a	151.8^a	146.8	153.4^a	148.4^a
5	133.3^b	113.9^c	115.4^c	121.7^b	114.3^c	121.2^c
6	148.7^a	136.3^b	136.5^b	136.8^a	127.7^b	137.8^b
6-Me	15.9^c	16.2^d	16.2	16.3	16.2	16.5^d
1′	27.7	28.4	28.2	28.2	30.5	28.8
2′	118.4	123.2	122.9	122.6	122.0	121.6
3′	139.9	131.8	132.1	131.5	138.7	129.0
3′-Me	16.1^c	16.4^d	16.2	16.3	16.2	16.2^d
4′	39.7	39.9	39.8	39.8	39.8	39.7
5′	26.6	26.8	26.8	26.7	26.5	26.7
6′	124.2	124.5	124.5	124.5	124.1	124.4
7′	131.9	131.5	131.6	132.2	132.1	131.7
7′-Me	17.7	17.7	17.7	17.7	17.7	17.7
8′	25.7	25.7	25.7	25.7	25.7	25.7
–OMe	—	55.4	—	—	55.7	—
–OMe	—	60.5	60.5	60.3	—	—
$-CO\underline{C}H_3$	—	—	—	21.1	—	20.4,21.1
$\underline{C}OMe$	—	—	—	169.8	—	168.8,169.5

^{a,b,c,d} Values with identical superscript within a column may be interchanged.

platforms off Cosy Corner (SW coast of Western Australia) in Oct. 1980, were frozen and stored at 4°. The CH_2Cl_2–MeOH (1:1) extract of the coarsely diced alga (589 g) was partitioned by addition of 10 % (by vol.) H_2O and the CH_2Cl_2 fraction was dried and the solvent removed to yield a mobile oil (16 g). A portion (5 g) of this extract was filtered rapidly through silicic acid (petrol–CH_2Cl_2 gradient) and the individual fractions were purified by Al_2O_3 chromatography to yield three known compounds: (a) β-carotene (0.007 %, 40 mg), (b) fucoxanthin (0.09 %, 530 mg) and (c) fucosterol (0.01 %, 100 mg), and three new compounds: **1** (0.03 %, 200 mg), **2** (0.03 %, 200 mg) and **4** (0.07 %, 500 mg) whose physico-chemical characteristics are given below.

(2′E)-2-(3′,7′-*Dimethylocta*-2′,6′-*dienyl*)-6-*methyl*-2,5-*cyclohexadiene*-1,4-*dione* (**1**). Yellow oil which darkens on standing, bp 210° (bath)/1.5 mm. (Found: C, 79.07; H, 8.83; M^+: 258.161. $C_{17}H_{22}O_2$ requires C, 79.07; H, 8.53 %; M^+: 258.162.) UV λ_{max}^{EtOH} (nm): 250 (ε, 22 900); IR ν_{max}^{film} cm^{-1}: 1662, 1620; ^{1}H NMR (90 MHz, $CDCl_3$): δ 1.62 (6 H) and 1.70 (3 H) (*s* (*br*), 3′-, 7′-Me and 8′-H_3), 2.05 (*s*, 6-Me), 2.07 (*s* (*br*), 4′- and 5′-H_2), 3.13 (*d* (*br*), *J* = 7.5 Hz, 1′-H_2), 5.12 (*m*, 2′-, 6′-H), 6.50 (AB*q*, *J* = 2.5 Hz, 3-, 5-H); MS *m/z* (rel. int.): 258 $[M]^+$ (6), 243 (6), 215 (20), 189 (15), 175 (50), 161 (15), 137 (10), 121 (15), 91 (20), 77 (20), 69 (100).

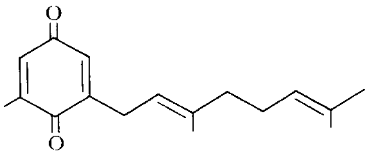
(2′E)-1,4-*Dimethoxy*-2-(3′,7′-*dimethylocta*-2′,6′-*dienyl*)-6-*methylbenzene* (**2**). Clear oil, bp 182° (bath)/1.5 mm. (Found: C, 79.81; H, 9.62; M^+: 288.207. $C_{19}H_{28}O_2$ requires C, 79.27; H, 9.72 %; M^+: 288.209.) UV λ_{max}^{EtOH} nm: 280 (ε, 2500); IR ν_{max}^{film}: 1610 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$): δ 1.60, 1.67 and 1.72 (*s* (*br*), 3′-, 7′-Me and 8′-H_3), 2.06 (*s* (*br*), 4′-, 5′-H_2), 2.28 (*s*, 6-Me), 3.35 (*d* (*br*), *J* = 7.5 Hz, 1′-H_2), 3.68 (3 H) and 3.74 (3 H) (*s*, 2 × –OMe), 5.30 (*m* (*br*), 2′-, 6′-H), 6.56 (*s* (*br*), 3-, 5-H); MS *m/z* (rel. int.): 288 $[M]^+$ (41), 219 (53), 204 (10), 189 (25), 151 (30), 123 (55), 69 (100).

(2′E)-2-(3′,7′-*Dimethylocta*-2′,6′-*dienyl*)-4-*hydroxy*-1-*methoxy*-6-*methylbenzene* (**4**). Clear oil, bp 200° (bath)/1.5 mm. (Found: C, 78.73; H, 9.73; M^+: 274.190.) $C_{18}H_{26}O_2$ requires C, 78.83; H, 9.49 %; M^+: 274.193.) UV λ_{max}^{EtOH} (nm): 282 (ε, 5300); IR ν_{max}^{film} (cm^{-1}): 3400, 1605; ^{1}H NMR ($CDCl_3$, 90 MHz): δ 1.60 (3 H) and 1.70 (6 H) (3′-, 7′-Me and 8′-H_3), 2.05 (*m*, 4′-, 5′-H_2), 2.24 (*s*, 6-Me), 3.31 (*d* (*br*), *J* = 7.5 Hz, 1′-H_2), 3.67 (3 H, *s*, –OMe), 4.72 (*s* (*br*), 4-O$\underline{H}$), 5.10 (*t* (*br*), *J* = 7.5 Hz, 6′-H), 5.28 (*t* (*br*), *J* = 7.5 Hz, 2′H), 6.47 (*s* (*br*), 3-, 5-H); MS *m/z* (rel. int.): 274 $[M]^+$ (67), 205 (100), 190 (33), 151 (75), 137 (65), 123 (100), 69 (100). Methylation of a sample of **4** with NaH/MeI in tetrahydrofuran gave a compound identical to **2**.

1,4-*Dimethoxy*-2-(3′,7′-*dimethyloctyl*)-6-*methylbenzene* (**3**). Hydrogenation of a sample of the benzoquinone (**1**) in Et_2O over 10 % Pd–C followed by methylation of the product with NaH/MeI in tetrahydrofuran at room temp. overnight yielded the dimethoxybenzene (**3**) as a clear oil, bp 170° (bath)/1 mm. (Found: C, 78.07; H, 10.83 %; M^+: 292.238. $C_{19}H_{32}O_2$ requires C, 78.03; H, 11.03, M^+: 292.240.) IR ν_{max}^{film} (cm^{-1}): 1602, 1612; ^{1}H NMR ($CDCl_3$, 90 MHz): δ 0.87 (*d*, *J* = 7 Hz, 3′-, 7′-Me and 8′-H_3), 2.27 (*d*, *J* = 1.5 Hz, 6-Me), 2.59 (*m*, 1′-H_2), 3.68 and 3.74 (6 H, *s*, 2 × –OMe), 6.55 (*s* (*br*), 3-, 5-H); MS *m/z* (rel. int.): 292 $[M]^+$ (70), 166 (100), 151 (90), 135 (40).

Hydrogenation of a sample of **2** in Et_2O over 10 % Pd–C yielded a compound which was shown to have identical GLC (R_t 15.3 min, SE-30 (5 %), initial temp. 100°, programmed at 8°/min) and spectral properties to **3** prepared above.

(2′E)-1-*Hydroxy*-2-(3′,7′-*dimethylocta*-2′,6′-*dienyl*)-4-*methoxy*-6-*methylbenzene* (**6**). To 1-hydroxy-4-methoxy-2-methylbenzene (0.5 g) in dry benzene (40 ml) was added BuLi (5 ml, 1.6 M in Et_2O) and the soln heated under reflux for 1 hr. Geranyl chloride (1.0 g) was added dropwise and the mixture heated under reflux overnight. The reaction mixture was quenched with ice and 1 M HCl and the product recovered was adsorbed on a column of Al_2O_3 (Act III, neutral). Elution with a petrol–CH_2Cl_2 gradient afforded **6** (200 mg), bp 170° (bath)/0.75 mm. (Found: C, 79.09; H, 9.19 %; M^+: 274.192. $C_{18}H_{26}O_2$ requires C, 78.83, H, 9.49; M^+: 274.193.) IR ν_{max}^{film}: 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz): δ 1.61, 1.69 and 1.78 (*s*, 3′-, 7′-Me and 8′-H_3), 2.08 (*m*, 4′-, 5′-H_2), 2.21 (*s*, 6-Me), 3.32 (*d* (*br*), *J* = 7.5 Hz, 1′-H_2), 3.73 (3 H, *s*, –OMe), 4.80 (*s*, –O$\underline{H}$), 5.06



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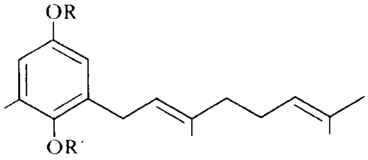

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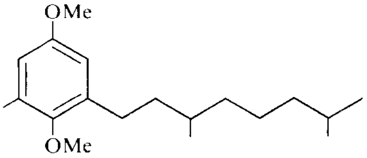
9	COMe	COMe



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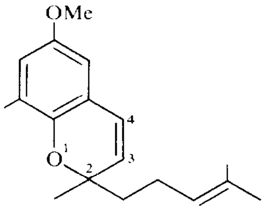

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(*m*, 6'-H), 5.30 (*t* (*br*), $J = 7.5$ Hz, 2'-H), 6.55 (AB*q*, $J = 2.5$ Hz, 3-, 5-H); MS *m*/*z* (rel. int.): 274 $[M]^+$ (100), 205 (25), 189 (65), 151 (100), 123 (45), 69 (70).

Transformation of **6** *to the chromene* (**7**). To a solution of **6** (118 mg) in C_6H_6 (20 ml) was added DDQ (120 mg) and the mixture was heated under reflux overnight. After cooling the mixture was filtered through celite and the filtrate taken to dryness. The residue was adsorbed on a column of Al_2O_3 (Act I, neutral) and elution with a petrol–CH_2Cl_2 gradient gave fractions (18 mg) of the 2,8-dimethyl-6-methoxy-2-(4'-methylpent-3'-enyl)-chromene (**7**), oil, bp (110° (bath)/0.4 mm. (Found: C, 79.58; H, 9.13; M^+: 272.175. $C_{18}H_{24}O_2$ requires C, 79.36; H, 8.89 %; M^+: 272.178.) IR $\nu_{\max}^{\text{film}}$ (cm^{-1}): 1610, 1600; ^{1}H NMR ($CDCl_3$, 90 MHz): δ 1.36 (*s*, 2-Me), 1.58, 1.67 (*s* (*br*), 4'-Me and 5'-H_3), 2.16 (*s*, 8-Me), 3.72 (3 H, *s*, –OMe), 5.10 (*t* (*br*), $J = 7$ Hz, 3'-H), 5.56 (*d*, $J = 10$ Hz, 3-H), 6.28 (*d*, $J = 10$ Hz, 4-H), 6.38 and 6.56 (AB*q*, $J = 3$ Hz, 5-, 7-H); MS *m*/*z* (rel. int.): 272 $[M]^+$ (30), 276 (10), 189 (100), 146 (20), 115 (10), 91 (15), 77 (10), 69 (20).

Compounds from the acetylated extract of Cystophora *sp.* A portion of the fresh algal extract (CH_2Cl_2) was treated with Ac_2O–pyridine under N_2. The product recovered was adsorbed on a column of Al_2O_3 (Act II, neutral). Elution with a petrol–CH_2Cl_2 gradient gave fractions of (a) **2**; (b) (2 *E*)-4-acetoxy-2-(3',7'-dimethylocta-2',6'-dienyl)-1-methoxy-6-methylbenzene (**5**) as an oil, bp 180° (bath)/1 mm. (Found: M^+: 316.201. $C_{20}H_{28}O_3$ requires M^+: 316.204.) IR $\nu_{\max}^{\text{film}}$: 1775 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz): δ 1.60 (3 H) and 1.69 (6 H), (*s* (*br*), 3'-, 7'-Me and 8'-H_3), 2.25 (3 H, *s*, –OCOMe), 2.28 (*s*, 6-Me), 3.37 (*d* (*br*), $J = 7.5$ Hz, 1'-H_2), 3.68 (3 H, *s*, –OMe), 5.20 (*m* (*br*), 2'-, 6'-H_2), 6.72 (*m*, 3-, 5-H); MS *m*/*z* (rel. int.): 316 $[M]^+$ (20), 274 (10), 231 (10), 205 (100), 175 (20), 151 (30), 123 (90), 69 (51); and (c) (2'*E*)-1,4-diacetoxy-2-(3',7'-dimethylocta-2',6'-dienyl)-6-methyl benzene (**9**), oil, bp 170° (bath)/0.2 mm. (Found: C, 73.20; H, 8.26; M^+: 344.193. $C_{21}H_{28}O_4$ requires C, 73.23; H, 8.19 %; M^+: 344.199.) IR $\nu_{\max}^{\text{film}}$: 1770 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz); δ 1.60, 1.66 and 1.68 (*s* (*br*), 3'-, 7'-Me and 8'-H_3), 2.13 (*s* (*br*), 6-Me), 2.25 and 2.30 (6 H, *s*, 2 × –OCOMe), 3.19 (*d* (*br*), $J = 7.5$ Hz, 1'-H_2), 5.13 (*m* (*br*), 2'-, 6'-H), 6.80 (AB*q*, $J = 2.5$ Hz, 3-, 5-H); MS *m*/*z* (rel. int.): 344 $[M]^+$ (7), 301 (15), 260 (55), 205 (20), 191 (55), 175 (35), 149 (100), 137 (35), 123 (100), 69 (80).

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