Debromocymopolone from the green alga, *Cymopolia barbata*

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Investigation of a Jamaican green alga, *Cymopolia barbata* led to the isolation of a new geranyl-1,4-dihydroxybenzene, debromocymopolone, the structure of which was elucidated by spectroscopic techniques.

Keywords: debromocymopolone, *Cymopolia barbata*, cymopolone, marine natural products

Marine green algae are among the least investigated of the algal types. The examination of the secondary metabolites from algae of the Chlorophyta Phylum represent about 10% of all the marine algae that have been investigated. Halogenated compounds are uncommon secondary metabolite of the marine green algae which have been examined, accounting for just about 7% of the compounds isolated.[1] It has been suggested that the low secondary metabolite production is due to a greater propensity of the green algae to adapt to the environment. *Cymopolia barbata* is a lightly calcified green alga that may not need to produce secondary metabolites as a defence mechanism although the compounds identified in this organism have been found to exhibit a wide range of bioactivities including inhibition of plant growth, feeding inhibition and antibacterial, antifungal and antimutagenic activity. Specimens from various tropical locations in the Caribbean (Cuba, The Bahamas, Puerto Rico, Florida Keys) and Canary Island have been studied and compounds of mixed terpenoid and aromatic biogenesis have been isolated.[2-6]

In our investigation of marine organisms for secondary metabolites, a series of previously isolated halogenated compounds including cymopolone, 7-hydroxycymopolone, 3,7-dihydroxycymopolone,3-hydroxycymopolone,7-hydroxy-cymopochromanone and cymopol monomethyl ether were identified by comparison with reported ^{1}H NMR and ^{13}C NMR data.[2,6] In addition, a new non-halogenated compound of the cymopol type was found in the Jamaican extract of *C. barbata*, debromocymopolone, **1**.

The alga was air-dried over a three day period and extracted with CH_2Cl_2: methanol (1 : 1) to yield a dark green gum which was subjected to vacuum liquid chromatography (VLC) on silica gel and eluted with increasing proportions of CH_2Cl_2 in hexanes. A final elution was with 20% methanol: CH_2Cl_2. Further purification using silica gel afforded several members of the series of compounds known as the cymopols. In one fraction which eluted in ethyl acetate: hexane, the ^{1}H NMR (see Table 1) spectrum revealed the absence of the singlets in the 7.15 to 7.6 ppm range which typify the cymopols. These resonances were replaced by three one-proton resonances at 6.90 (doublet, $J = 9.0$ Hz), 7.02 (doublet of doublets, $J = 2.9$, 9.0 Hz) and 7.25 ppm (doublet, $J = 2.9$ Hz), a coupling pattern typical of a 1,2,4-trisubstituted aromatic system. This therefore suggested that the 1,2,4,5 tetrasubstitution pattern known for all the cymopols to date was absent. This compound (**1**) was isolated as a transparent oil and gave a molecular ion of *m/z* 261.1487 (M + H), corresponding to a molecular formula of $C_{16}H_{20}O_3$. Of the seven double bond equivalents implied by this formula, two could be readily attributable to olefinic groups (119.6, 122.9, 132.9 and 161.2 ppm), while another denoted a carbonyl resonance (196.0 ppm) leading one to surmise that the other double bond equivalents could be accounted for by an aromatic ring. The absorption at 703 and 731 cm^{-1} in the IR spectrum suggested the presence of the 1,2,4 substitution pattern. The ^{1}H NMR spectrum consisted of singlet methyl groups at 1.62 and 1.75 ppm, overlapping methylenes (2.31 ppm) and olefinic methine signals at 5.15 and 6.70 ppm. This led to the structural formula **1**, debromocymopolone, for the new compound.

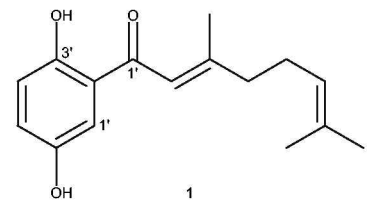

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Fig. 1

Table 1 ^{1}H, ^{13}C, and HMBC NMR data for debromocymopolone[a,b]

Position	^{13}C	^{1}H	HMBC (^{1}H–^{13}C)
1	196.0		
2	119.6	6.70, br s	C-1, C-3, C-4, C-10
3	161.2		
4	41.6	2.31, m	C-2, C-3
5	26.2	2.31, m	C-6, C-7
6	122.9	5.15, m	C-5, C-8, C-9
7	132.9		
8	17.8[c]	1.62, s	C-6, C-7
9	25.7[c]	1.75, s	C-6, C-7, C-8
10	20.1	2.22, s	C-1, C-2, C-3, C-4
1'	115.0	7.25, d (2.9)	C-1, C-3', C-5', C-6'
2'	120.5		
3'	157.4		
4'	119.2	6.90, d (9.0)	C-2', C-3'
5'	124.1	7.02, dd (2.9, 9.0)	C-1', C-3'
6'	147.1		
3' - OH		12.4, s	C-2', C-3', C-4'
6' - OH		4.55, s	C-1', C-5', C-6'

[a]NMR spectra were recorded in $CDCl_3$. [b]*J* values given in Hz are recorded in parentheses. [c]Signals may be interchanged.

While it has been reported that the extracts from *C. barbata* have been subjected to a range of biological assays, specific applications have not been ascribed to the individual compounds. Some of the cymopols which have been isolated from the Jamaican specimens are currently undergoing evaluation for activity with respect to the inhibition of cytochrome P450 enzymes.

This represents, to the best of our knowledge, the first report of a cymopol from *C. barbata* which does not contain a bromine atom.

Experimental

General procedure

Optical rotations were determined on a Perkin–Elmer 241 MC polarimeter. UV spectra were recorded on a Perkin Elmer Lambda 19 spectrometer. IR spectra were obtained on a Perkin Elmer 1600 FTIR instrument.

^{1}H and ^{13}C spectra were recorded on either a Bruker 500 spectrometer or a Bruker 200 MHz instrument. Mass spectral data were measured on Micromass 70-SE magnetic sector running CI with methane reagent gas in positive mode.

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Plant material

The algal sample was collected in June 2004 from the shoreline of the north eastern coast of Jamaica at Fairy Hill Beach in the parish of Portland at a depth of 0.5 m.

Extraction and isolation

The air-dried sample (962.15 g) was extracted with methanol: dichloromethane (1:1) to yield a dark green gum (30.91 g), a portion of which (12.8 g) was subjected to vacuum liquid chromatography on silica gel in a 2 L sintered funnel (10.3 cm high × 13.2 cm diameter) with a gradient elution system consisting of increasing proportions of CH_2Cl_2 in hexanes, 100% CH_2Cl_2 with final elution in 20% methanol: CH_2Cl_2. Of the 56 fractions obtained, fraction 22–24 (2.35 g), which eluted in 20% methanol: CH_2Cl_2, were subjected to further column chromatography to afford 172 fractions. From this column, fraction 20–22 was found to contain 7-hydroxycymopochromanone, fraction 33–38 contained 3-hydroxycymopolone while fraction 57–63 contained 3-methoxy-7-hydroxycymopol, all identified by comparison of their ^1H and ^{13}C NMR data with the literature.[6] Fractions 28–32 (58.5 mg) from this column was subjected to further column chromatography in 50% CH_2Cl_2 and subsequent purification in 20% ethyl acetate: hexane afforded compound **1** (4.2 mg).

Debromocymopolone (**1**): Yellow oil; UV (MeOH) λ_{max} (ε) 260 (0.70), 360 (0.18) nm; IR (film) υ_{max} 3054, 1421, 1264, 895, 731, 703 cm^{-1}; ^1H NMR and ^{13}C NMR ($CDCl_3$), see Table 1; LREIMS (M + H) *m/z* (rel int) 261 (15), 227 (25), 177 (35), 137 (100), 109 (80); HREIMS (M + H) *m/z* 261.1487 [calcd for $C_{16}H_{20}O_3$, 261.1491 (M + H)].

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