

A New Brominated Phenylpropylaldehyde and its Dimethyl Acetal from Red Alga *Rhodomela confervoides*

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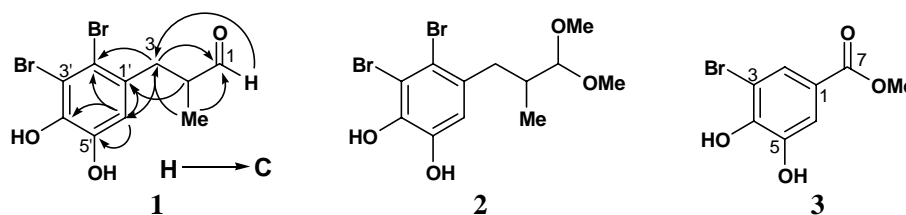
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Abstract: A new brominated phenylpropylaldehyde and its dimethyl acetal together with a new natural brominated phenol were isolated from *Rhodomela confervoides*. Their structures were elucidated as 2-methyl-3-(2,3-dibromo-4,5-dihydroxyphenyl)propylaldehyde, 2-methyl-3-(2,3-dibromo-4,5-dihydroxyphenyl) propylaldehyde dimethyl acetal and 3-bromo-4,5-dihydroxybenzoic acid methyl ester by spectroscopic techniques including IR, HRFABMS, 1D and 2DNMR experiments.

Keywords: Red alga, Rhodomelaceae, *Rhodomela confervoides*, brominated phenylpropyl- Aldehyde derivatives.

Red alga *Rhodomela confervoides* is widely distributed in the gulf of Yellow Sea, China. It belongs to the Rhodomelaceae family reported being rich in bromaphenols¹⁻⁹. The previous report indicated that 2, 3-dibromo-4, 5-dihydroxybenzyl alcohol and 3, 5-dibromo-4-hydroxybenzyl alcohol were isolated from this alga¹⁰, while some chlorinated bromophenols and 2, 3, 2', 3'-tetrabromo-4, 5, 4', 5'-tetrahydroxydipenylmethane were identified by stepwise extraction followed by GC-MS⁵. In our investigation of chemical constituents of *R. confervoides* collected at the coast of Qingdao, two unique bromophenols with oxygenated 2-methylpropyl side chains, along with a new natural brominated phenol were obtained. This paper deals with the isolation and structural elucidation of these compounds.

Figure 1 The key HMBC correlations of **1** and **2**



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The air-dried and grounded red alga *R. confervoides* was extracted with 95% EtOH, the concentrated extract was suspended in water, and then partitioned with EtOAc. The EtOAc extract was chromatographed over silica gel eluting with a gradient increasing MeOH (0-100%) in CHCl₃. The fraction eluted by 10% MeOH in CHCl₃ was separated by size-exclusion chromatography over Bio-Beads SX-3 with CHCl₃-EtOAc (1:1) as eluent to yield a mixture which was further purified by reverse phase HPLC to yield **1** and **2**.

Compound **1** was obtained as a gum. The IR spectrum (KBr) of **1** showed absorption bands for hydroxyl (3386 cm⁻¹) and carbonyl (1712 cm⁻¹) groups and aromatic rings (1600, 1576, 1498 and 1469 cm⁻¹). Its EIMS spectrum gave characteristic tribrominated molecular ion peaks at *m/z* 339, 337 and 335 (1:2:1). The molecular formula was determined as C₁₀H₁₀Br₂O₃ by HREIMS at *m/z* 335.8982 (calcd. for C₁₀H₁₀⁷⁹Br₂O₃ 335.8997). The ¹H NMR spectrum of **1** in acetone-d₆ showed a diagnostic signal at δ 9.70 (d, 1H, *J*=1.5 Hz, H-1) for aldehyde proton, and signals attributed to a aromatic proton at δ 6.88 (s, 1H, H-6') and a methyl at δ 1.07 (d, 3H, *J*=7.0 Hz, H-4), as well as an ABX coupling system at δ 2.66 (dd, 1H, *J*=13.5 and 7.8 Hz, H_A-3), 2.74 (m, 1H, H-2) and 3.18 (dd, 1H, *J*=13.5 and 6.3 Hz, H_B-3). The ¹H-¹H COSY spectrum of **1** confirmed the presence of a 2-methylpropylaldehyde unit with a substitution group at C-3 position in the structure of **1**. In addition to carbon signals of this unit, the ¹³C NMR and DEPT spectrum (see **Table 1**) exhibited six methylene signals attributed to a *penta*-substituted benzene ring. All of the above spectral data revealed that the structure of **1** is 2-methyl-3-phenylpropylaldehyde possessing substitution groups of two hydroxyls and two bromines at the aromatic moiety. In the HMBC spectrum of **1** (see **Figure 1**), long range correlations from H₂-3 to C-2' and C-6' and from H-6' to C-1', C-2', C-4' and C-5' unambiguously established substitution

Table 1 ¹H and ¹³C NMR data of compounds **1** - **3**^a

No.	1		2		3	
	δ _H	δ _C	δ _H	δ _H	δ _H	δ _H
1	9.70 d (1.5)	203.7 d	4.11 d (5.1)	108.5 d		128.0 s
2	2.74 m	46.5 d	2.15 m	36.3 d	7.70 d (1.8)	117.5 d
3a	2.66 dd (13.5, 5.7)		2.44 dd (13.5, 3.6)			
3b	3.18 dd (13.5, 6.3)	37.7 t	2.96 dd (13.5, 4.8)	39.2 t		116.8 s
4	1.07 d (7.0)	12.8 q	0.80 d (6.6)	13.3 q		149.1 s
5						151.2 s
6					7.56 d (1.8)	125.3 d
7						165.5 s
1'		131.4 s		133.0 s		
2'		115.8 s		115.9 s		
3'		113.3 s		113.2 s		
4'		143.4 s		143.0 s		
5'		144.9 s		144.7 s		
6'	6.88 s	117.0 d	6.83 s	117.0 d		
OMe			3.35 s	54.0 q	3.90 s	60.2 q
OMe			3.33 s	53.9 q		

^a Measured in acetone-d₆ at 300 MHz for proton and at 75 MHz for carbon. ¹H coupling constants (*J*) in Hz are given in parentheses. The assignments were based on DEPT, ¹H-¹H COSY, HMQC and HMBC experiments.

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pattern of the phenyl moiety. Therefore, the structure of **1** was determined as 2-methyl-3-(2', 3'-dibromo-4', 5'-dihydroxyphenyl)propylaldehyde. It was considered to be an enantiomer since no optical rotation was observed.

Compound **2** was obtained as a white amorphous powder (Me₂CO), m.p. 117-118 °C. Its IR spectrum (KBr cm⁻¹) showed absorption bands for hydroxyl groups (3462) and aromatic rings (1599, 1581 and 1496). The EIMS spectrum exhibited characteristic tribrominated molecular ion peaks at *m/z* 382, 384 and 386 (1:2:1). The molecular formula was determined as C₁₂H₁₆Br₂O₄ by HREIMS at *m/z* 381.9425 (calcd. for C₁₂H₁₆⁷⁹Br₂O₄ 381.9415). The ¹H NMR spectrum of **2** was very similar to that of **1** (see **Table 1**), except for disappearances of the signal attributed to the aldehyde proton and appearances of signals at δ_H 4.11 (d, 1H, *J*=5.1 Hz, H-1), 3.35 (s, 3H) and 3.34 (s, 3H), and δ_C 108.5 (d), 54.0 (q) and 53.9 (q), which could assigned to a dimethyl acetal moiety. Thus, the structure of **2** was established as 2-(*S*)-2-methyl-3-(2,3-di-bromo-4,5-dihydroxyphenyl)propylaldehyde dimethyl acetal. This assignment was confirmed by the HMBC experiment. **2** is an enantiomer since it is optically inactive. Although the structure of **2** is novel, it might be an artifact produced in the isolation procedure because **1** was refluxed with methanol at 40 °C for 8 h to yield **2**.

Compound **3** was a white amorphous powder, m.p. 176-178 °C. Its IR spectrum showed absorption bands for hydroxyl (3425 cm⁻¹), carbonyl (1685 cm⁻¹) groups and aromatic rings (1608 and 1496 cm⁻¹). The structure of **3** was established as 3-bromo-4, 5-dihydroxybenzoic acid methyl ester by 1D NMR data (**Table 1**) and 2D NMR experiments. Although this compound has been synthesized, no spectral data were reported¹¹.

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