

Two New Bromophenols from Red Alga *Rhodomela confervoides*^{††}

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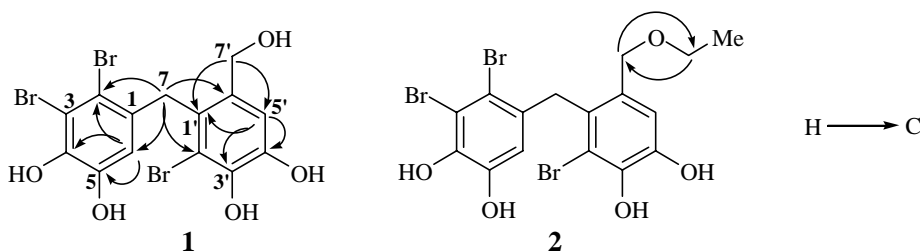
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Abstract: Two new bromophenols were isolated from *Rhodomela confervoides*. Their structures were elucidated as 2, 2', 3-tribromo-3', 4, 4', 5-tetrahydroxy-6'-hydroxymethyldiphenylmethane and 2, 2', 3-tribromo-3', 4, 4', 5-tetrahydroxy-6'-ethyloxymethyldiphenylmethane by spectroscopic methods including IR, HREIMS, 1D and 2D NMR techniques.

Keywords: Red alga, Rhodomelaceae, *Rhodomela confervoides*, bromophenol.

Red algae of the family Rhodomelaceae were reported being rich in bromophenols¹⁻⁹. *Rhodomela confervoides* is widely distributed in the gulf of Yellow Sea, China. 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'-tetrahydroxydiphenylmethane were identified by stepwise extraction followed by GC-MS⁵. In our recent systematic investigation of chemical constituents of *R. confervoides* collected at the coast of Qingdao, two new bromophenols **1** and **2** were obtained. We report here the isolation and structural elucidation of these compounds.

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



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

[†] This paper is dedicated to Professor Xiao-Tian Liang on the occasion of his 80th birthday

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EtOAc extract was chromatographed over silica gel eluting with a gradient increasing MeOH (0-100%) in CHCl₃. The fraction eluted by 20% 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 yellowish white needles (Me₂CO), mp 127-129 °C. The IR spectrum (KBr) of **1** showed strong broadened absorption bands for hydroxyl groups at 3477 and 3425 cm⁻¹ and characteristic bands for aromatic rings at 1608, 1577, 1491 and 1469 cm⁻¹. Its EIMS spectrum gave the tri-brominated molecular ion peaks at *m/z* 502, 500, 498 and 496 with a abundance ratio of 1:3:3:1. The molecular formula was determined as C₁₄H₁₁Br₃O₅ by HREIMS at *m/z* 495.8134 (calcd. for C₁₄H₁₁Br₃O₅ 495.8157). In addition to a very broadened exchangeable signal integrated for four protons at δ 8.52, the ¹H NMR spectrum of **1** in acetone-d₆ showed only four singlets attributed to aromatic protons at δ 7.09 (s, 1H, H-5'), 6.08 (s, 1H, H-6), and two methylenes at δ 4.42 (s, 2H, H-7') and 4.12 (s, 2H, H-7). The ¹³C NMR and DEPT spectra of **1** (see **Table 1**) displayed 14 carbons assignable to two methylenes and two *penta*-substituted benzene rings with four oxygenated carbons which were recognized by their chemical shifts (δ >142 ppm). All of the above spectral data indicated that **1** possessed a diarylmethane structure with substitution groups of four hydroxyls, three bromines and one hydroxymethyl group. In the HMBC spectrum (see **Figure 1**), long range correlations from H₂-7 to C-2, C-6, C-2' and C-6' confirmed the diarylmethane structure of **1**. The substituted patterns of the aromatic rings were unambiguously established by correlations from H-6 to C-2, C-4, C-5 and C-7, from H-5' to C-1', C-3', C-4' and C-7' and from H₂-7' to C-1' and C-5'. Therefore, the structure of **1** was

Table 1 ¹H and ¹³C NMR data of compound **1** and **2**^a

No.	1		2	
	δ _H	δ _C	δ _H	δ _C
1		131.7 s		131.8 s
2		115.7 s		115.6 s
3		113.1 s		112.9 s
4		142.9 s		142.8 s
5		144.8 s		144.7 s
6	6.08 s	114.1 d	6.08 s	114.3 d
7	4.12 s	38.6 t	4.13 s	38.8 t
1'		127.7 s		128.8 s
2'		114.2 s		114.4 s
3'		142.3 s		142.7 s
4'		144.4 s		144.1 s
5'	7.09 s	114.4 d	7.00 s	114.3 d
6'		133.5 s		130.5 s
7'	4.42 s	62.1 t	4.25 s	70.7 t
O-CH ₂			3.40 q (7.0)	65.5 t
CH ₃			1.06 t (7.0)	14.7 q

^a NMR data were measured in acetone-d₆ at 300 MHz for proton and at 75 MHz for carbon. δ_H, δ_C in ppm, the proton coupling constants (*J*) in Hz are given in parentheses. Assignments were based on DEPT, ¹H-¹H COSY, HMQC and HMBC experiments.

determined as 2,2',3-tribromo-3',4,4',5-tetrahydroxy-6'-hydroxymethyldiphenyl methane.

Compound **2** was obtained as yellowish white needles (Me₂CO), mp 197-199 °C. Its EIMS spectrum showed the molecular ion peak cluster at *m/z* 530, 528, 526 and 524 (1:3:3:1), which indicated the presence of three bromine atoms in the molecule of **2**. The molecular formula was determined as C₁₆H₁₅Br₃O₅ by HREIMS at *m/z* 523.8466 (calcd. for C₁₆H₁₅Br₃O₅ 523.8470). The IR and NMR spectra of **2** were very similar to those of **1** (see **Table 1**), except for appearances of characteristic signals attributed to a ethyloxyl group at δ_H 1.06 (t, 3H, *J*=7.0 Hz) and 3.40 (q, 2H, *J*=7.0 Hz) and δ_C 65.5 (t) and 14.7 (q) in the ¹H and ¹³C NMR spectra of **2**. In addition, H₂-7' was shifted upfield from δ 4.42 in **1** to δ 4.25 in **2**, while C-6' and C-7' were shifted from δ 133.5 and 62.1 in **1** to 130.5 and 70.7 in **2**, respectively, by comparing the NMR data of **2** with those of **1**. These evidences revealed that **2** is a 7'-ethyloxyl derivative of **1**, which was confirmed by the HMBC experiment of **2** (see **Figure 1**). Thus, the structure of **2** was assigned as 2,2',3-tribromo-3',4,4',5-tetrahydroxy-6'-ethyloxymethyldiphenylmethane.

2 might be an artifact of **1** produced in the extraction procedure, because **2** was obtained by refluxing **1** with 95% ethanol at 60 °C for 72 h. The methyl derivative of **1** 2,2',3-tribromo-3',4,4',5-tetrahydroxy-6'-methoxy methyldiphenylmethane was isolated from the methanolic extract of red alga *R. larix*⁴, it could be an artifact also.

Acknowledgments

The authors are grateful to professor Ablez Zeper for mass spectra measurements, and financial support from the NNSF (Grant No.99-929-01-26), and National "863" Program (Grant No. 2001AA620403).

References

1. N. Katsui, Y. Suzuki, S. Kitamura, T. Irie, *Tetrahedron*, **1967**, 23, 1185.
2. P. Saenger, M. Pedersen, K. S. Rowan, *Phytochemistry*, **1976**, 15, 1957.
3. K. Kurata, T. Amiya, N. Nakano, *Chem. Lett.*, **1976**, (6), 821.
4. K. Kurata, T. Amiya, *Chem. Lett.*, **1977**, (12), 1435.
5. M. Pedersen, *Phytochemistry*, **1978**, 17, 291.
6. K. Kurata, T. Amiya, *Bull. Chem. Soc. Jpn.*, **1980**, 53, 2020.
7. M. Akinin, A. Samb, J. Mirailles, V. Costantino, E. Fattorusso, A. Mangoni, *Tetrahedron Lett.*, **1992**, 33 (4), 555.
8. K. Kurata, K. Taniguchii, K. Takashima, I. Hayashi, M. Suzuki, *Phytochemistry*, **1997**, 45 (3), 485.
9. L. Lundgren, K. Olsson, O. Theander, *Acta Chem. Scand. B*, **1979**, 33 (2), 105.
10. J. S. Craigia, D. E. Gruening, *Science*, **1967**, 157 (3792), 1058.

Received 27 September, 2002