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BIS(2,3,6-TRIBROMO-4,5-DIHYDROXYBENZYL) ETHER FROM THE RED ALGA, *SYMPHYOCLADIA LATIUSCULA*[*]

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Key Word Index—*Symphyocladia latiuscula*; Rhodomelaceae; red alga; bromophenol; bis(2,3,6-tribromo-4,5-dihydroxybenzyl) ether; antimicrobial activity.

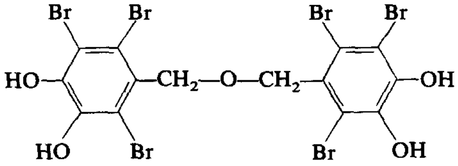
INTRODUCTION

Since Saito and Ando [1] obtained 3-bromo-4,5-dihydroxybenzaldehyde from *Polysiphonia morrowii*, many simple bromophenols have been isolated from the red algae, Rhodomelaceae. In a survey of 23 Rhodophycean species, Pedersén *et al.* [2] reported the presence of 10 simple bromophenols in Rhodomelaceae as well as in 4 other families using the GC–MS technique. Further, simple bromophenols were identified in *Fucus vesiculosus* [3], the blue green alga *Calothrix brevissima* and its culture filtrate [4], and an axenically cultured marine Ascomycete isolated from *Ascophyllum nodosum* by Pedersén and Fries [5]. Weinstein *et al.* [6] obtained one brominated phenol, dipotassium 2,3-dibromo-5-hydroxybenzyl-1′,4-disulfate, only from *Rhodomela larix*, and stated that other simple bromophenols previously isolated from the same alga could be artifacts which were derived during the isolation procedure. Recently, Chevolot-Magueur *et al.* [7] isolated 5,6,3′,5′-tetrabromo-3,4,2′,4′,6′-pentahydroxydiphenylmethane from *Rytiphlea tinctoria*. We reported the isolation of 3,3′-dibromo-4,5,4′,5′-tetrahydroxybibenzyl [8] from *P. urceolata* and two brominated diphenylmethanes, 2,3,2′,3′-tetrabromo-4,5,4′,5′-tetrahydroxydiphenylmethane and 2,3,2′-tribromo-4,5,3′,4′-tetrahydroxy-6′-methoxymethyldiphenylmethane [9], from *R. larix*. Pedersén [10] has identified the same diphenylmethane, 2,3,2′,3′-tetrabromo-4,5,4′,5′-tetrahydroxydiphenylmethane, together with bromochlorophenols in *P. nigrescens* and *R. confervoides*. Lundgren and Theander [11] also have isolated the same bromophenol from *P. brodiaei*.

Reports on the constituents of the red marine alga, *Symphyocladia latiuscula* have not been so extensive [12]. We have obtained 2,3,6-tribromo-4,5-dihydroxybenzyl methyl ether from the methanol extract and the corresponding ethyl ether from the ethanol extract of this alga (Kurata, K. and Amiya, T., unpublished results). These compounds could be artifacts which have been derived from a bromophenol precursor during the extraction procedure. A structurally related alcohol, 2,3,6-tribromo-4,5-dihydroxybenzyl alcohol, has been identified in *P. lanosa* and *R. subfusca* on the basis of the study of the TMSi derivative following GLC [13]. In the course of the investigation of the bromophenol precursor of this alga, a new bromophenol, bis(2,3,6-tribromo-4,5-dihydroxybenzyl) ether (**1**) has been obtained. We now report the isolation and structural elucidation of this compound.

RESULTS AND DISCUSSION

Si gel chromatography of a Me_2CO extract of the frozen alga gave bis(2,3,6-tribromo-4,5-dihydroxybenzyl) ether (**1**), mp 177–178°. Compound **1** showed an intense green colour with ferric chloride and gave a precipitate after standing overnight at room temperature or on heating over a steam bath, after addition of lead acetate. These facts suggested that **1** would be a catechol having substituents on both sides of the vicinal OH groups [9]. Compound **1** was analysed for $C_{14}H_8O_5Br_6$ by elemental analysis. Although the molecular ion peaks of **1** were not noticed in MS spectrum, the tetramethyl derivative (**2**) of **1** gave 798, 796, 794, 792, 790, 788 and 786 (M^+). The IR of **1** showed the presence of OH groups at 3480 cm^{-1}, phenyl rings at 1585, 1560 cm^{-1} and an aliphatic ether at 1075 cm^{-1}. The UV in EtOH exhibited a maximum at 297 nm (log ε 3.65). The ^1H NMR spectrum (60 MHz, Me_2CO-d_6) showed a signal for methylene protons at δ 4.98 (4H, *s*), a signal of phenolic protons at δ 8.68 (4H, *bs*), but revealed no presence of an aromatic ring proton. A total of nine carbon peaks were observed in the ^{13}C NMR spectrum ($CDCl_3$) of **2** (Table 1). These assignments were made by the gated decoupling technique. The gated decoupled spectrum of **2** was adequate to illustrate structure **1**. On the basis of these facts, as well as from the biogenetic view point, bis(2,3,6-tribromo-4,5-dihydroxybenzyl) ether was proposed for **1**.



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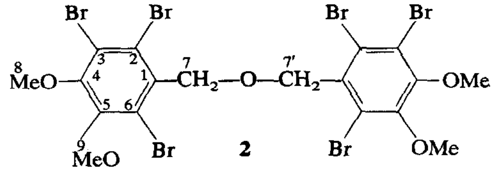

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[*] Part 5 in the series "Chemical Studies on Constituents of Marine Algae". For Part 4 see Kurata, K. and Amiya, T. (1977) *Chem. Letters* 1435.

Table 1. ^{13}C NMR data for **2***

Carbon No.	^{13}C δ	Gated decoupled multiplicity, $J_{C—H}$ (Hz)
8 and 9	60.77 (*q*)† 60.84 (*q*)	$J_{C_8—H_8}, J_{C_9—H_9} = 146$ (*q*)
7	73.8 (*t*)	$J_{C_7—H_7} = 145$ (*t*), $J_{C_7—H_{7'}} = 3.3$ (*t*)
3	121.8 (*s*)	
2 and 6	122.1 (*s*) 124.2 (*s*)	$J_{C_2—H_7}, J_{C_6—H_7} = 5.8$ (*t*)
1	133.6 (*s*)	$J_{C_1—H_7} = 3.7$ (*t*)
4 and 5	150.7 (*s*) 152.2 (*s*)	$J_{C_4—H_8}, J_{C_5—H_9} = 4.0$ (*q*)

* Proton decoupled values of **2** (ppm downfield from TMS) in $CDCl_3$ solvent on a JEOL FX-100 spectrometer.

† Off-resonance decoupling.

Compound **1** showed *in vitro* activity below the 50 μg/ml level against *Aspergillus niger* and another 4 fungal species, at the 100 μg/ml level against *Candida albicans*, and at the 100–200 μg/ml level against 13 gram-positive and gram-negative bacteria.

EXPERIMENTAL

Symphyocladia latiuscula was collected in April 1978 at Hakodate Bay, Hokkaido.

Bis(2,3,6-tribromo-4,5-dihydroxybenzyl) ether (**1**). The frozen alga (8.4 kg) was refluxed with 80% Me_2CO for 1 hr. The extract was evapd to dryness and treated with dried Me_2CO. The Me_2CO extract (37 g) was chromatographed on Si gel. Elution with C_6H_6–Et_2O (9:1) furnished a brownish crystalline material (0.8 g). This material was purified by recrystallization from C_6H_6–Me_2CO to yield fine colourless needles of **1**, mp 177–178°; (Found: C, 23.07; H, 1.06; Br, 65.24. $C_{14}H_8O_5Br_6$ requires: C, 22.86; H, 1.01; Br, 65.17%). IR ν_{max}^{KBr} cm^{-1}: 3480, 1585, 1560, 1075; UV λ_{max}^{EtOH} nm (log ε): 297 (3.65); ^{1}H NMR (60 MHz, Me_2CO-d_6): δ 4.98 (4H, *s*, methylene), 8.68 (4H, *s*, OH); MS *m/e*: 363, 361, 359, 357 ($M^+ - C_7H_4O_3Br_3$), 362, 360, 358, 356 ($M^+ - C_7H_4O_3Br_3 - 1$).

Tetramethyl derivative (**2**) *of* **1**. **1** in Et_2O was treated with CH_2N_2, yielding a tetramethyl ether, mp 137–138°; ^{1}H NMR (100 MHz, $CDCl_3$): δ 3.871 (6H, *s*, OMe), 3.876 (6H, *s*, OMe), 5.034 (4H, *s*, methylene). (Found: C, 27.28; H, 1.78. $C_{18}H_{16}O_5Br_6$ requires: C, 27.31; H, 2.04%). MS *m/e*: 798, 796, 794, 792, 790, 788, 786 (M^+), 392, 390, 388, 386 ($M^+ - C_9H_8O_3Br_3 + 1$), 391, 389, 387, 385 ($M^+ - C_9H_8O_3Br_3$), 311, 309, 307, 305 ($M^+ - C_9H_8O_3Br_3 + 1 - Br$).

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REFERENCES

1. Saito, T. and Ando, Y. (1955) *J. Chem. Soc. Jpn* (*Nippon Kagaku Zasshi*) **76,** 478.
2. Pedersén, M., Seanger, P. and Fries, L. (1974) *Phytochemistry* **13,** 2237.
3. Pedersén, M. and Fries, L. (1975) *Z. Pflanzenphysiol.* **74,** 272.
4. Pedersén, M. and DaSilva, E. J. (1973) *Planta* (*Berlin*) **115,** 83.
5. Pedersén, M. and Fries, N. (1977) *Z. Pflanzenphysiol.* **82,** 363.
6. Weinstein, B., Rold, T. D., Harrel, C. E., Jr., Burns, III, M. W. and Waaland, B. (1975) *Phytochemistry* **14,** 2667.
7. Chevolot-Magueur, A. M., Cave, A., Potier, P., Teste, J., Chiaroni, A. and Roche, C. (1976) *Phytochemistry* **15,** 767.
8. Kurata, K., Amiya, T. and Nakano, N. (1976) *Chem. Letters* 821.
9. Kurata, K. and Amiya, T. (1977) *Chem. Letters* 1435.
10. Pedersén, M. (1978) *Phytochemistry* **17,** 291.
11. Lundgren, L. and Theander, O. (1979) *Acta Chem. Scand.* (in press).
12. Saito, K. and Sameshima, M. (1955) *J. Agric. Chem. Soc. Jpn* **29,** 427.
13. Glombitza, K. W., Stoffelen, S., Murawski, U., Bielaczek, U. and Egge, H. (1974) *Planta Med.* **25,** 104.