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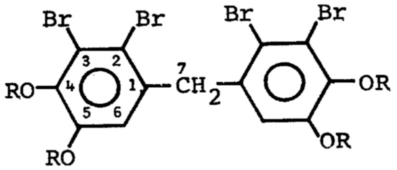
TWO NEW BROMOPHENOLS FROM THE RED ALGA, RHODOMELA LARIX[1)]

Kazuya KURATA* and Takashi AMIYA**
* Department of Industrial Chemistry, Hakodate Technical College, Hakodate 042
** Hokkaido Institute of Pharmaceutical Sciences, Otaru 047

Two new bromophenols, 2,2′,3,3′-tetrabromo-4,4′,5,5′-tetrahydroxydiphenylmethane and 2,2′,3-tribromo-3′,4,4′,5-tetrahydroxy-6′-methoxymethyldiphenylmethane have been isolated from the red alga, *Rhodomela larix*.

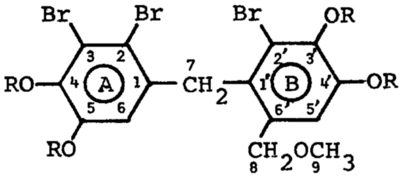
Many bromophenols have been previously isolated from the red algae, Rhodomelaceae.[2-13)] In the course of the investigation of the constituents of the red marine algae, the present authors obtained two new bromophenols, 2,2′,3,3′-tetrabromo-4,4′,5,5′-tetrahydroxydiphenylmethane (I) and 2,2′,3-tribromo-3′,4,4′,5-tetrahydroxy-6′-methoxymethyldiphenylmethane[17)] (II) together with bromophenols, 2,3-dibromo-4,5-dihydroxybenzyl methyl ether[5,7,8,10,11,17)] (III), 2,3-dibromo-4,5-dihydroxybenzaldehyde[5,7,8,11)] (IV) and 2,3-dibromo-4,5-dihydroxybenzyl alcohol (lanosol)[3,7,8,11)] (V) from *Rhodomela larix*.

In this paper the isolation and structural elucidation of the above two new compounds are described. The alga was collected in May at Usujiri Bay near Hakodate, Hokkaido and air dried. The dried alga (20.5 kg) was soaked for ten days at room temperature in methanol (120 l). The methanol extract was evaporated to a syrup, which was treated with ether. The ether extract (770 g) was chromatographed on silica gel (2.5 kg). Elution with benzene – ether (9 : 1) furnished 38 fractions, 2 l each. The fractions 1-12 furnished a crystalline material, compound I, m.p. 200 – 201°, 1.41 g, after recrystallization from benzene – methanol. Compound I gave an intense green color with ferric chloride and precipitated easily on addition of lead acetate. These facts strongly suggested that I would be a catechol derivative. Compound I was analyzed for $C_{13}H_8O_4Br_4$ by elemental analysis and gave parent molecular ion peaks (M^+ 552, 550, 548, 546, 544) by mass spectrometry. The ir showed the presence of OH groups at 3400 cm^{-1}, phenyl rings at 1603, 1595, and 875 cm^{-1}. The uv in ethanol exhibited maximum at 295 nm (ε 5,800). The pmr showed four peaks which were all singlets; δ 3.95 (2H, s, $-CH_2-$), 6.45 (2H, s, aromatic H), 9.24 (2H, s, OH) and 9.75 (2H, s, OH). Six downfield carbon peaks observed in cmr (solvent CD_3SOCD_3) were aromatic carbon peaks (C-1 – C-6, δ 113.3 – 145.1). Although a methylene carbon peak was not noticed for overlapping solvent peak, it was noticed at δ 44.6 in CD_3COCD_3. The six aromatic carbon signals in the downfield region and a methylene carbon (C-7) signal were assigned on the basis of off-resonance decoupling and the chemical shifts as follows. The ^{13}C signals at δ 113.3, 115.0, 115.7, 130.5, 143.1 and 145.1 correspond to the carbons C-3, C-2, C-6, C-1,



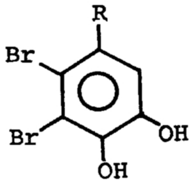
(I) R=H

(Im) R=CH_3



(II) R=H

(IIm) R=CH_3



(III) R=CH_2OCH_3

(IV) R=CHO

(V) R=CH_2OH

Table 1 ^{13}C-NMR Data for II and IIm

Carbon No	^{13}C δ^a		Gated Decoupled Multiplicity, J_{C-H} (Hz)
7	37.8	(t)[b]	$J_{C_7-H_7}$=130 (t), $J_{C_7-H_6}$=2 (d)*
9	57.3	(q)	$J_{C_9-H_9}$=140 (t)
8	72.0	(t)	$J_{C_8-H_8}$=140 (t), $J_{C_8-H_7}$=5 (t)*, $J_{C_8-H_{5'}}$=2 (d)*
3	113.0	(s)	$J_{C_3-H_6}$=2 (d)
5′	113.7	(d)	$J_{C_{5'}-H_{5'}}$=159 (d), $J_{C_{5'}-H_8}$=5 (t)
2	114.33	(s)	$J_{C_2-H_6}$=11.25 (d), $J_{C_2-H_7}$=5 (t)
2′	114.44	(s)	$J_{C_{2'}-H_7}$=5 (t)
6	115.3	(d)	$J_{C_6-H_6}$=159 (t), $J_{C_6-H_7}$=5 (t)
6′	127.5	(s)	$J_{C_{6'}-H_8}$=5 (t), $J_{C_{6'}-H_7}$=5 (t), $J_{C_{6'}-H_{5'}}$=2 (d)
1′	128.5	(s)	$J_{C_{1'}-H_7}$=6.8 (t)
1	130.4	(s)	$J_{C_1-H_7}$=6.8 (t), $J_{C_1-H_6}$=2 (d)
3′, 4	142.5	(s)	$J_{C_{3'}-H_{5'}}$=8 (d), $J_{C_4-H_6}$=8 (d)
5	144.5	(s)	$J_{C_5-H_6}$=2 (d)
4′	144.8		$J_{C_{4'}-H_{5'}}$=2.5 (d)

[a] Proton decoupled values of II (ppm downfield from TMS) in CD_3SOCD_3 solvent on a JEOL FX-60 spectrometer. [b] off-resonance decoupling.

* J_{C-H} was observed in the expanded spectrum of IIm.

J_{C-H} without asterisk showed that of spectrum of II.

C-4 and C-5, respectively. These assignments were identified by gated decoupling technique. A methylene carbon (δ 45.1 in $CDCl_3$) of tetramethyl derivative[15] (Im) of I in gated decoupled spectrum showed $J_{C_7-H_7}$=128 Hz (triplet) and $J_{C_7-H_6}$=5 Hz (doublet). The carbon C-6 of I showed $J_{C_6-H_6}$=162 Hz (doublet) and $J_{C_6-H_7}$=5 Hz (triplet). The C-1 of I showed $J_{C_1-H_7}$=5 Hz (triplet) and $J_{C_1-H_6}$=2 Hz (doublet). These long range couplings indicate that the aromatic H must be at *ortho*-position for the methylene. The carbons C-4 and C-5 of I showed $J_{C_4-H_6}$=8 Hz and $J_{C_5-H_6}$=2 Hz (each doublet), respectively. The long range couplings indicate that C-4 must be at *meta*-position and c-5 must exist at *ortho*- or *para*-position for the aromatic H. The carbon C-2 showed $J_{C_2-H_6}$=8 Hz (doublet) and $J_{C_2-H_7}$=5 Hz (triplet). The carbon C-3 showed $J_{C_3-H_6}$=2 Hz (doublet). The long range couplings indicate that C-2 must be at *meta*-position for the aromatic H and at *ortho*-position for the methylene, and C-3 at *ortho*- or *para*-position for the aromatic H. Although six isomers are possible for a tetrabromo and tetrahydroxy methylene bisphenol, 2,2',3,3'-tetrabromo-4,4',5,5'-tetrahydroxy and 2,2',5,5'-tetrabromo-3,3',4,4'-tetrahydroxydiphenylmethane are satisfied with above mentioned evidence. On the other hand, III was precipitated at room temperature easily on addition of lead acetate, but 2,3,6-tribromo-4,5-dihydroxybenzyl methyl ether from the red alga, *Symphiocladia latiuscula*[14], was precipitated by standing overnight at room temperature or heating on the steam bath. As mentioned above, compound I was precipitated at room temperature easily by this reagent as in the case of III. On the basis of these facts as well as the biogenetic view point 2,2',3,3'-tetrabromo-4,4',5,5'-tetrahydroxydiphenylmethane was proposed for compound I. For the selection of the structure I this test is not enough, and more data are necessary

The fractions 13-28 furnished a crystalline material, compound II 9.4 g, after recrystallization from benzene – methanol. This compound decomposed at about 540° without melting. Compound II was analyzed for $C_{15}H_{13}O_5Br_3$ by elemental analysis. λ_{max}^{EtOH} 291 nm (ε 5,700). IR ν_{max}^{KBr} cm^{-1} : 3250, 3420 (OH), 1615, 1590, 1565, 1470, 880 (aromatic ring), 2820 (aliphatic OCH_3), 1100 (aliphatic ether). PMR (CD_3SOCD_3) : δ 3.19 (3H, s, $-CH_2O\underline{CH_3}$), 3.99 (2H, s, $-\underline{CH_2}OCH_3$), 4.12 (2H, s, ø-CH_2-ø), 6.02 (1H, s, aromatic H), 6.86 (1H, s, aromatic H), 9.02 (2H, broad s, OH), 9.60 (2H, broad s, OH). MS (m/e) M^+ (516, 514, 512, 500), M^+-OCH_3 (485, 483, 481, 479), $M^+-OCH_3-H_2O$ (467, 465, 463, 461), M^+-OCH_3-Br (404, 402, 400). It was estimated from above spectral data that II was a diphenylmethane derivative similar to I. The properties of II for ferric chloride and lead acetate were quite similar to I. Then, two of four phenolic OH groups would have to be vicinal at least. Two aromatic protons of II in pmr appeared as singlets, and therefore, two aromatic rings seem to consist of two penta-substituted rings, or of hexa-substituted ring and tetra-substituted ring which was not substituted in *para*-position. The evidence and the biogenetic consideration suggest that II is formulated as 2,2',3-tribromo-3',4,4',5-tetrahydroxy-6'-methoxymethyldiphenylmethane. The structure II was confirmed by the gated decoupling of cmr (solvent CD_3SOCD_3) in analogy with I. The ^{13}C signals at δ 37.8, 57.3 and 72.0 correspond to the carbons C-7, C-9 and C-8, respectively. The eleven aromatic carbon peaks appeared in downfield (δ 113.3 – 144.8) were assigned on the basis of off-resonance decoupling and the chemical shifts of I as follows. Ring A was the same as that of I, and then the carbon peaks of the ring A were assigned on the basis of the chemical shifts of I. The gated decoupled spectrum of these carbon peaks supports that the ring A is the same that of I. The carbons C-5′ (δ 113.7) and C-2′ (δ 114.44) of ring B were assigned on the basis of the chemical shifts and off-resonance decoupling. The assignment of C-6′ was established by comparison of peak intensities between C-6′ and C-1′ related to relaxation time T_1. The carbons C-3′ (δ 142.5) and C-4′ (δ 144.8) were assigned on the basis of the chemical shifts and the gated decoupled spectrum. The gated decoupled spectra of II and the tetramethyl derivative$^{16)}$ (IIm) of II were adequate to illustrate II (see Table 1).

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14) This study was presented at annual meetings of Japanese Society of Scientific Fisheries held in Tokyo, April 1973 and in Kagoshima, October 1973.
15) Compound I in acetone containing anhyd. K_2CO_3 was treated with Me_2SO_4, yielding a tetramethyl ether. M.p. 159 – 160°. PMR δ 3.67 (6H), 3.76 (6H), 4.16 (2H), 6.51 (2H). MS (m/e) M^+ (608, 606, 604, 602, 600).
16) Tetramethyl derivative of II was obtained in a similar manner as I. M.p. 121 – 122°. PMR δ 3.36 (3H), 3.57 (3H), 3.81 (3H), 3.88 (3H), 3.92 (3H), 4.22 (2H), 4.26 (2H), 6.17 (1H), 7.02 (1H). MS (m/e) M^+ (572, 570, 568, 566).
17) Compounds II and III can be artifacts which are derived by methylation of the corresponding alcohols during the extraction procedure.$^{8,10)}$

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