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NEW GERANYLGERANYLBENZOQUINONE DERIVATIVES FROM SARGASSUM TORTILE

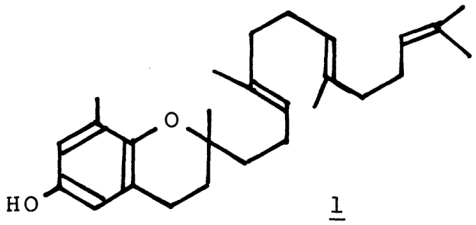
Midori ISHITSUKA, Takenori KUSUMI, Yukihiro NOMURA, Toshinori KONNO[+], and Hiroshi KAKISAWA*

Department of Chemistry, The University of Tsukuba, Sakura-mura, Ibaraki 300-31

[+]Laboratory of Phycology, Tokyo University of Fisheries, Minato-ku, Tokyo 108

From the brown alga, Sargassum tortile, seven new benzoquinones and hydroquinones bearing diterpenoid side chains were isolated. 2-Geranylgeranyl-6-methylbenzoquinone, which is likely to be a basic substance of the diterpenoid-substituted benzoquinones distributed in many Sargassum species, was also obtained.

In the course of our investigations on the constituents of the brown algae belonging to Sargassum family, we have found that some species of this family contain geranylgeranylbenzoquinone derivatives[1a] and norditerpenes which were supposed to be derived from such diterpenoid-substituted benzoquinones.[1b] In the present paper, we wish to describe the isolation of new geranylgeranylbenzoquinone derivatives from Sargassum tortile C. Agardh, Yoremoku in Japanese. Isolation of δ-tocotrienol (1) and its epoxide, and sargatriol (2) from this alga was reported.[1c,d]



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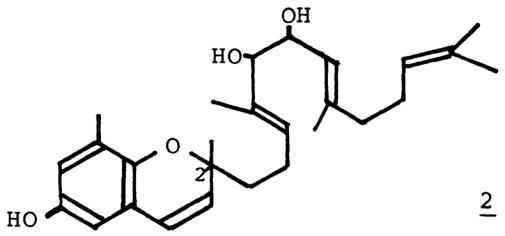

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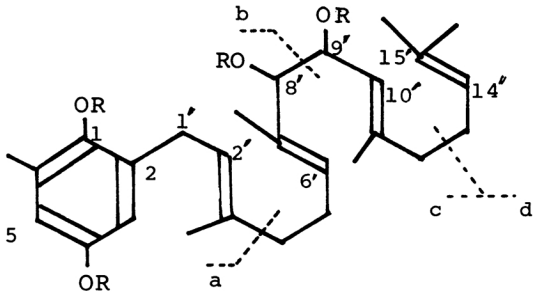
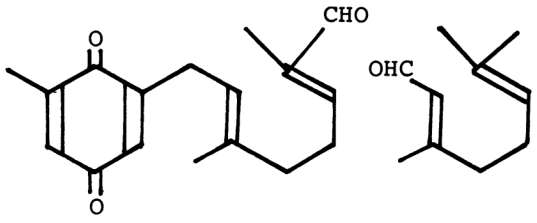
The ether-soluble material of the methanol extract of fresh S. tortile, collected at Awa-kominato, Chiba, in May, was fractionated by 'flash chromatography'[2] using hexane-ethyl acetate (1:1). Repeated preparative TLC and HPLC of the resulting fractions afforded seven new compounds, 3, 7, 9, 11, 12, 13, and 14, spectral properties of which are listed in the Table, together with 15.

The major component, which was named as sargatetraol (3), afforded tetraacetate (4). Presence of an α-glycol moiety was deduced from the NMR spectra of 3 and 4, and oxidative cleavage of 3 with periodic acid. Thus, treatment of 3 with periodic acid in dry ether[3] yielded geranial (6)[4] [IR(CCl_4) 1675 cm^{-1} ; NMR($CDCl_3$)δ 10.08(1H,d,J=8 Hz), 5.90(1H,d,J=8 Hz), 5.1(1H,m), 2.15(3H,s), 1.67(3H,s), 1.59(3H,s)] and the quinone (5) [IR(CCl_4) 1690, 1655, 1610 cm^{-1}; NMR($CDCl_3$)δ 9.48(1H,s), 6.62(1H,m), 6.50(1H,m), 6.50 (1H,t), 5.26(1H,t,J=7 Hz), 3.17(2H,d,J=8 Hz), 2.07(3H,d,J=1.5 Hz), 1.76(3H,s), 1.70 (3H,s)]. The production of these aldehydes settled the position of the two hydroxy groups at C-8′ and 9′. The chemical shifts of 3-Me protons (δ 2.15) of 6 and the aldehyde proton (δ 9.48)[1a,5] of 5 were consistent with the E,E-configurations of C-6′ and 10′ double bonds of 3. The configuration of C-2′ double bond was determined to be E from the upfield chemical shifts[6] of the signals (δ 15.6, 16.1, 16.8, 17.6) due to 3′, 7′, 11′, and 15′ (trans to the olefin proton) methyls, in the ^{13}C-NMR spectrum of 3. The structure was further confirmed by the following transformation. Oxidation of 3 with silver oxide in ether[7] afforded the quinone 13, which was also isolated from this alga as a minor component (vide infra). When the synthesized quinone 13 was heated in pyridine, it changed into the chromenol (2) in a good yield. This



3 ; R=H, 4 ; R=Ac



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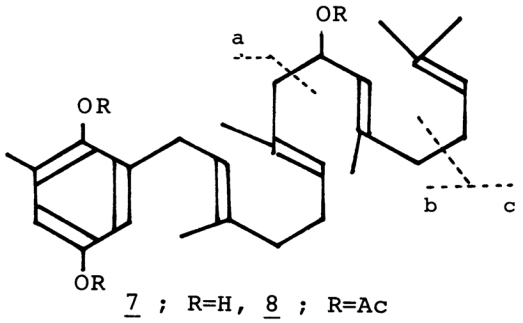

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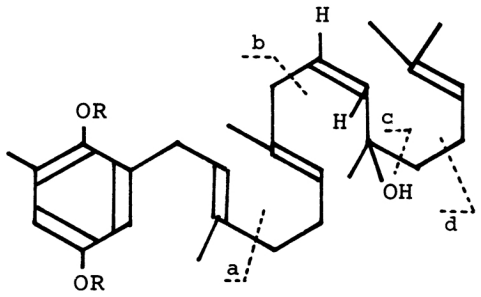
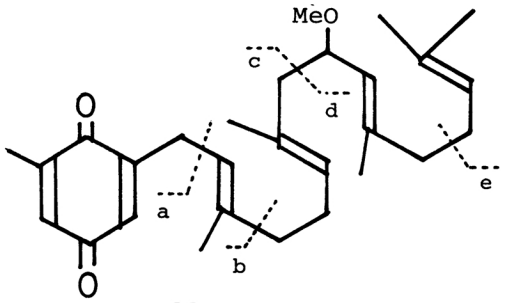


9 ; R=H, 10; R=Ac



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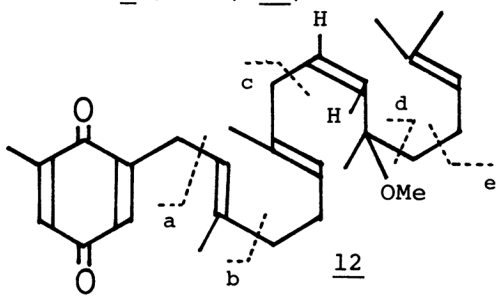

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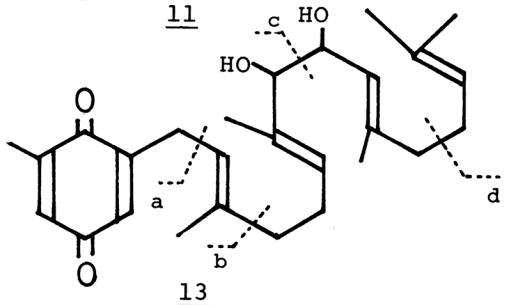

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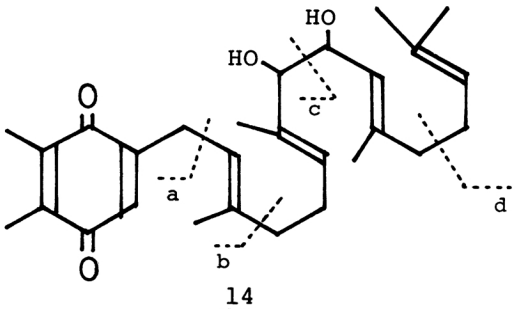

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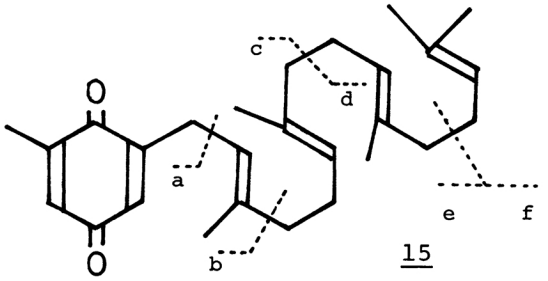

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Table 1.
Spectral and physical properties of the compounds isolated from S. tortile and their derivatives.

	$[\alpha]_D$ ($CHCl_3$)	IR (cm^{-1}) (CCl_4)	UV (nm) (ε, EtOH)	NMR (δ) (CCl_4)	MS (m/e) *
3	-25.4° c=0.47	3610, 3600-3100, 1210, 1180, 1140	290 (2840)	1.57(6H,s),1.63(9H,s),2.12(3H,s), 3.12(2H,d,J=7 Hz),3.87(1H,d,J=8Hz), 4.31(1H,t,J=8 Hz),5.0-5.4(4H,m), 6.44(2H,s)	410(M-H_2O),408(M-2H-H_2O),392(M-$2H_2O$),323 (c-$2H_2O$),275(b),175 (a-2H),69(d)
4	+31.1° c=0.54	1765, 1740, 1245, 1225, 1210, 1170	260 (588)	1.56,1.60,1.65,1.73,1.94,1.97,2.11, 2.19,2.24(each 3H,s),3.16(2H,d,J=7 Hz),4.9-5.3(3H,m),5.11(1H,d,J=8Hz), 5.5(1H,m),5.66(1H,dd,J=8,10 Hz), 6.77(2H,ABq,J=3 Hz),1.65(3H,s)	536(M-AcOH),494(536-C_2H_2O),476(M-2AcOH), 434(476-C_2H_2O),401(b), 359(b-C_2H_2O),317(b-2C2H2O)
7	-12.8° c=0.89	3610, 3600-3200	290 (2470)	1.58(3H,s),1.62(3H,s),1.66(9H,s), 2.10(3H,s),3.18(2H,d,J=7 Hz),4.40 (1H,q,J=7 Hz),5.0-5.3(4H,m),6.36 (2H,ABq,J=3 Hz)	412(M),410(M-2H),394 (M-H_2O),392(410-H_2O), 325(b-H_2O),257(a-2H)
8	+7.36° c=1.10	1765, 1730, 1370, 1240, 1210, 1170	262 (605)	1.59,1.67,1.67,1.68,1.70,1.91,2.12, 2.19,2.24(each 3H,s),3.17(2H,d,J=7 Hz),5.0-5.3(4H,m),5.60(1H,q,J=8Hz), 6.78 (2H,ABq,J=2 Hz)	478(M-AcOH),436(478-C_2H_2O),409(b-AcOH), 394(436-C_2H_2O),301(a -C_2H_2O),69(c)
9	+3.51° c=0.57	3610, 3600-3200	290 (1950)	1.23(3H,s),1.57(6H,s),1.65(6H,s), 2.11(3H,s),2.66(2H,br.s),3.20(2H, d,J=7 Hz),4.8-5.6(5H,m),6.36(2H, br.s)	410(M-2H),392(410-H_2O) 327(c-2H),325(d-H_2O), 323(325-2H),257(b-2H), 175(a-2H)
10	+3.17° c=0.82	3600, 1765, 1370, 1210, 1170, 975	end absorption	1.18,1.57,1.57,1.66,1.66,2.11,2.19, 2.24(each 3H,s),2.65(2H,br.s),3.16 (2H,d,J=7 Hz),4.9-5.5(5H,m),6.75 (2H,ABq,J=3 Hz)	478(M-H_2O),413(c), 371(c-C_2H_2O),329(c -2C_2H_2O),175(a-2H-2C_2H_2O)
11	+2.68 c=0.56	1655, 1615, 1295, 1100	253 (14700)	1.60(6H,s),1.65(9H,s),2.05(3H,d,J= 1.5 Hz),3.10(2H,d,J=8 Hz),3,12(3H, s),3.88(1H,q,J=8 Hz),4.9-5.2(4H,m), 6.40(1H,br.m),6.50(1H,br.m)	424(M),392(M-MeOH), 257(c),175(b),167(d), 135(a),69(e)
12	0 c=0.83	1655, 1615, 1295, 1075, 980	253 (15800)	1.16(3H,s),1.58(6H,s),1.65(6H,s), 2.04(3H,d,J=1.5 Hz),2.70(2H,d,J=5 Hz),3.07(3H,s),3.10(2H,d,J=8 Hz), 5.0-5.5(5H,m),6.39,6.50(each 1H,br. m)	424(M),392(M-MeOH), 341(d),257(c),175(b), 135(a),69(e)
13	-15.5° c=0.39	3600-3300, 1655, 1630, 1615	253 (13100)	1.58(6H,s),1.61(3H,s),1.65(6H,s), 2.04(3H,d,J=1.5 Hz),3.09(2H,d,J=8 Hz),3.71(1H,d,J=8 Hz),4.15(1H,t,J= 8 Hz),5.0-5.4(4H,m),6.45,6.53(each 1H,br.m)	426(M),410(M+2H-H_2O), 273(c),175(b),137 (a+2H),69(d)
14	-7.75° c=0.40	3600-3300, 1650, 1630, 1615	255 (13400)	1.60(9H,s),1.66(6H,s),2.01(6H,s), 3.09(2H,d,J=8 Hz),3.71(1H,d,J=8 Hz), 4.14(1H,t,J=8 Hz),5.0-5.4(4H,m), 6.44(1H,finely splitted triplet)	440(M),424(M+2H-H_2O), 422(M-H_2O),287(c), 189(b),151(a+2H),69 (d)
15		1650, 1610, 1290, 915	252 (12400)	1.59(9H,s),1.66(6H,s),2.05(3H,d, J=1.5 Hz),3.12(2H,d,J=8 Hz),5.1 (4H,m),6.42(1H,br.m),6.53(1H,br.m)	396(M+2H),394(M),325 (e),257(c),175(b), 137(d),135(a),69(f)

*Letters a,b,c,d,e,and f correspond to the fragments depicted in the Figure.

chromenol and its triacetate (acetic anhydride-pyridine) exhibited the same spectral and chiloptical properties as those of sargatriol (2), which has been reported to be a constituent of this alga,[1d] although the synthesized chromenol (2) was seemingly a mixture of epimers at C-2′.

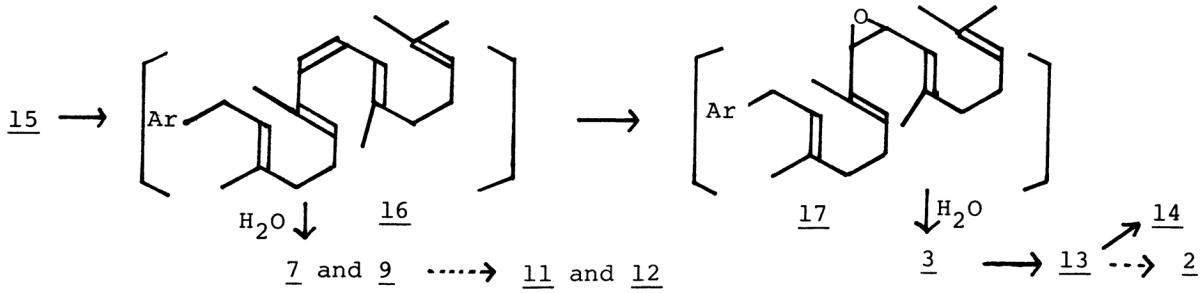
From the fraction slightly less polar than that containing 3, two hydroquinone isomers, 7 and 9, were obtained. Acetylation of 7 and 9 with acetic anhydride-pyridine afforded the triacetate (8) and the diacetate (10), respectively, suggesting the presence of a secondary hydroxyl in 7 and a tertiary hydroxyl in 9. The position of the hydroxy groups of these compounds was determined on the basis of their mass spectra (Figure). The trans-geometry of C-9′ double bond of 9 was deduced from the IR band at 975 cm^{-1}.

Analogous pair of methyl ethers, 11 and 12, were also isolated from a colored fraction. The isomer 11 exhibited a distinct optical rotation. Although $[\alpha]_D$ value of another isomer 12 was zero, it showed plus optical rotation at shorter wave length. Whether the methoxy groups of 11 and 12 were incorporated from methanol or not was obscure.

Two quinones, 13 and 14, were obtained from less polar fraction. The Rf value of these two quinones were quite identical under various solvent system, and the two compounds were only separable by preparative HPLC (TSK GEL, LS-410, 7.5 mm x 30 cm, MeOH : H_2O = 7 : 1). The mass (M^+440) and the NMR (δ 2.01, 6H,quinone Me's) spectra of 14 revealed that this compound had one additional methyl group on the quinone nucleus of 13. The position of the methyl group was determined to be C-5, because the broad triplet at δ 6.44 due to the quinone proton collapsed into a sharp singlet on irradiation at δ 3.09 (1′-methylene protons).

From the least polar fraction, 2-geranylgeranyl-6-methylbenzoquinone (15), which we named sargaquinone, was isolated. Though sargaquinone has been synthesized,[8] this compound had not been found in the natural source. Sargaquinone (15) is possibly a precursor of geranylgeranylbenzoquinone derivatives found in some Sargassum species.

As for the biosynthesis of the present diterpenoid-substituted benzoquinone derivatives, the following scheme, involving the pentaene (16) and epoxide (17), is proposed.



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