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NEW FARNESYLACETONE DERIVATIVES FROM SARGASSUM MICRACANTHUM

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From the brown alga, Sargassum micracanthum, eight new farnesylacetone derivatives were isolated and their structures were elucidated from spectral and chemical properties.

Many species of the brown algae of Sargassum family are known to contain prenyl phenyl derivatives,[1] methylhydroquinones and methylbenzoquinones bearing geranylgeranyl side chain. In the course of our investigations on the constituents of Sargassum family growing on the Japanese coast, we isolated new terpenoids which biogenetically seemed to be derived from these prenyl phenyl derivatives.

The methanol extracts of fresh S. micracanthum (Kützing) Yendo,[2] togemoku in Japanese, were chromatographed on silica gel, affording three fractions, I-III. The fraction I consisted of almost pure farnesylacetone (**1**); IR(CCl_4) 1715 cm^{-1}; NMR (CCl_4) δ 1.62 (9H,s), 1.68 (3H,s), 2.08 (3H,s), 5.08 (3H,br.t), which was identified by converting into the semicarbazone; mp 79-80° (lit.[3] mp 80.5-81.5°). Although the TLC of the fraction II showed only one spot, its HPLC exhibited five distinct peaks, and four new compounds (**2**-**5**) were obtained from this fraction by preparative HPLC (TSK-GEL LS-410, 7.5 mm x 30 cm column, $CH_3CN : H_2O = 3:1$). The fraction III was a mixture of four compounds (**7**-**10**) which was separated by preparative TLC and HPLC.

The molecular formula, $C_{18}H_{30}O_2$ (M^+ 278.2230, calcd 278.2245), of COMPOUND **2** corresponded to that of dihydromonooxofarnesylacetone. The presence of $-COCH=C(CH_3)$ moiety and an acetyl group was deduced from the IR absorption bands at 1680 and 1715 cm^{-1}, the UV absorption maximum at 239 nm (ε 10500), and the NMR signals at δ 1.85 (3H,d,J=1.5 Hz), 5.95 (1H,br.s), and 2.07 (3H,s). The NMR spectrum also suggested the presence of isopropyl [δ 0.92 (6H,d,J=7 Hz)], vinyl methyl [1.62 (3H,s)], and trisubstituted olefin [5.10 (1H,br.t,J=7 Hz)] groups. The stereochemistry of the double bonds at C-5 and C-10 was determined to be E and Z, respectively, from the chemical shifts of the methyl groups at C-6 (δ 1.62) and C-10 (δ 1.85).[4] The structure was further verified by high resolution mass spectrum as described in the Figure. Hydrogenation of **2** afforded the tetrahydro derivative (**6**), $C_{18}H_{34}O_2$; m/e 282(M^+), 267(M^+-CH_3), 225(M^+-C_4H_9,M^+-CH_2COCH_3),182 (M^+-$Me_2CHCH_2COCH_3$); IR(CCl_4) 1715 cm^{-1}.

COMPOUND **3**, $C_{18}H_{32}O_2$; m/e 280.2378(M^+), 262 (M^+-H_2O), 223 (M^+-C_4H_9,M^+-CH_2COCH_3) was a dihydro derivative of compound **2**. The IR spectrum (1710 cm^{-1}) showed the absence of an α,β-unsaturated carbonyl group, and the NMR spectrum revealed the presence of an acetyl (δ 2.05,3H,s), isopropyl (0.90,6H,d,J=7 Hz), and secondary methyl (0.87,3H,d,J=7 Hz) groups, together with a trisubstituted olefin group (5.02, 1H,m). The structure **3** was confirmed by converting it into the diketone (**6**) by hydrogenation.

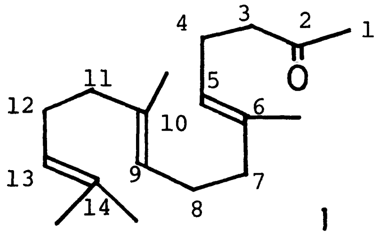
COMPOUND **4**, $C_{18}H_{28}O_2$; m/e 276.2141(M^+) and 219 (M^+-CH_2COCH_3), showed a strong absorption maximum at 246 nm (ε20900) in its UV spectrum, and exhibited IR absorption bands due to α,β-unsaturated carbonyl system at 1670 and 1625 cm^{-1}. The molecular formula corresponded to that of dehydro derivative of compound **2**, and the presence of an isopropylidene group instead of isopropyl group was confirmed by its NMR spectrum; δ 1.62 (3H,s,6-Me), 1.86 (3H,s,14-Me,<u>trans</u> to C=O), 2.05 (3H,s,$COCH_3$), 2.11 (6H,d,J=1 Hz,10-Me and 14-Me,<u>cis</u> to C=O), 5.02 (1H,t,J=7 Hz,5-H), and 5.90 (2H,m,11-H, and 13-H). The E-configuration of the double bond at C-10 was obvious from the downfield chemical shift (δ 2.11) of the methyl group at C-10.

COMPOUND **5**, $C_{18}H_{28}O_2$, was an isomer of **4**, and showed the following spectral properties; m/e 276.2042 (M^+), 261 (M^+-CH_3), 233 (M^+-$COCH_3$), 83 (Me_2C=CHCO); IR(CCl_4) 1715, 1685, 1615 cm^{-1}; NMR(CCl_4)δ 1.62 (6H,s), 1.87 (3H,s), 2.04 (6H,s), 2.93 (2H,s), 5.0-5.3 (2H,m), 6.01 (1H,s). The stereochemistry of the double bonds at C-5 and C-9 was determined to be E from the chemical shifts of the methyl signals.

The structures **7**-**10** were assigned for the remaining new compounds on the basis of the following spectral properties.

COMPOUND **7**, $C_{18}H_{34}O_2$; m/e 282.2561 (M^+), 264 (M^+-H_2O), 225 (M^+-C_4H_9), 85 (Me_2CH-CH_2CO); IR(CCl_4) 3620, 1710, 1615 cm^{-1}; NMR(CCl_4)δ 0.87 (3H,d,J=7 Hz), 0.92 (6H,d, J=7 Hz), 1.13 (3H,d,J=7 Hz), 3.70 (1H,m), 5.10 (1H,m), 1.62 (3H,s).

COMPOUND **8**, $C_{18}H_{32}O_2$; m/e 280.2393 (M^+), 265 (M^+-CH_3), 223 (M^+-C_4H_9), 85 (Me_2CH-CH_2CO); $[\alpha]_D$ -3.75° (chloroform, c 0.53); λ_{max}^{EtOH} 241 nm (ε 9500); IR(CCl_4) 3620, 1685, 1620, 1110, 1050 cm^{-1}; NMR(CCl_4)δ 0.92 (6H,d,J=7 Hz), 1.13 (3H,d,J=7 Hz), 1.61 (3H,s),



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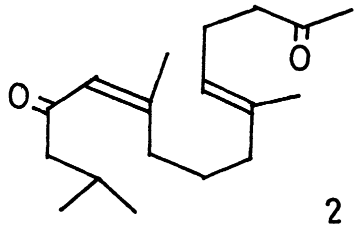

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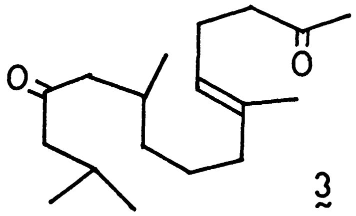

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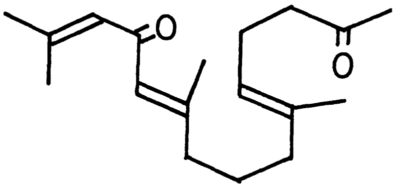

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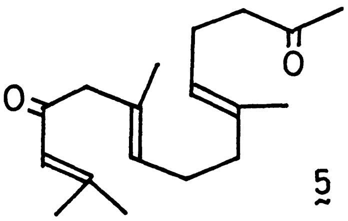

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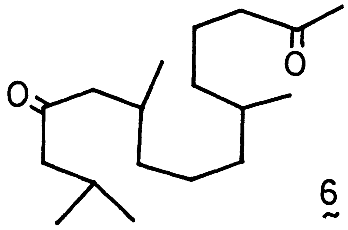

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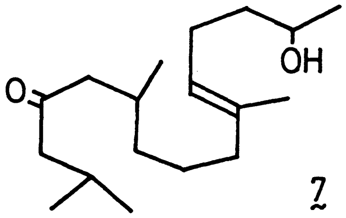

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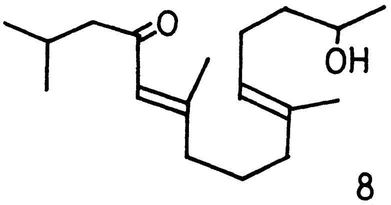

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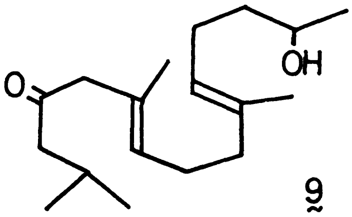

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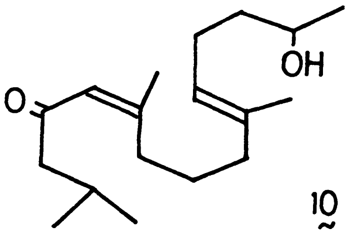

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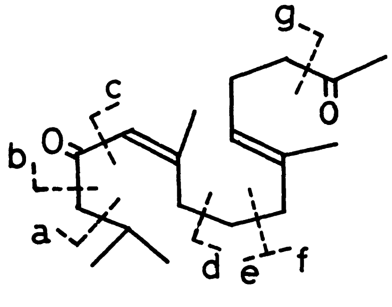
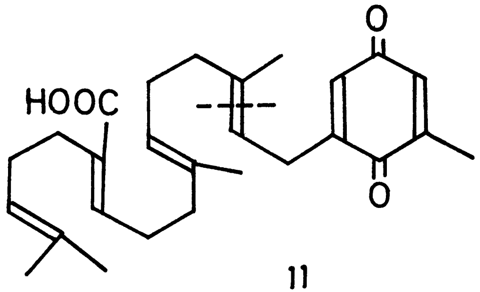


Fragment	Found	Calcd	Formula
a	235.1667	.1698	$C_{15}H_{23}O_2$
b	221.1545	.1541	$C_{14}H_{21}O_2$
c	193.1581	.1592	$C_{13}H_{21}O$
d	140.1198	.1201	$C_9H_{16}O$
e	153.1257	.1279	$C_{10}H_{17}O$
f	125.0950	.0966	$C_8H_{13}O$
g	235.2029	.2061	$C_{16}H_{27}O$



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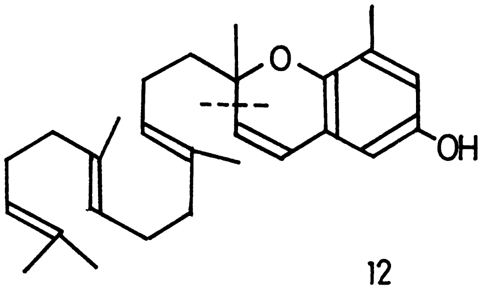

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2.09 (3H,s), 3.70 (1H,sextet,J=7 Hz), 5.10 (1H,t,J=7 Hz), 5.94 (1H,s).

COMPOUND 9, $C_{18}H_{32}O_2$;m/e 280.2360 (M^+), 262 (M^+-H_2O), 247 (262-CH_3), 237 (M^+-C_3H_7), 223 (M^+-C_4H_9), 85 (base,Me_2CHCH_2CO); $[\alpha]_D$ -3.31° (chloroform, c 0.45); IR(CCl_4) 3620, 1710 cm^{-1}; NMR(CCl_4)δ 0.90 (6H,d,J=7 Hz), 1.12 (3H,d,J=7 Hz), 1.61 (6H,s), 2.93 (2H,s), 3.73 (1H,sextet,J=7 Hz), 5.16 (2H,m).

COMPOUND 10, $C_{18}H_{32}O_2$; m/e 280.2383 (M^+), 262 (M^+-H_2O), 223 (M^+-C_4H_9), 85 (Me_2CH-CH_2CO); $[\alpha]_D$ -3.16° (chloroform,c 0.25), λ_{max}^{EtOH} 239 nm (ε 10600), IR(CCl_4) 3620, 1685, 1615, 1170, 1150 cm^{-1}; NMR(CCl_4)δ 0.92 (6H,d,J=7 Hz), 1.13 (3H,d,J=7 Hz), 1.64 (3H,s), 1.85 (3H,s), 3.68 (1H,sextet,J=7 Hz), 5.10 (1H,t), 5.90 (1H,s).

From the brown algae belonging to Sargassum group, geranylgeranylquinones and chromenols such as sargaquinoic acid (11)[1c] and δ-tocotrienol (12)[1a] have been isolated. The farnesylacetone derivatives reported here are supposed to be "norditerpene"s, derived from these quinones and chromenols by the oxidative cleavage of the C-C bonds pointed by the dotted lines in the Figure.

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