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The Granulation-Inhibiting Principles from *Eucalyptus globulus* LABILL. III.[1) The Structures of Euglobal-III, -IVb and -VII[2)

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The structures of three novel potent granulation-inhibiting principles, euglobal-III (1), -IVb (2) and -VII (3) were deduced, except for the absolute configurations, on the basis of proton magnetic resonance, ^{13}C-nuclear magnetic resonance and mass spectral evidence.

Keywords——euglobal-III; euglobal-IVa; euglobal-IVb; euglobal-V; structure determination; physicochemical data; acetogenin-sesquiterpene structure; granulation-inhibiting principle; *Eucalyptus globulus*

As a result of the continuing research on granulation-inhibiting principles from *Eucalyptus globulus* LABILL., eleven novel compounds were isolated.[3) A preliminary communication[2) described the isolation and structure determination of the potent granulation-inhibiting principle, euglobal-III (1). We have also reported the structure elucidation of seven of the new compounds which have acetogenin-monoterpene structures.[1) The purpose of this paper is to present the full account of the structural determination of the remaining three new compounds having acetogenin-sesquiterpene structures, euglobal-III (1), -IVb (2) and -VII (3), by means of physical methods.

These three compounds have the same composition, $C_{28}H_{38}O_5$ (mass spectra and elemental analyses),[3) and showed ultraviolet (UV), infrared (IR) and mass spectra (MS) similar to those of euglobals with acetogenin-monoterpene structures.[1) The UV data [$\lambda_{\max}^{\mathrm{EtOH}}$ nm (ε): 275—276 (32000—36000), 340 (3900—5000, inflection)] of these three compounds were also very closely related to the data reported for grandinol (4) isolated from *Eucalyptus grandis*,[4) and indicated the presence of a similarly substituted phloroglucinol chromophore. These compounds, like the other euglobals,[1) showed the presence of hydrogen-bonded conjugated carbonyls, as evidenced by their IR bands at 1620—1630 cm^{-1}. The proton magnetic resonance (PMR) spectra and ^{13}C-nuclear magnetic resonance (CMR) spectra (Table I) showed that the carbonyls are two aldehydic groups in euglobal-III (1) and -IVb (2), and one aldehydic and one ketonic carbonyl in euglobal-VII (3). The presence of two hydrogen-bonded hydroxyl groups was revealed by IR bands at 3400—3500 cm^{-1}, and the disappearance of two singlet signals at δ 12.96—15.37 in the PMR spectra on addition of deuterium oxide. The MS of these three compounds exhibited the same fragmentation pattern as shown in Chart 1. The peaks at m/z 251 and 195 with the compositions $C_{13}H_{15}O_5$ and $C_9H_7O_5$, respectively, are in common with the MS of the other euglobals.[1) The above spectral data strongly suggested that euglobal-III (1), and -IVb (2) have the same aromatic part [A] found in the previously reported euglobals exclusive of euglobal-IIc (5).[1) It was also shown that these three compounds were split into two fragments, m/z 251 ($C_{13}H_{15}O_5$) and 203 ($C_{15}H_{23}$), which were supposed to be formed by retro-Diels-Alder cleavage of the molecular ions, and were assigned from their compositions as an aromatic part and a sesquiterpene moiety. The ions at m/z 251 and 203 suffered further cleavage to give m/z 195 and 161 with, the loss of C_4H_8 and C_3H_6, respectively. The CMR spectra (Table I) of these three compounds exhibited six aromatic

Table I. PMR and CMR Spectral Data for Euglobal-III (1), -IVb (2) and -VII (3)

Carbon	Euglobal-III (1)			Euglobal-IVb (2)			Euglobal-VII (3)		
	M[a]	δ ^{13}C	δ ^{1}H	M[a]	δ ^{13}C	δ ^{1}H	M[a]	δ ^{13}C	δ ^{1}H
1	s	109.6		s	110.8		s	101.7	
2	s	164.4		s	165.2		s	162.5	
3	s	104.0		s	106.9		s	104.0	
4	s	167.2		s	167.3		s	168.0	
5	s	103.5		s	104.6		s	103.6	
6	s	167.9		s	167.5		s	171.8	
7	d	30.3[e]	3.05(m)	d	32.9[e]	3.26 (br. dd J= 11, 3 Hz)	t	30.8[e]	2.76, 2.17 (ABq J=16 Hz)
8	d	191.6[b]	10.03[d] (s)	d	191.7[b]	10.24[d] (s)	d	191.7	10.02(s)
9	d	191.3[b]	10.16[d] (s)	d	191.5[b]	10.02[d] (s)	s	206.1	
10	t	42.3	1.46[f]	t	44.6[e]	1.39, 1.79[f]	t	52.7	2.99(d J=6 Hz)
11	d	26.2	1.40[f]	d	26.3		d	25.1	2.30[f]
12, 13	q	21.0, 24.6[e]	1.01, 0.84 (d J=6 Hz)	q	21.9, 24.0	0.98, 0.80 (d J=6 Hz)	q	22.7	1.00(d J=7 Hz)
1′	d	39.5[e]	2.0[f]	d	123.0	5.26 (br. d J= 10 Hz)	d	127.5	5.23(m)
2′	t	26.5		t	23.9[e]	22.9[f]	t	22.7[b]	
3′	t	39.6[c]		t	34.9		t	37.9[c]	
4′	s	136.0		s	91.3		s	36.1	
5′	d	121.9	4.84 (br. d J= 9 Hz)	d	48.1[e]	2.05[f]	d	83.6	3.71(d J=7 Hz)
6′	d	24.6[e]	1.25[f]	d	29.7[c,e]	0.26 (m)	d	30.4	0.82 (t like J= 7, 8 Hz)
7′	d	27.7[e]	0.60[f]	d	28.5[c,e]	0.26 (m)	d	31.1[e]	0.60 (dd like J= 8, 10 Hz)
8′	t	19.2		t	25.3		t	23.0[b]	
9′	t	39.9[c]		t	45.0[e]	2.29[f]	t	39.5[c]	
10′	s	88.8		s	133.8		s	130.9	
11′	s	20.3		s	16.7		s	19.5	
12′, 13′	q	15.1, 28.6[e]	1.02, 0.95(s)	q	29.9, 16.9	1.06, 0.93(s)	q	26.8, 17.6	1.14[d], 0.94(s)
14′	q	26.1[e]	1.45(s)	q	20.8[e]	1.70(s)	q	19.3	1.63 (br. s)
15′	q	16.8[e]	1.70(s)	q	24.0[e]	1.17(s)	q	21.4	1.17[d] (s)
OH			13.37(s)			13.08(s)			15.37(s)
			13.20(s)			12.96(s)			14.56(s)
			1.1—2.3(12H)			0.7—2.7(12H)			0.9—2.6(10H)
			0.5—0.75(2H)						

Chemical shifts are expressed in δ (ppm) values.

a) Multiplicity.

b), *c*), *d*) Assignments may be interchangeable among the signals with the same superscripts in any one spectrum.

e) These δ values were assigned by selective proton decouplings.

f) These δ values were estimated by the double resonance technique.

carbons, and the chemical shifts were similar to those of grandinol (4). In addition to these observations, additivity of the chemical shifts of the substituents[5] on the aromatic ring in CMR led to the partial structure [A] for the aromatic part.[1]

The data described above suggested that euglobal-III (1), -IVb (2) and-VII (3) have phloroglucinol-terpene structures similar to those of the other euglobals.[1] The structures of the non-aromatic portions of these three compounds will be discussed below.

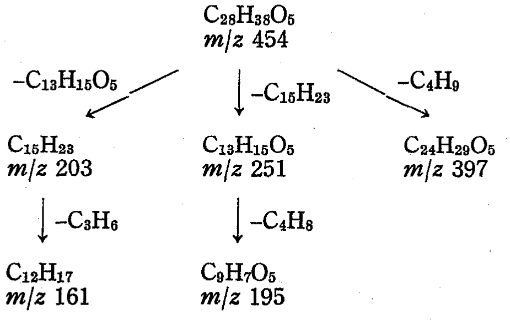
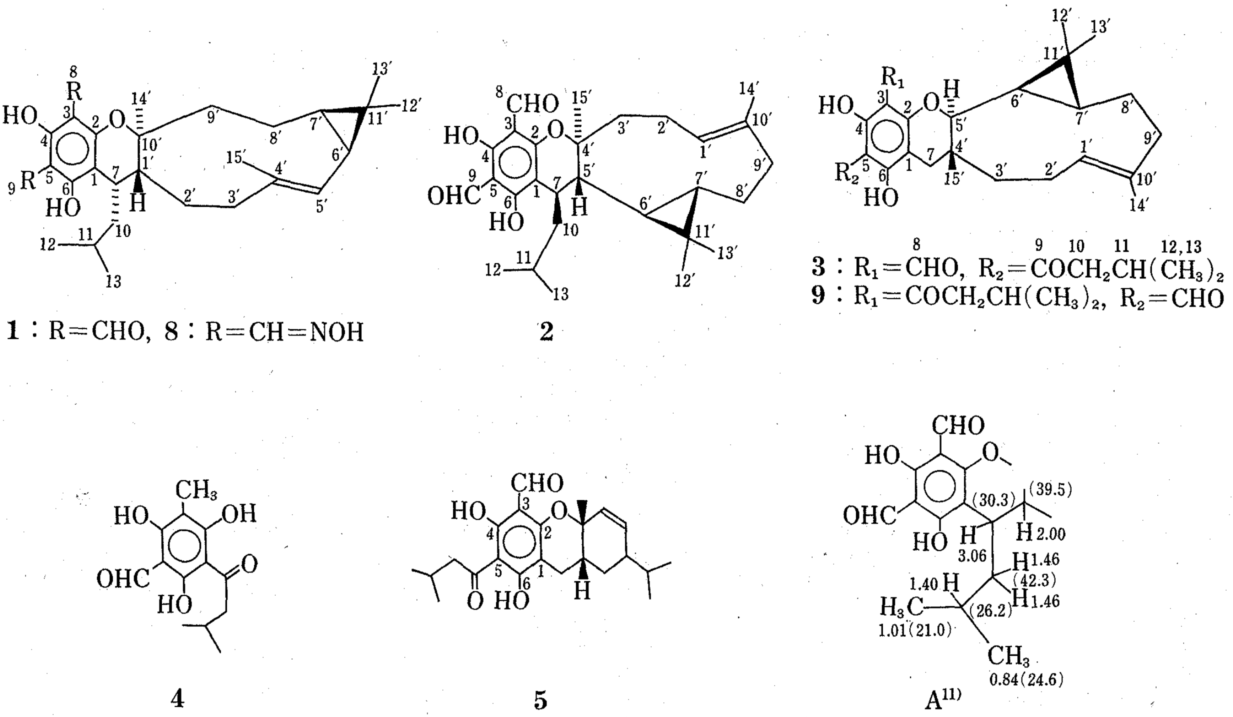


Chart 2. The Fragmentations of Euglobal-III (1), –IVb (2) and –VII (3) in MS



1 : R=CHO, 8 : R=CH=NOH

2

3 : R_1=CHO, R_2=$COCH_2CH(CH_3)_2$

9 : R_1=$COCH_2CH(CH_3)_2$, R_2=CHO

4

5

A[11]

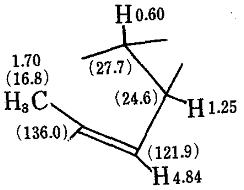
Chart 2

Euglobal-III (**1**), mp 169—171 °C, colorless needles, was the first isolated and the major component from the active fraction of the buds and leaves of *Eucalyptus globulus* Labill. The high-field region of the PMR spectrum of **1** exhibited an olefinic proton (δ 4.84, 1H, broad d, J=9 Hz), a methine proton (δ 3.05, 1H, m), six methyl groups (δ 1.70, 1.45, 1.02 and 0.95, each 3H, s; δ 1.01 and 0.84, each 3H, d, J=6 Hz), twelve methylene and/or methine protons (δ 1.1—2.3, a highly complicated splitting pattern), and two protons (δ 0.5—0.75, m). The saturated carbon region of CMR indicated the presence of two quaternary carbons (δ 88.8 and 20.3, each s), five methines (δ 39.5, 30.3, 27.7, 26.2 and 24.6), five methylenes (δ 42.3, 39.9, 39.6, 26.5 and 19.2) and six methyls (δ 28.6, 26.1, 24.6, 21.0, 16.8 and 15.1). The multiplet at δ 3.05 in PMR was assigned to a methine proton adjacent to an aromatic ring from its chemical shift. In decoupled PMR spectra, saturation of the signals at δ 1.46 collapsed the multiplet at δ 3.05 into a doublet. Saturation of the proton at δ 2.00 changed the multiplet to a double doublet-like signal. When the protons at δ 3.05 and 2.00 were irradiated, the ^{13}C-signals at δ 30.3 (d) and 39.5 (d), respectively, were sharpened, whereas irradiation at δ 1.46—1.45 sharpened two signals at δ 42.3 (t) and 26.1 (q). The methylene and methyl carbon signals were correlated with protons at δ 1.46 and 1.45, respectively. Thus, the benzylic methine at δ 3.05 is adjacent to a methine and a methylene. Saturation of the proton at δ 1.40 caused the methyl doublets at δ 0.84 and 1.01 to coalesce into singlets. When the protons at δ 1.40, 1.01 and 0.84 were saturated, the signals at δ 26.2 (d), 21.0 (q) and 24.6 (q) were sharpened, respectively. These results suggested the presence of an isopropyl group in euglobal-III (**1**). The fact that the isopropyl group constitutes a part of the isobutyl group in [A] was suggested by the chemical shift of the methine carbon signal of the isopropyl group. Further, the high resolution MS[3] of **1** showed the fragmentation pattern of the isobutyl side-chain ($M-CH_3$, $M-C_3H_7$, $M-C_4H_9$). The base peak (m/z 195.0301) was formed from the aromatic part fragment with the loss of C_4H_8.

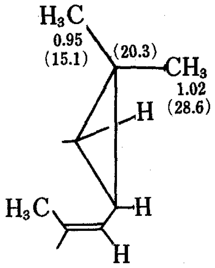
The data described above confirmed the partial structure [A] for the aromatic part, and thus fourteen carbons in compound **1** were assigned.

Two of the fourteen remaining carbons were present as olefinic carbons, δ 136.0 (s) and 121.9 (d), and the latter seemed to be attached to the olefinic proton at δ 4.84. Saturation of the olefinic methyl broad singlet at δ 1.70 caused sharpening of the olefinic proton (δ 4.84) without any increase in the integrated intensity, and the (*E*)-configuration was suggested for the double bond.6) Saturation of the one-proton double doublet at δ 1.25 caused the doublet at δ 4.84 to collapse into a broad singlet and the one-proton multiplet at δ 0.60 to be modified. When the proton signals at δ 4.84, 1.70, 1.25 and 0.60 were irradiated, the signals at δ 121.9 (d), 16.8 (q), 24.6 (d) and 27.7 (d) were decoupled and sharpened, respectively. Thus, the partial structure [B] was confirmed.

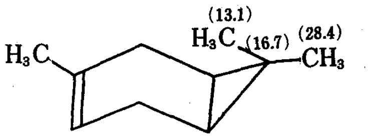
Of the two quaternary carbons in the sesquiterpene moiety, the low-field chemical shift (δ 88.8) of one implied that it is attached to an oxygen atom. It is also clear that three singlet methyls at δ 1.45, 1.02 and 0.95 in the PMR are attached to quaternary carbons. When the methyl protons at δ 1.45, 1.02 and 0.95 were irradiated, the signals at δ 26.1 (q), 28.6 (q) and 15.1 (q), respectively, in the CMR were decoupled. The chemical shift of the methyl carbons at δ 28.6 and 15.1 showed a good agreement with those (δ 28.4 and 13.1) reported for the tow methyl groups on the three-membered ring in carene (**6**).7) Thus, the quaternary carbon at δ 20.3 is assumed to be in the cyclopropane ring. In the MS of euglobal-III (**1**), a peak was observed at *m/z* 161.1327 ($C_{15}H_{23}-C_3H_6$), indicative of a *gem*–dimethyl group attached to the cyclopropane ring. The signals at δ 20.3 (s), 28.6 (q) and 15.1 (q) were assigned to the quaternary carbon in the three–membered ring and to the *gem*–dimethyl carbons attached to the quaternary carbon, respectigely. The methyl carbon at δ 26.1 must be attached to the quaternary carbon (δ 88.8) adjacent to the oxygen atom. Since the remaining four carbons of **1** are methylenes, the three–membered ring was formed including two methines in the partial structure [B]. These data allowed the partial structure [B] to be expanded to [C].



B11



C11)



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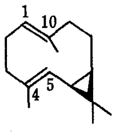

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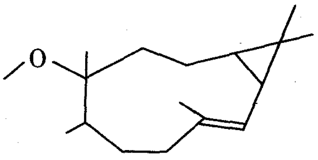


D

Chart 3

From the index of hydrogen deficiency of euglobal-III (**1**), the sesquiterpene moiety must be bicyclic or tricyclic. On the other hand, among hitherto known naturally occurrnig bicyclo- and tricyclosesquiterpenes, bicylogermacrene (**7**)6) is the only compound having the partial structure [C]. The PMR spectrum of **1** was comparable with that of **7** but lacked the characteristic signals due to C(10)- methyl and C(1)- hydrogen in **7**. This suggested that the C(1), C(10) double bond was absent in **1**. Thus, a partially saturated bicyclogermacrene structure [D] for the sesquiterpene moiety was suggested for euglobal-III (**1**).

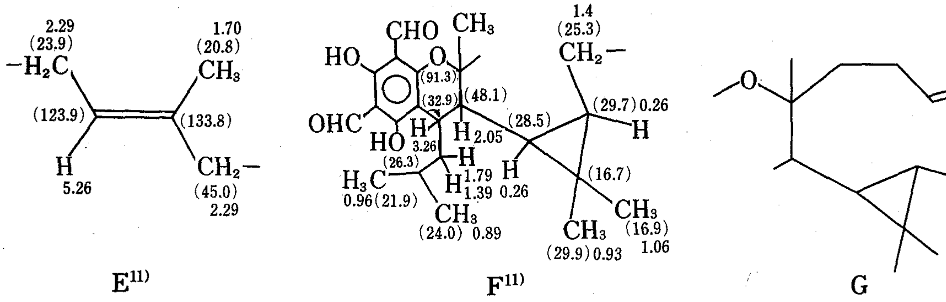
The above discussions thus allow merging of the partial structures [A] and [D] into the formula **1** to represent euglobal-III.

To confirm the structure and determine the stereochemistry of **1**, an X-ray analysis[8] was conducted of the dioxime (**8**), and the structure of **1** was established except for its absolute configuration.

Euglobal-IVb (2), mp 187—190°C, was isolated as colorless prisms. As is apparent from the physicochemical data, this compound has the same aromatic part [A] as in the case of euglobal-III (**1**). The foregoing evidence led to the conclusion that compound **2** was a structural variant of **1** in the sesquiterpene moiety. The CMR of the terpene moiety of euglobal-IVb (**2**) indicated, by analogy with that of euglobal-III (**1**), the presence of a double bond consisting of two olefinic carbons (δ 133.8, s; 123.0, d), a quaternary carbon attached to an oxygen atom (δ 91.3, s), another quaternary carbon (δ 16.7, s) involved in a threemembered ring and bearing *gem*-dimethyl carbons (δ 29.9 and 16.9, each q), two methyls (δ 24.0 and 20.8, each q), four methylenes (δ 45.0, 34.9, 25.3 and 23.9, each t) and three methines (δ 48.1, 29.7 and 28.5, each d). The (*E*)-configuration was suggesteed for the double bond on the basis of an experiment similar to that described before. When the methyl proton signal at δ 1.70 coupled over long range with the olefinic proton at δ 5.26 was irradiated, the quartet signal at δ 20.8 was decoupled.

The signal at δ 24.0 was assigned to the methyl group attached to the quaternary carbon atom adjacent to the oxygen atom, since the corresponding PMR signal was a singlet (δ 1.17) upon selective proton decoupling. Irradiation of the signal at δ 2.29 converted the olefinic proton signal at δ 5.26 (broad d) to a broad singlet. When the overlapped proton signals at δ 2.29 were irradiated, the two methylene carbon signals at δ 23.9 (t) and 45.0 (t) were decoupled. The methylene coupled with the olefinic proton (δ 5.26) can be assigned to the signal at δ 23.9 (t), since it must be *cis* to the methyl group at δ 20.8. The signal at δ 45.0 was assigned to the methylene carbon attached to the other end of the double bond from its PMR chemical shift. These data suggested the partial structure [E] for the terpene moiety of euglobal-IVb (**2**). A broad doublet at δ 2.05 changed to a broad singlet when the signal at δ 0.26 (2H, m), assignable to the protons on the three-membered ring, was irradiated. There was also a change in the methylene signals at about δ 1.4. Conversely, irradiation of the signal at δ 2.05 caused the higher field part of the signals at δ 0.26 to be modified, and the benzylic proton (δ 3.26, broad dd) to change into a double doublet. These observations revealed that the three-membered ring was not adjacent to the double bond, leading to the partial structure [F]. The NMR assignments given in [F] were confirmed by selective proton decouplings. From the partial structures [E] and [F], and a remaining methylene, thus, a partially saturated bicyclogermacrene structure [G] for the sesquiterpene moiety would be suggested from the biogenetic point of view. These data led to the elaboration of a planar structure corresponding to formula **2** for euglobal-IVb. Recently, a new compound designated as euglobal-IVa was isolated, and the structure, including relative stereochemistry, was determined to be **16** by X-ray analysis.[8] A PMR comparison of both compounds, **2** and **16**, showed that they were apparently diastereomeric (Tables I and II). This assignment was also supported by a comparison of the chemical shifts of the CMR signals (Tables I and II) of euglobal-IVa (**16**) and -IVb (**2**). The CMR spectra of both compounds were similar, but a major difference was observed among the carbon signals at C(10) [**16**: δ 38.7; **2**: δ 44.6]. A consideration using a Dreiding model indicated that the upfield shift in euglobal-IVa (**16**) could be explained by a steric compression effect attributable to a difference in configuration of the isobutyl group. Thus, the formula **2** represents euglobal-IVb except for its absolute configuration.

Euglobal-VII (**3**), isolated as an oil, showed IR and MS similar to those of euglobal-III (**1**) and -IVb (**2**) except for the part described below. The NMR data of this compound are summarized in Table I. Two signals (δ 15.37 and 14.56, each 1H, s) due to hydroxyl protons appeared in the PMR, while only one aldehydic proton (δ 10.02, 1H, s) and carbon (δ 191.7, d), and ketonic carbon signal (δ 206.1, s) were observed. These data indicated that the structure of the aromatic part of euglobal-VII (**3**) is different from those of euglobal-III



E[11] F[11] G

Chart 4

(**1**) and -IVb (**2**). In the CMR spectrum, the six aromatic carbons were all singlets and their chemical shifts coincided with those of euglobal-III (**1**) and -IVb (**2**), indicating that the substitution pattern in euglobal-VII (**3**) was fairly similar to those of euglobal-III (**1**) and -IVb (**2**). The above data suggest that one of the two aldehyde groups in **1** or **2** was substituted by an acyl group in euglobal-VII (**3**). The acyl group was found to be an isovaleryl group from the following NMR experiments. Irradiation of the signal at δ 2.30 (1H, m) changed the signals of a methylene at δ 2.99 (2H, d, $J=6$ Hz) and two methyls at δ 1.00 (6H, d, $J=7$ Hz) to singlets. The assignment was also confirmed by the fact that the CMR spectrum revealed the presence of a ketone (δ 206.1), a methylene adjacent to the ketone (δ 52.7), a methine (δ 25.1) and two methyls (δ 22.7). The chemical shifts in the PMR and CMR of the acyl group coincided with those of the isovaleryl group of grandinol (**4**). It was also confirmed that the methine at δ 3.71 attached to an oxygen atom and seen as the carbon signal at δ 83.6 (d) was decoupled when the methine proton signal(d, $J=7$ Hz) was irradiated. An isolated methylene signal (δ 2.76 and 2.17, AB-type q, $J=16$ Hz) was observed as the signal corresponding to C(7)-H observed in the PMR spectrum of euglobal-III (**1**) or euglobal-IVb (**2**). The above data also suggested that the methylene group was attached to a quaternary carbon. These observations led to a partial structure [H] for the moiety including the aromatic ring. The CMR of the terpene moiety of this compound indicated the presence of two olefinic carbons (δ 130.9, s; 127.5, d), two quaternary carbons (δ 36.1 and 19.5), three methines (δ 83.6, 31.1 and 30.4), four methylene carbons (δ 39.5, 37.9, 23.0 and 22.7), and four methyls (δ 26.8, 21,4, 19.3 and 17.6). Irradiation of the proton signal due to the methly group at δ 1.63 (broad s) caused the olefinic proton multiplet at δ 5.23 to collapse into a double doublet, but no nuclear Overhauser effect (NOE) was observed. This result demonstrated that the olefinic proton was adjacent to a methylene and indicated the presence of partial structure [I]. The methyl signal at δ 1.63 was related to the carbon signal at δ 19.3 (q) by selective proton decoupling. The presence of the *gem*-dimethyl group on the three-membered ring was supported by the diagnostic peak ($C_{15}H_{23}-C_3H_6$) in the MS, and was also confirmed by the CMR signals at δ 19.5 (s), 17.6 (q) and 26.8 (q). The signals at δ 0.60 (1H, dd, $J=8$, 10 Hz) and δ 0.82 (IH, t-like, $J=7$, 8 Hz), assignable to methines in a cyclopropane ring, were related to the carbon signals at δ 31.1 (d) and 30.4 (d), respectively, by selective proton decouplings. The three-membered ring was constructed from the two methines and the carbon bearing the *gem*-dimethyl group. Irradiation of the proton signal (δ 3.71) due to the methine adjacent to the oxygen atom changed the methine proton signal at δ 0.82 to a doublet ($J=8$ Hz). Conversely, irradiation of the signal at δ 0.82 converted the methine doublet at δ 3.71 to a singlet. Consequently, it was concluded that the other bond of the methine adjacent to the oxygen atom was linked to a quaternary carbon atom (δ 36.1, s), and thus that the partial structure [H] was to be extended into a six-membered oxygen heterocyclic structure. The metyl group at δ 21.4 in the CMR must be attached to the quaternary carbon atom, because the proton signal (δ 1.14) due to the methyl group was a singlet. These data supported the partial structure [J] of **3**. The terpene portion of euglobal-VII (**3**) will be constructed from the partial structures [I] and [J], and the three methylenes. Thus, a partially saturated bicyclogermacrene structure [K] was suggested for the sesquiterpene moiety, and a planar structure corresponding to the formula **3** or **9** should represent euglobal-VII.

To choose the correct structure from **3** and **9**, detailed analysis of the long-range $^{13}C-^{1}H$ coupling was carried out. The higher-field spectrum of the high-resolution CMR of euglobal-VII (**3**) is shown in Fig. 1. The isovaleryl group was attached to C(**5**), since the coupling pattern in the C(3) and C(5) region consisted of a double doublet [$^2J(\underline{C}-C\underline{H}O)=16.9$ Hz, $^3J(\underline{C}-C-O\underline{H})=6.6$ Hz] and a triplet [$^3J(\underline{C}-C-O\underline{H})=6.6$ Hz], respectively, so the planar formula **3** was assigned to euglobal-VII. The aromatic carbon signals at lower field of th spectrum at δ 171.8 (m), 168.0 (t, $J=5.1$ Hz) and 162.5 (broad s) can be assigned to C(6), C(4) and C(2), respectively, by comparison with the spectrum of euglobal-Ic (**10**).[9] The carbon signal due to C(4) of euglobal-VII (**3**) was observed as a triplet similar to those of euglobal-Ic (**10**) and-IIc (**5**). This is compatible with an earlier detalied discussion.[1]

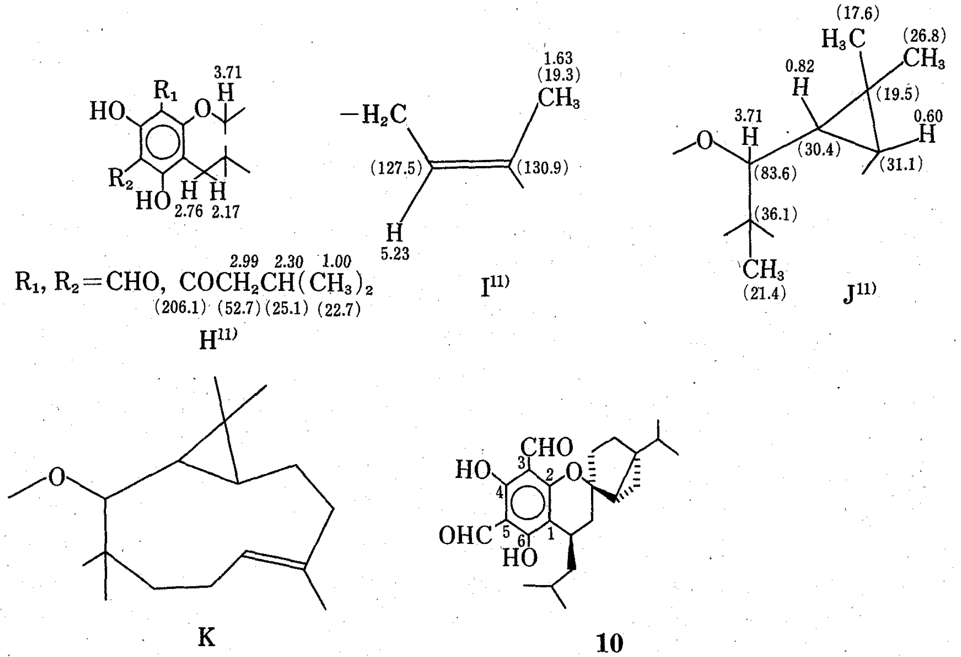


Chart 5

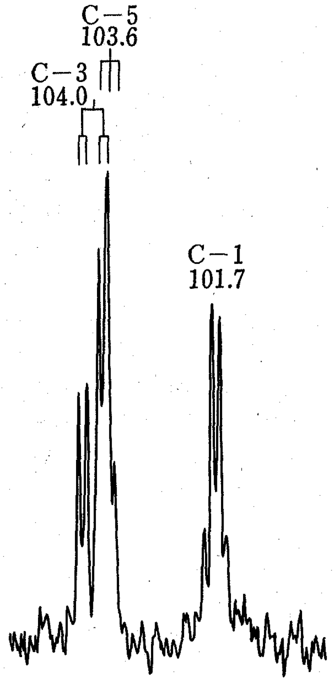


Fig. 1. The Higher Field Signals of the Aromatic Carbons in the 50.2 MHz CMR of Euglobal-VII (3) with Gated ^1H Decoupling

Based on biogenetic considerations and the circular dichroism (CD) data, the stereochemical assignments of euglobal-III (**1**), -IVb (**2**) and -VII (**3**) can be discussed as follows. These compounds may be derived biogenetically from isovaleryl phloroglucinol dialdehyde precursor (**11**) and bicyclogermacrene (**7**), which is the common precursor of aromadendrane derivatives isolated from *Eucalyptus globulus* Labill., such as α-grujunene (**12**), aromadendrene (**13**) and globulol (**14**). The euglobals could be produced by a Diels-Alder-type condensation of the precursors.

If the addition of the phloroglucinol precursor (**11**) to C(1) and C(10) of bicyclogermacrene (**15**) occurred from the less hindered side, and if euglobal-III (**1**) retained the configuration[6] of **15**, the formula **1** could be drawn for euglobal-III. The CD spectrum of euglobal-IVa (**16**) in ethanol, exhibiting positive Cotton effects as shown in Table III, was very similar to that of euglobal-III (**1**). In these compounds, the chiral center at C(7) was expected to exert a Cotton effect at 280—285 nm and to contribute to the sign. Hence, the absolute configuration at C(7) of euglobal-IVa (**16**) will be identical with that of **1**. The absolute configurations of euglobal-IVb (**2**) are also suggested by its CD spectrum. The CD spectrum of **2** showed negative Cotton effects (Table III), and therefore, takineg the biogenetic consider-

TABLE II. PMR and CMR Spectral Data for Euglobal-IVa (**16**) and -V (**17**)

Carbon	Euglobal-IVa (**16**)			Euglobal-V (**17**)		
	M$^{a)}$	δ ^{13}C	δ ^{1}H	M$^{a)}$	δ ^{13}C	δ ^{1}H
1	s	112.2		s	119.6$^{b)}$	
2	s	165.4		s	167.6$^{c)}$	
3	s	106.5		s	119.2$^{b)}$	
4	s	166.9		s	169.2$^{c)}$	
5	s	104.5		s	116.6$^{b)}$	
6	s	167.5		s	172.1$^{c)}$	
7	d	30.9	3.29 (m)	d	43.0	3.28 (m)
8	d	191.9$^{b)}$	10.24$^{d)}$ (s)	d	193.2$^{d)}$	10.36$^{f)}$ (s)
9	d	191.7$^{b)}$	10.06$^{d)}$ (s)	d	191.8$^{d)}$	10.23$^{f)}$ (s)
10	t	38.7	1.20$^{g)}$, 1.67$^{g)}$	t	43.2$^{h)}$	1.21$^{g)}$
11	d	26.5		d	25.7	
12, 13	q	22.4, 24.8	1.01, 0.78 (d $J=6$ Hz)	q	21.5, 24.6	
1′	d	122.7	5.13 (m)	s	105.2	
2′	t	23.7		t	36.0$^{e)}$	
3′	t	36.2		t	37.5$^{e)}$	
4′	s	91.1		s	47.1	
5′	d	46.0	1.83$^{g)}$	d	49.1$^{h)}$	2.15 (br, d $J=12$ Hz)
6′	d	28.9$^{c)}$	0.75 (t like $J=8$ Hz)	d	26.3$^{h)}$	0.32 (dd $J=9$, 12 Hz)
7′	d	28.2$^{c)}$	0.40 (br, dd $J=11$, 8 Hz)	d	23.8$^{h)}$	0.75$^{g)}$
8′	t	24.8		t	20.2	
9′	t	46.4		t	29.8$^{e)}$	
10′	s	134.4		d	40.2$^{h)}$	2.47 (m)
11′	s	16.3		s	19.5	
12′, 13′	q	30.4, 17.3	1.18, 1.08 (s)	q	28.6, 15.7	
14′	q	19.5	1.66 (s)	q	17.3$^{h)}$	1.00 (d $J=7$ Hz)
15′	q	25.4	1.56 (s)	q	24.0$^{h)}$	1.21 (s)
OH			13.09 (s)			13.38 (s)
			13.02 (s)			13.55 (s)
			0.8—2.4 (12H)			0.6—2.0 (18H)

Chemical shifts are expressed in δ (ppm) values.

a) Multiplicity.

b—*f*) Assignments may be interchangeable among the signals with the same superscripts in any one spectrum.

g) These δ values were estimated by the double resonance technique.

h) These δ values were assigned by selective proton decouplings.

TABLE III. CD Data for Euglobals (Ethanol)

Euglobals	$\Delta\varepsilon$ (nm)	c (%)
III(**1**)	10.4(280), −2.7(310), 2.3(344)	0.0030
IVa(**16**)	13.5(282), −4.0(312), 6.0(345)	0.0023
IVb(**2**)	−15.9(285), 5.8(314), −4.3(348)	0.0031

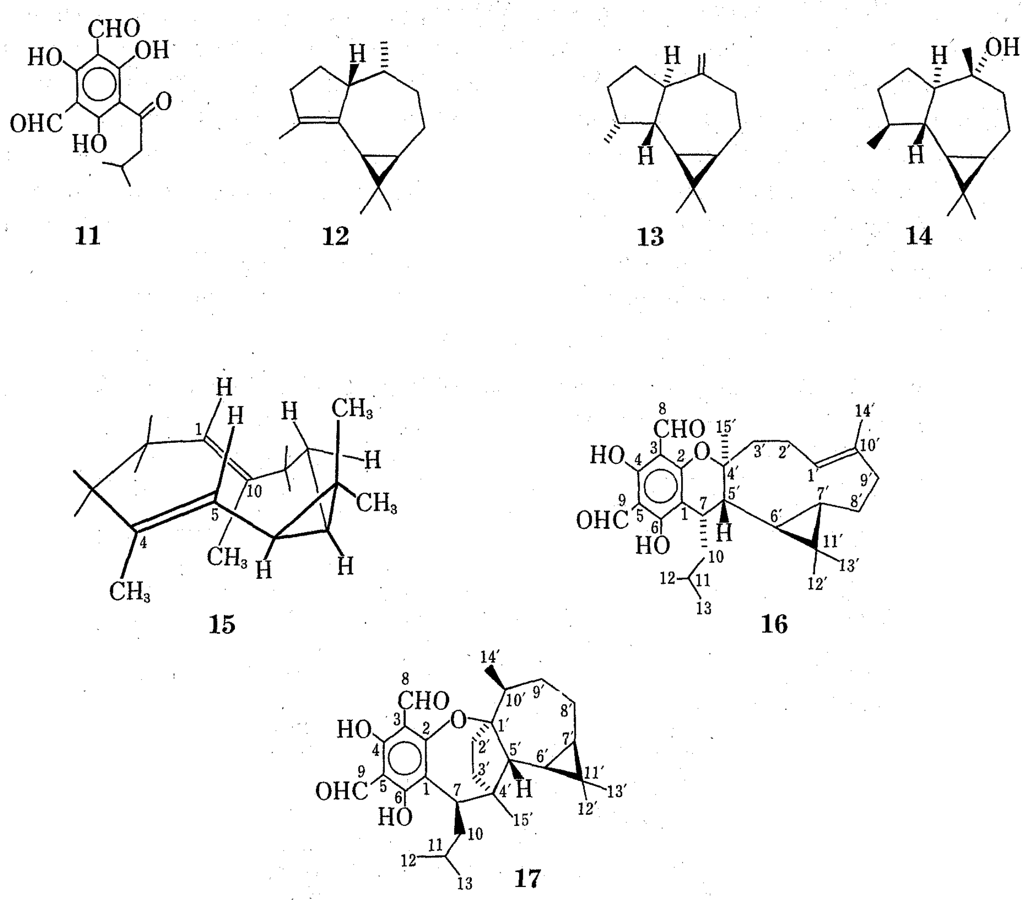


Chart 6

ations into account the absolute configuration of this compound should be as shown in **2**.

Euglobal-VII (**3**) could be produced by a Diels-Alder-type condensation involving the C(4) and C(5) double bond of bicyclogermacrene (**15**) and the phloroglucinol precursor (**11**) through different reaction sites from the other euglobals. If euglobal-VII (**3**) also retained the configuration[6] of **15**, formula **3** would represent the most probable structure. Thus, the structures including absolute configurations, of euglobal-III, -IVb, -IVa and -VII are proposed to be **1**, **2**, **16**, and **3**, respectively. On the other hand, the previously reported euglobal-V (**17**)[3,10] is presumably formed from the aromatic precursor (**11**) and α-grujunene (**12**). However, its biogenesis seems rather exceptional with respect to oxepine ring formation and the stereochemical course during the product formation.

Further studies on the biosynthesis and the biological activities of these four compounds are in progress.

Experimental

All melting points were determined on a microscopic hot stage (Yanagimoto micro melting point apparatus) and are uncorrected. IR, UV and MS spectra were recorded using Hitachi 260-10, Perkin-Elmer 450 and JEOL JMS-01SC spectrometers, respectively. PMR spectra were taken on a Varian XL-100-12 spectrometer. The samples (20—40 mg) were dissolved in $CDCl_3$ (0.4 ml), and measured by the continuous wave method. Chemical shifts are given in δ values downfield from tetramethylsilane (TMS) as an internal standard. CMR spectra were recorded on a JEOL FX-200 spectrometer and a Varian XL-100-12 Fourier-transform spectrometer operating at 50.2 and 25.2 MHz with proton noise decoupling, off-resonance decoupling, selective proton decoupling and gated decoupling techniques. The spectral width was 6000 Hz (6000—12000 Hz) for euglobal-VII and 5000 Hz for euglobal-III, -IVa, -IVb and -V, and 8K (32K) data points were used for 5000—70000 accumulations in the Varian XL-100-12 (JEOL FX-200). The samples (40—80 mg) were dissolved in $CDCl_3$ (0.4 ml or 0.8 ml) and the ^{13}C-chemical shifts were measured relative to the ^{13}C-signal of $CDCl_3$ and converted to ppm from TMS using δ ($CDCl_3$)$=76.9$. Optical rotations and CD spectra were measured with a Perkin–Elmer 141 spectropolarimeter and a JASCO ORD/UV-5, respectively.

Euglobal-III (1)——Colorless needles from ethanol, mp 169—170°C. UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (ε): 276 (35000), 340 (4500, inflection). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3400 (OH), 1620 (C=O). $[\alpha]_{\mathrm{D}}^{20}$ $+229°$ ($c=1.0$, $CHCl_3$). The NMR, CD and MS data are shown in Tables I and III and Chart 1, respectively. *Anal.* Calcd for $C_{28}H_{38}O_5$: C 73.98; H 8.43. Found: C 73.96; H 8.41.

Euglobal-IVb (3)——Amorphous powder. UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (ε): 275 (34600), 340 (4400, inflection). IR $\nu_{\max}^{\mathrm{liq.film}}$ cm^{-1}: 3450 (OH); 1630 (C=O). $[\alpha]_{\mathrm{D}}^{20}$ $-230°$ ($c=1.0$, $CHCl_3$). The NMR, CD and MS data are shown in Tables I and III and Chart 1, respectively.

Euglobal-VII (5)——Colorless oily substance. UV $\lambda_{\max}^{\mathrm{EtOH}}$ nm (ε): 276 (36000), 340 (3900, inflection). IR $\nu_{\max}^{\mathrm{liq.film}}$ cm^{-1}: 3450 (OH), 1620 (C=O). $[\alpha]_{\mathrm{D}}^{20}$ $-137°$ ($c=1.0$, $CHCl_3$). The NMR, CD and MS data are shown in Tables I and III and Chart 1, respectively.

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References and Notes

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7) L.F. Johnson and W.C. Jankowski, Carbon-13 NMR Spectra—A Collection of Assigned, Coded and Indexed Spectra—No. 394.
8) The X-ray crystallographic studies of these compounds will be reported elsewhwere.
9) The assignments of the aromatic carbons were already reported in Part II of this series.
10) The structure of euglobal-V was determined by an X-ray analysis, and will be reported elsewhere. The NMR data of this compound were shown in Table II.
11) The figures in the structural formulas are δ ^1H (δ ^{13}C) in the NMR.