CHEMISTRY LETTERS, pp. 2187-2190, 1990.

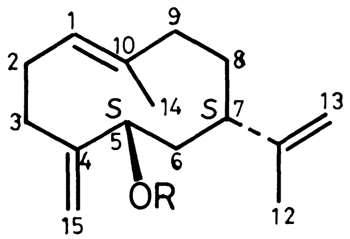
The Structure of a Germacrane-Type Sesquiterpene Alcohol, a Possible Precursor of Guaiane-Type Sesquiterpenes from the Brown Alga *Dictyopteris divaricata*[1)]

Minoru SUZUKI,* Nobuhiko KOWATA,† Hirokazu KOBAYASHI,†† and Isao TANAKA ††*
Department of Chemistry, Faculty of Science,
Hokkaido University, Sapporo 060
††Department of Polymer Science, Faculty of Science,
Hokkaido University, Sapporo 060

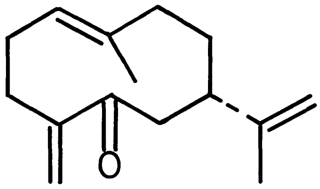
A new sesquiterpene alcohol was isolated from the title alga, and its structure established as (*E*,5*S*,7*S*)-germacra-1(10),4(15),11-trien-5-ol by an X-ray crystallographic analysis of the *p*-bromobenzoate derivative.

In connection with our continuing studies on the constituents of the brown alga *Dictyopteris divaricata* (Okamura) Okamura (family Dictyotaceae), we have reported previously the isolation of several cadinane-type sesquiterpenes.[2)] Further investigation of the polar fraction has resulted in the isolation of a new sesquiterpene alcohol with a germacrane skeleton, whose structure is described in this communication.

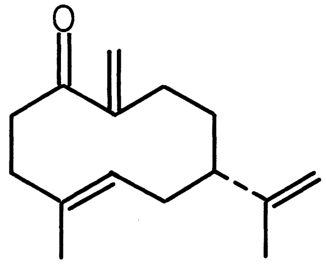
The fraction eluted with diethyl ether on the column chromatography of the neutral extract[2)] was repeatedly subjected to a combination of column and thin-layer chromatography to give a new sesquiterpene alcohol (1) in 0.1% yield based on the neutral extract.



1 : R=-H
2 : R=-CO-CH_3
4 : R=-CO-C_6H_4-Br



3



5

---

†Present address: Nippon Chemiphar Co. Ltd., Hikokawato, Misato 341.

Compound 1, $C_{15}H_{24}O$, $[\alpha]_D$ -23.6° (c 0.970; $CHCl_3$), exhibited in its spectra$^{3)}$ the presence of two olefinic methyl groups [δ_H 1.62 and 1.77 (3H each, br s)], two *exo*-methylene group [δ_H 4.72, 4.87, 5.14, and 5.30 (1H each, br s); δ_C 110.5 (t) and 109.8 (t)], and a hydroxyl group (δ_H 4.05 (1H, m); ν_{max} 3560 and 3460 cm^{-1}]. Acetylation of 1 with acetic anhydride in pyridine afforded the corresponding acetate (2), $C_{17}H_{26}O_2$, ν_{max} 1735 and 1240 cm^{-1}; δ_H 1.95 (3H, s),$^{3)}$ which regenerated the parent alcohol on mild saponification with potassium carbonate in methanol. The spin decoupling studies in the ^1H NMR spectrum of 1 coupled with the ^{13}C NMR data indicated the presence of the following partial structural units (A, B, C, D, and E; Fig. 1) in the molecule. The allylic alcohol nature of the hydroxyl group in 1 was further confirmed by the following oxidation reaction. Sarett oxidation of 1 gave an α,β-unsaturated ketone (3), $C_{15}H_{22}O$, λ_{max} 226 nm (ε 4380) and ν_{max} 1680 cm^{-1}.$^{3)}$ The ^{13}C NMR spectrum revealed that there were no other double bonds apart from three double bonds mentioned above and hence compound 1, having four degrees unsaturation, must be composed of monocarbocyclic skeleton, which is probably a ten-membered ring. From the above data along with the biogenetic viewpoint (co-occurence of 1 and (-)-germacrene A$^{4)}$), compound 1 might be a germacrene-type sesquiterpene. The complete structure, including the absolute configuration, was established unequivocally by an X-ray crystallographic analysis of the *p*-bromobenzoate derivative (4).

$-CH_2-CH(OH)-\underset{|}{C}=CH_2$ $\quad CH_3\underset{|}{C}=CH-CH_2-$ $\quad -C(CH_3)=CH_2$ $\quad CH_2 \times 3$ $\quad CH \times 1$

A B C D E

Fig. 1. Partial structural units for 1.

The *p*-bromobenzoate (4),$^{5)}$ $C_{22}H_{27}O_2Br$, mp 77-78 °C, crystallized from methanol in the monoclinic space group C2, a=24.77(7), b=8.442(2), c=9.969(9)Å, β=89.49 (9)°, z=4, D_C=1.28 g/cm^3. The intensity of 1789 independent reflections with 2θ< 45° were measured on a MAC Science imaging plate diffractometer DIP-100 with graphite-monochromated Mo Kα radiation. The structure was solved by the direct method, and was refined by the block-diagonal least-squares method.

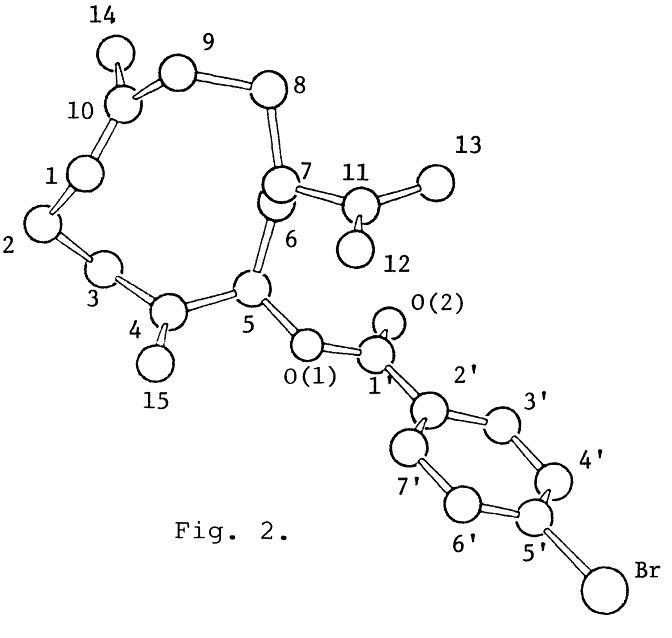
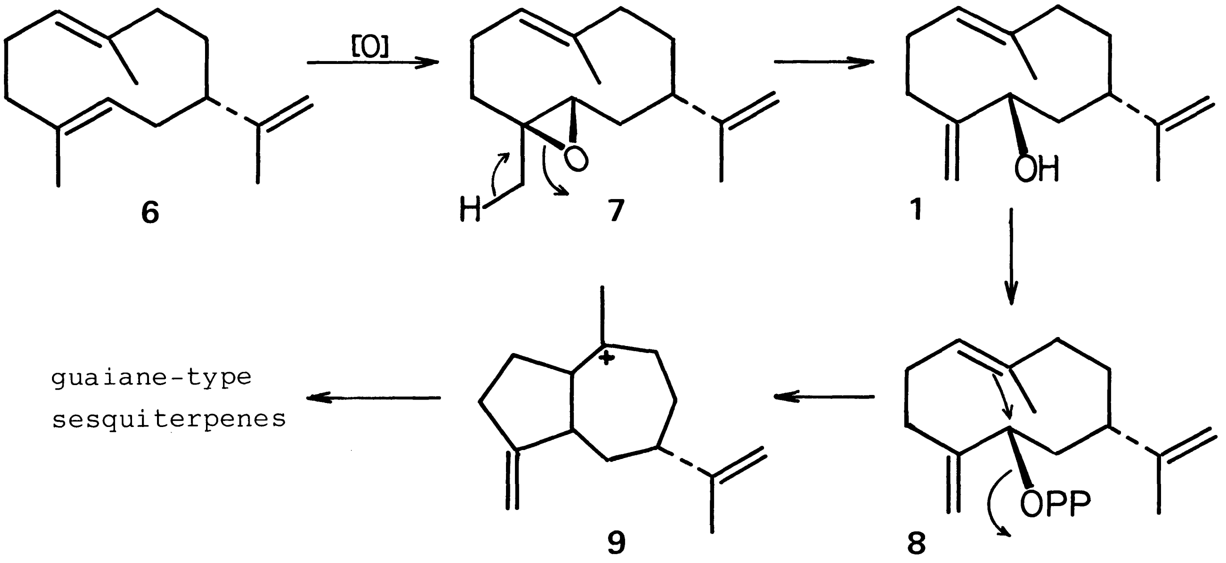


Fig. 2.

No hydrogen atoms were included in the structure factor calculation. The final R value was 0.118. The absolute configuration was established by comparison of 123 Bijvoet pairs of reflections. A computer generated perspective drawing of the X-ray model of 4 is illustrated in Fig. 2.

Two germacrane-type sesquiterpenes, (*E*,1*S*,7*R*)-germacra-4(15),6-10(14)-trien-1-ol acetate$^{6)}$ and (*E*,*S*)-germacra-4,10(14),11-trien-1-one (5),$^{7)}$ have already been isolated from the brown algae *Dilophus fasciola* and *Dictyopteris divaricata*, respectively.

Compound 1 may enzymatically be synthesized from (-)-germacrene A (6)$^{4)}$ via 4,5-epoxide 7 (Scheme 1). Furthermore, as shown in Scheme 1 the guaiane-type sesquiterpenoids seem to be biosynthesized from compound 1 via cyclization of pyrophosphate 8 to cation 9.$^{8)}$



Scheme 1. Possible biogenesis from (-)-germacrene A.

References

1) Part 81 of "Constituents of Marine Plants." Part 80; M. Suzuki, N. Kowata, and A. Furusaki, *Bull. Chem. Soc. Jpn.*, in preparation.

2) M. Suzuki, N. Kowata, and E. Kurosawa, *Bull. Chem. Soc. Jpn.*, 54, 2366 (1981).

3) 1: oil; $[\alpha]_D$ -23.6° (c 0.970, $CHCl_3$); IR (film), ν_{max} 3560, 3460, 3080, 1640, 1095, 1055, and 890 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$), δ 1.62 (3H, br s), 1.77 (3H, br s), 4.05 (1H, m), 4.72 (1H, br s), 4.87 (1H, br s), 5.14 (1H, br s), 5.30 (1H, br s), and 5.40 (1H, br t, J=7 Hz); ^{13}C NMR (22.6 MHz, $CDCl_3$), δ 154.3 (s), 150.2 (s), 132.6 (s), 126.5 (d), 110.5 (t), 109.8 (t), 76.0 (d), 39.8 (d), 39.1 (t), 32.8 (t), 31.0 (t), 30.4 (t), 26.4 (t), 19.6 (q), and 15.8 (q); MS (70 eV), m/z (rel intensity) 220 (2; M^+), 202 (54; M^+-H_2O), 187 (31; $M^+-H_2O-CH_3$), 161 (16; $M^+-H_2O-C_3H_5$), 159 (100; $M^+-H_2O-C_3H_5-H_2$), 146 (30), 145 (61), 133 (30), 131 (54), 119 (58), 107 (42), 105 (80), 95 (40), 93 (61), 91 (91), 81 (66),

79 (60), 77 (31), 69 (32), 67 (40), 55 (55), and 41 (80). HRMS, m/z 220.1835, calcd for $C_{15}H_{24}O$, 220.1827 (M).

2: oil; $[\alpha]_D$ +5.95° (c 0.830; $CHCl_3$); IR (film), ν_{max} 3080, 1735, 1643, 1240, 1081, 1050, 1040, 1028, 890, and 880 cm^{-1}; ^1H NMR, δ 1.65 (3H, br s), 1.70 (3H, br s), 1.95 (3H, s), 4.62 (2H, s), 5.05 (1H, m), 5.10 (1H, br s), 5.21 (1H, br s), and 5.36 (1H, br t, J=7 Hz); ^{13}C NMR, δ 170.2 (s), 151.6 (s), 146.2 (s), 133.7 (s), 125.9 (d), 112.3 (t), 108.2 (t), 75.6 (d), 39.9 (d), 39.0 (t), 32.0 (t), 31.6 (t), 31.3 (t), 26.7 (t), 20.7 (q), 20.7 (q), and 16.4 (q); MS, m/z 262 (1; M^+), 220 (3; $M^+-C_2H_2O$), 202 (4; $M^+-CH_3CO_2H$), 187 (5), 159 (9), 119(15), 105 (15), 93 (20), 81 (20), 79 (16), 55 (16), 43 (100), and 41 (28). HRMS, m/z 262.1925, calcd for $C_{17}H_{26}O_2$, 269.1930 (M).

3: oil; $[\alpha]_D$ -167° (c 0.300; $CHCl_3$); IR (film), ν_{max} 3060, 1680, 1645, 1148, 1080, 925, and 895 cm^{-1}; ^1H NMR, δ 1.58 (3H, br s), 1.75 (3H, br s), 4.66 (1H, br s), 4.72 (1H, br s), 4.8-5.2 (1H, m), 5.31 (1H, s), and 5.40 (1H, s); MS, m/z 218 (3; M^+), 203 (4), 185 (7), 135 (21), 122 (30), 109 (31), 107 (44), 93 (45), 81 (100), 79 (38), 68 (37), 67 (49), 55 (37), 53 (22), and 41 (58). HRMS, m/z 218.1683, calcd for $C_{15}H_{22}O$, 218.1671 (M).

4) (-)-Germacrene A, (1*E*,4*E*)-germacra-1(10),4,11-triene, has been isolated from this alga as a major component (10% of the neutral oil) of the hydrocarbon fraction. Its structure was confirmed by chemical transformation. These results will be reported in near future.

5) Compound 1 (10 mg) was treated with *p*-bromobenzoyl chloride (20 mg) in dry pyridine (0.5 ml) at room temperature by the usual methods to give 4 (11 mg): mp 77-78 °C (methanol); $[\alpha]_D$ -11.4° (c 1.25; $CHCl_3$); IR ($CHCl_3$), ν_{max} 1705, 1640, 1590, 1280, 1270, 1173, 1115, 1105, 1013, and 890 cm^{-1}; ^1H NMR, δ 1.64 (3H, br s), 1.67 (3H, br s), 4.55 (1H, br s), 4.68 (1H, br s), 5.13 (1H, br s), 5.21 (1H, br s), 5.3-5.5 (2H, m), 7.54 (2H, br d, J=8.8 Hz), and 7.88 (2H, br d, J=8.8 Hz); MS, 404, 402 (1.7:1.8; M^+), 202 (18; $M^+-BrC_6H_4COO$), 185, 183 (98:100; $M^+-C_{15}H_{23}O$). HRMS, m/z 402.1179, calcd for $C_{22}H_{27}O_2{}^{79}Br$, 402.1194 (M).

6) E. Fattorusso, S. Magno, L. Mayol, V. Amico, G. Oriente, M. Piatteli, and C. Tringali, *Tetrahedron Lett.*, 1978, 4149.

7) M. Segawa, K. Yamano, and H. Shirahama, *Phytochemistry*, 29, 937 (1990).

8) The anti-Markownikoff cyclization (attack of the double bond at C-1 to that at C-4 in a germacra-1(10),4-diene precursor) has long been accepted as the mode of formation of the guaiane-type sesquiterpenes. To our knowledge the guaiane-type metabolites have not yet been found from the algae, but from the soft corals.

(Received September 10, 1990)