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THE STRUCTURES OF FUKURINOLAL AND FUKURINAL, TWO NEW DITERPENOIDS FROM THE BROWN SEAWEED *DILOPHUS OKAMURAI* DAWSON

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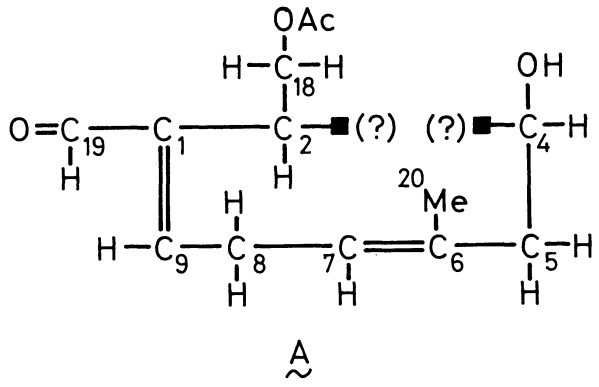
The structures of fukurinolal and fukurinal, two new diterpenoids isolated from the brown seaweed *Dilophus okamurai* Dawson, have been established as 1 and 2, the latter possessing a novel bicyclic ring system, on the basis of spectral and chemical evidence.

In 1979 Finer *et al.*[1] reported the isolation of dictyodial (3), which showed good antibiotic and antifungal activities, from two *Dictyota* species. During a search for the antimicrobial constituents of marine algae,[2] we observed that the allied species *Dilophus okamurai* Dawson contained metabolites whose spectral properties are strongly reminiscent of those of dictyodial. These compounds, fukurinolal and fukurinal, were isolated in 0.015 and 0.0004% yields respectively from the dichloromethane soluble fraction of a methanol extract of the fresh alga by conventional open-column (silica gel) and preparative high-performance liquid (TSK-gel, LS-410KG) chromatography. We propose biogenetically related structures 1 and 2 for these compounds, the latter possessing a novel carbon framework derived from that of the former.

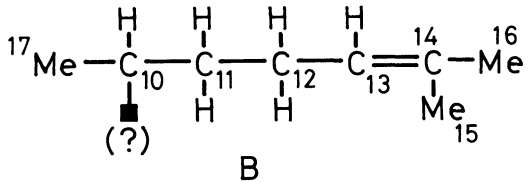
The major diterpenoid, fukurinolal (1),[3] $C_{22}H_{34}O_4$, mp 79-80 °C, $[\alpha]_D^{18}$ -189° (*c* 0.20, $CHCl_3$), showed IR ($CHCl_3$) and UV (EtOH) absorptions indicative of hydroxyl (ν_{max} 3540 cm^{-1}) and α,β-unsaturated enal [ν_{max} 2720, 1680, and 1600 cm^{-1}; λ_{max} 230 nm (ε 16300)] groups. The 400-MHz ^1H NMR spectrum ($CDCl_3$) displayed signals due to one secondary methyl group at δ 1.00, three vinylic methyl groups at δ 1.56, 1.66, and 1.98, one acetoxyl group at δ 1.98, one oxygen-bearing methine proton at δ 4.26, one acetoxymethyl group at δ 4.53 and 4.64, three olefinic protons at δ 5.02, 5.23, and 6.82, and one formyl group at δ 9.32. In addition, extensive ^1H NMDR studies[4] and NOE measurements revealed the presence of the partial structures (A) and (B), the former showing significant long-range couplings ($J_{H_2,H_{19}}$=1.4 Hz, $J_{H_5\beta,H_{20}}$=∿1.0 Hz, and $J_{H_7,H_{20}}$=1.4 Hz) and an NOE (∿10%) between H_9 and H_{19}. The secondary nature of the hydroxyl group was evident from the ^1H NMR spectrum recorded in acetone-d_6 which exhibited a doublet of OH proton [δ 3.75 (J=4.0 Hz)] coupled with H_4. The ^{13}C NMR spectrum[4] showed the presence of one methine carbon atom (C_3) in addition to carbon atoms characterized in the above partial structures.

The E geometry of the C_6 double bond was proved by the observation of an NOE (∿9%) between $H_8\beta$ and H_{20}. These facts inevitably led to the gross structure 1 for fukurinolal. Small J values of vicinal couplings of the protons on the contiguous C_2-C_3-C_4 carbon atoms ($J_{H_2,H_3}=J_{H_3,H_4}=J_{H_3,H_{10}}=$∿0 Hz), in connection with the examination of the model, defined the relative stereochemistry in this system as shown in the structure 1.

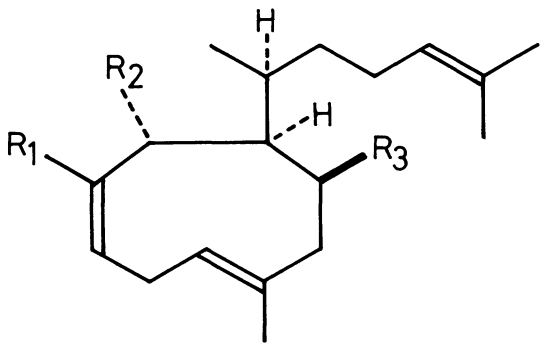
Final confirmation of the assigned structure was achieved by the spectral correlation of the lactone (5), which was derived from 1, with dictyolactone (6).[1] The reduction of 1 with $LiAlH_4$ afforded a triol (4), $C_{20}H_{34}O_3$, mp 151-154 °C, in 60% yield. The oxidation of 4 with Ag_2CO_3/Celite[5] gave the lactone (5), $C_{20}H_{30}O_3$ (M^+ 318), in 55% yield, the IR spectrum ($CHCl_3$) of which showed the presence of a newly introduced α,β-unsaturated γ-lactone (ν_{max} 1740 cm^{-1}). The ^1H and ^{13}C NMR spectra[6] of 5 were quite analogous to those of 6 except for the environs of the hydroxyl group. Thus, the ^1H NMR signals due to H_2, H_{17}, and H_{20} in 5 appeared in lower field (+0.69, +0.13, and +0.17 ppm respectively) compared with those of 6. The deshielding of these protons would be reasonably interpreted through the consideration of the paramagnetic anisotropy by 4β-OH disposed just as in 1,3-diaxial relationship. In the ^{13}C NMR spectrum of 5, the signals due to C_3, C_4, and C_5, as expected, appeared in lower field (+4.3, +44.3, and +9.2 ppm respectively) than those of 6, whereas the signal of C_2 was observed at a higher field (-7.9 ppm) compared with that of 6. The marked shielding of the last signal is excellently explainable by the γ-gauch effect of the 4β-OH group.



A



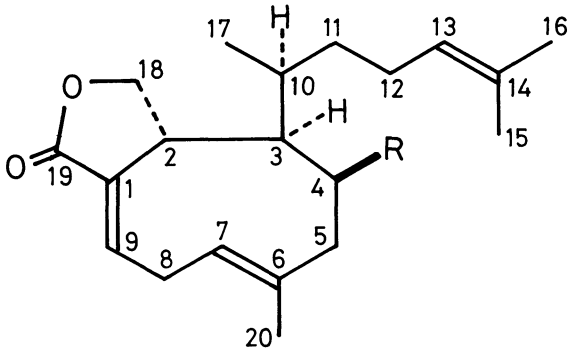
B



1 $R_1 = CHO$, $R_2 = CH_2OAc$, $R_3 = OH$

3 $R_1 = R_2 = CHO$, $R_3 = H$

4 $R_1 = R_2 = CH_2OH$, $R_3 = OH$



5 $R = OH$

6 $R = H$

The minor diterpenoid, fukurinal (2), $C_{24}H_{34}O_5$, mp 132-134 °C, had the spectroscopic properties similar to those of 1. IR (Nujol): 1725, 1690, 1630, and 1240 cm^{-1}; UV (EtOH): 234 nm (ε 13300); MS: m/z 402 (M^+), 342 (M^+ - AcOH), 282 (M^+ - 2AcOH), 260 (M^+ - AcOH - C_6H_{10}), 200 (M^+ - 2AcOH - C_6H_{10}), 82 ($C_6H_{10}^+$), and 69 ($C_5H_9^+$). The 400-MHz ^1H NMR spectrum ($CDCl_3$) of 2 contained signals due to two acetoxyl groups at δ 1.91 and 2.07, two methine protons attached to carbon atoms bearing an acetoxyl group at δ 4.92 and 5.06, and one exocyclic methylene group at δ 4.85 and 4.88, but lacked the signals of the acetylated hydroxymethyl group and the vinylic methyl group at C_6 which exist in 1. The exhaustive ^1H NMDR studies accomplished unequivocal characterization of all of the protons included in the bicyclic system 2a. The row C_2-C_1-C_9-C_8 was verified by the observation of a homoallylic coupling between H_2 and $H_8\alpha$ (J=2.5 Hz) and of an NOE on H_9 (17%) upon irradiation of H_{19}. The configurations of the protons attached to the carbon chain C_2-C_3-C_4 were established as β, α, and α respectively from their small vicinal coupling constants (J_{H_2,H_3}=∿0 Hz and J_{H_3,H_4}=2.0 Hz) and the W-coupling between H_2 and H_4 (J=0.8 Hz). Another W-coupling (J_{H_2,H_7}=2.5 Hz) supported the bicyclo[4,3,1]decane ring system including C_2 and C_7 at bridgehead positions. The presence of the side chain identical with that of 1 was evident from the MS fragments described above and the ^1H NMR data [δ 0.79 (3H, d, J=6.0 Hz), 1.61 and 1.69 (3H each, br s), and 5.15 (1H, ddqq, J=6.8, 6.8, 1.4, and 1.4 Hz)]. Observation of an NOE on H_{18} (∿6%) upon irradiation of $H_8\alpha$ suggested that the acetoxyl group at C_{18} was oriented to the side of the seven-membered ring. From the evidence outlined above, we proposed the structure 2 for fukurinal. This structure would be reasonable biogenetically if we assume that fukurinal is derived from a compound close to fukurinolal as illustrated in Scheme 1.

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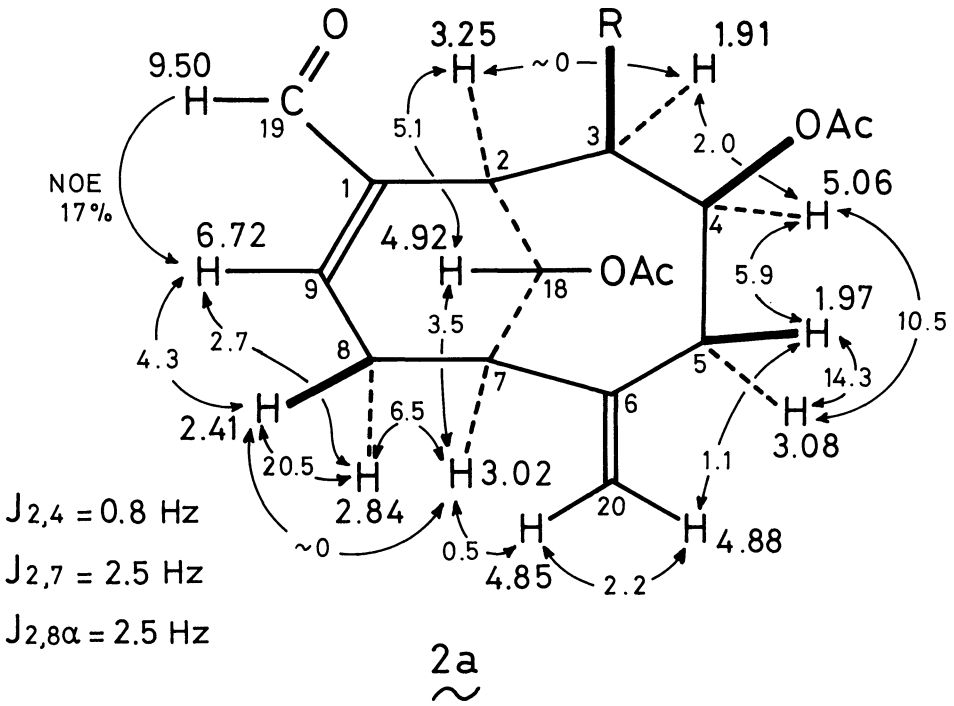
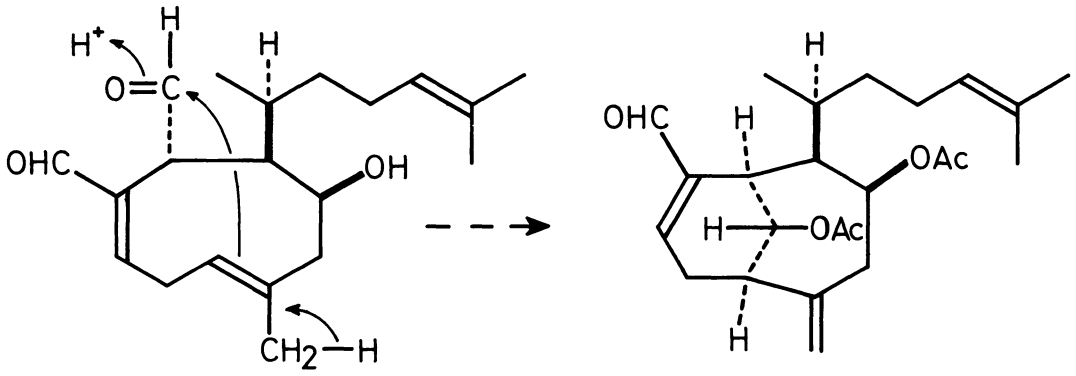


2a



Scheme 1

References

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2) M. Ochi, I. Miura, and T. Tokoroyama, *J. Chem. Soc., Chem. Commun.*, 1981, 100.

3) This compound has also been isolated independently from *Dictyota dichotoma*: Professor T. Matsumoto, Hokkaido University, private communication.

4) ^{1}H NMR (400-MHz, $CDCl_3$): δ 1.00 (3H, d, J=7.0 Hz, 17-H_3), 1.07 (1H, dddd, J= 13.5, 7.8, 7.5, and 7.5 Hz, 11-Ha), 1.22 (1H, dddd, J=13.5, 7.5, 7.5, and 5.9 Hz, 11-Hb), 1.56 and 1.66 (3H each, br s, 16- and 15-H_3), 1.84 (2H, m, 12-H_2), 1.97 (1H, br s, 3-H), 1.98 (6H, s, 20-H_3 and Ac), 2.08 (1H, dd, J=13.0 and 3.5 Hz, 5α-H), 2.32 (1H, ddq, J=7.8, 5.9, and 7.0 Hz, 10-H), 2.42 (1H, ddq, J=13.0, 3.5, and 1.0 Hz, 5β-H), 3.00 (1H, ddd, J=15.9, 8.6, and 1.6 Hz, 8α-H), 3.22 (1H, ddd, J=8.6, 7.0, and 1.4 Hz, 2-H), 3.35 (1H, ddd, J=15.9, 11.9, and 3.2 Hz, 8β-H), 4.26 (1H, dd, J=3.5 and 3.5 Hz, 4-H), 4.53 (1H, dd, J=10.5 and 8.6 Hz, 18-Ha), 4.64 (1H, dd, J=10.5 and 7.0 Hz, 18-Hb), 5.02 (1H, ddqq, J=7.0, 7.0, 1.4, and 1.1 Hz, 13-H), 5.23 (1H, ddq, J=11.9, 1.6, and 1.4 Hz, 7-H), 6.82 (1H, dd, J=8.6 and 3.2 Hz, 9-H), 9.32 (1H, d, J=1.4 Hz, 19-H); ^{13}C NMR (100-MHz, $CDCl_3$): δ 17.6 (C_{17}), 17.7 (C_{15}), 20.1 (C_{20}), 20.9 ($CO\underline{C}H_3$), 25.6 (C_{16}), 26.3 (C_{12}), 29.4 (C_8), 32.1 (C_{10}), 37.8 (C_2), 38.5 (C_{11}), 49.2 (C_5), 50.1 (C_3), 64.1 (C_{18}), 75.3 (C_4), 124.9 (C_7 and C_{13}), 131.4 (C_{14}), 138.1 (C_6), 150.7 (C_1), 156.7 (C_9), 170.7 ($\underline{C}OCH_3$), 195.9 (C_{19}).

5) S. C. Howell, S. V. Ley, and M. Mahon, *J. Chem. Soc., Chem. Commun.*, 1981, 507.

6) ^{1}H NMR (400-MHz, $CDCl_3$): δ 1.08 (3H, d, J=6.8 Hz, 17-H_3), 1.15 (1H, m, 11-Ha), 1.21 (1H, m, 11-Hb), 1.57 and 1.63 (3H each, br s, 16- and 15-H_3), 1.69 (1H, m, 10-H), 1.90 (3H, d, J=1.4 Hz, 20-H_3), ∿1.90 (2H, m, 12-H_2), 2.04 (1H, br s, 3-H), 2.18 (1H, dd, J=13.2 and 4.3 Hz, 5α-H), 2.33 (1H, dd, J=13.2 and 1.9 Hz, 5β-H), 2.96 (1H, ddd, J=17.6, 7.6, and 4.3 Hz, 8α-H), 3.21 (1H, dddd, J=17.6, 11.3, 2.2, and 2.2 Hz, 8β-H), 3.41 (1H, br d, J=7.8 Hz, 2-H), 4.10 (1H, dd, J= 9.7 and 7.8 Hz, 18β-H), 4.31 (1H, dd, J=4.3 and 1.9 Hz, 4-H), 4.46 (1H, dd, J= 9.7 and 1.6 Hz, 18α-H), 5.03 (1H, ddqq, J=7.3, 7.3, 1.4, and 1.4 Hz, 13-H), 5.32 (1H, ddq, J=11.3, 4.3, and 1.4 Hz, 7-H), 6.93 (1H, ddd, J=7.6, 2.2, and 2.2 Hz, 9-H); ^{13}C NMR (100-MHz, $CDCl_3$): δ 17.7 (C_{15}), 18.2 (C_{17}), 20.0 (C_{20}), 25.6 (C_{16}), 26.0 (C_{12}), 29.6 (C_8), 32.5 (C_{10}), 35.9 (C_2), 38.0 (C_{11}), 49.3 (C_5), 51.4 (C_3), 68.8 (C_{18}), 72.9 (C_4), 124.2 (C_7), 125.5 (C_{13}), 132.0 (C_{14}), 135.7 (C_1), 136.3 (C_6), 139.3 (C_9), 173.5 (C_{19}).

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