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BIOMIMETIC CYCLIZATION OF DICTYODIACETAL: THE STEREOCHEMISTRY OF FUKURINAL

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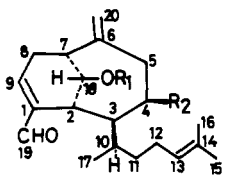
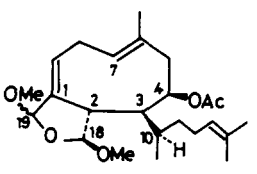
Diterpenoid constituents in brown algae of the Dictyotaceae family have been of current interest owing to their biological activities and unique structures (1,2). We determined the structure of acetylsanadaol (**1**), a component of *Pachydictyon coriaceum*, to possess a novel carbon skeleton (3,4). Biogenetically, compound **1** seems to be derived from dictyodial (**6**) (5), also a constituent of the same alga (6). We have shown that under a mild acidic condition, dictyodial was convertible into sanadaol (**2**) by transannular cyclization (3,4). Fukurinal, a diterpene, was recently isolated from *Dilophus okamurai*, with the same carbon skeleton as sanadaol (**2**) from spectroscopic analyses (7), but without data for the configuration at C-10. In our studies on acid-catalyzed cyclization of dictyodial derivatives (8), we have now synthesized fukurinal (**3**) from dictyodiacetal (**5**), a component of known stereochemistry (9). This transformation chemically establishes the complete stereochemistry of fukurinal (**3**).

On mild acid treatment, dictyodial (**6**) was converted into sanadaol (**2**) by transannular cyclization (3,4,8). Under the same conditions, dictyodiacetal (**5**) was not converted into a bicyclic compound but, instead, was hydrolyzed to a dialdehyde (**7**). On the other hand, treatment of dictyodiacetal with boron trifluoride etherate (10), for 30 min at room temperature, afforded three cyclization products, A (25%), B (8%), and C (5%).

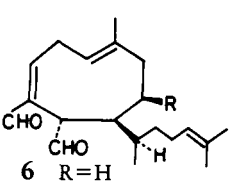
Compound A, $C_{22}H_{32}O_4$, was a colorless oil. Ir bands at 1735 and 1235 cm^{-1}, as well as the ^{1}H-nmr signals at δ 1.92 (3H, s) and 5.0 (1H, m), indicated that the acetoxyl group remained intact. Presence of an α,β-unsaturated aldehyde moiety was deduced from ir bands at 1695 and 1635 cm^{-1}, and also by ^{1}H-nmr signals at δ9.50 (1H, s, CHO) and 6.70 (1H, m, CH=C-CHO). Disappearance of one acetal (or aldehyde) group in dictyodiacetal (**5**) and the appearance of new signals at 4.96 (2H, s, $=CH_2$) and 3.88 (1H, m, CH-O) suggested that an intramolecular ene-type reaction occurred between the aldehyde and methyl vinyl groups afford-



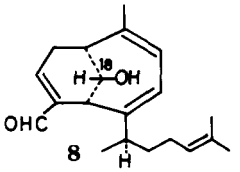
1 R_1=Ac, R_2=H (acetylsanadaol)
2 R_1=H, R_2=H
3 R_1=Ac, R_2=OAc (fukurinal)
4 R_1=H, R_2=OAc



5 (dictyodiacetal)



6 R=H
7 R=OAc



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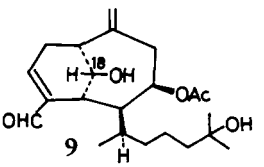

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ing a bicyclic compound **4**. *Acetylation* of compound **4** afforded an acetate **3** with ^{1}H- and ^{13}C-nmr properties identical in all respects to those reported for fukurinal (7). Thus, the configurations of fukurinal at C-2, -3, -4, and especially at C-10, have been established as identical with those of dictyodiacetal (**5**).[1]

Compound B, $C_{20}H_{28}O_2$, lacked an acetoxyl group and, instead, revealed a uv-absorption maximum at 258 nm due to a homodiene chromophore, confirmed by ^{1}H-nmr signals at δ 5.72 (1H, d, J=8 Hz; H-4) and 5.79 (1H, d, J=8 Hz; H-5). Furthermore, the ^{1}H-nmr spectrum exhibited a broad singlet ascribable to a highly deshielded olefinic methyl (CH_3-20) at δ 1.89, as well as signals due to an α,β-unsaturated aldehyde moiety at δ 9.40 (1H, s) and 6.72 (1H, bs). These data provide structure **8** for compound B. Configuration of the hydroxyl group at the newly formed chiral center C-18 was deduced from the coupling pattern of H-18 (δ 4.01, dd, J=6, 3.5 Hz).

Compound C, $C_{22}H_{34}O_5$, had an ^{1}H-nmr spectrum similar to compound **4**, except for the appearance of sharp singlets at δ 1.22 (3H) and 1.24 (3H) instead of olefinic methyl signals (1.64 and 1.70) as in bicyclic compound **4**. These properties suggested that the side chain olefinic bond was hydroxylated in compound C. A hydroxyl group at C-14 was confirmed by the fragment *m/z* 319 (M^+-C_3H_7O) in the mass spectrum of compound C, allowing the structure to be assigned as **9**. Configuration of C-18 was deduced from the coupling pattern of H-18 (δ 3.88, dd, J=5, 3 Hz) in the ^{1}H-nmr spectrum.

[1]Relative configurations of all the chiral centers of dictyodiacetal have been determined but not absolute configuration (9). Configuration at C-18 of sanadaol (**2**) was determined by means of lanthanide shift experiments. The coupling patterns of protons at C-3, -2, -18, and -7 of fukurinal (7) are coincident with those of sanadaol (3,4), determining the configuration of the new asymmetric carbon atom of fukurinal.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The nmr spectra were recorded in $CDCl_3$ and CCl_4 with TMS as internal standard, at 90 and 400 MHz; the ms were recorded at 70 eV.

REACTION OF DICTYODIACETAL (**5**) WITH BORON TRIFLUORIDE ETHERATE.—A 1% CH_2Cl_2 solution of boron trifluoride etherate was added to a CH_2Cl_2 solution of dictyodiacetal (8.7 mg) and allowed to stand for 30 min at room temperature. The reaction mixture was treated with H_2O and extracted with CH_2Cl_2 to obtain 6.1 mg of a crude product that was separated into components, A, B, and C by preparative tlc. Acetylation of compound A with Ac_2O and pyridine afforded fukurinal (**3**).

COMPOUND A (**4**).—Ir ν max (CCl_4) 1735, 1695, 1635, 1235 cm^{-1}; ms *m/z* (%) 360 (M^+, 1), 342 (M^+-18, 2), 300 (M^+-AcOH, 20), 218 (M^+-AcOH-C_6H_{10}, 56), 171 (26), 143 (20), 109 (29), 82 ($C_6H_{10}^+$, 100), 69 (14); ^{1}H nmr δ ($CDCl_4$, 90 MHz) 0.80 (3H, d, J=7, 17-Me), 1.64, 1.70 (each 3H, bs, 16-, 15-Me), 1.92 (3H, s, Ac), 3.88 (1H, m, 18-H), 4.96 (2H, s, 20-H_2), 5.0-5.4 (2H, m, 4-, 13-H), 6.70 (1H, m, 9-H), 9.50 (1H, s, 19-H).

COMPOUND B (**8**).—Uv λ max (EtOH) 229, 258 nm; ms *m/z* (%) 300 (M^+, 100), 143 (68), 82 (58), 69 (42); ^{1}H nmr δ ($CDCl_3$, 400 MHz) 1.02 (3H, d, J=6.5, 17-Me), 1.62, 1.67, 1.89 (each 3H, bs, 16-, 15-, 20-Me), 2.72 (3H, m, 7-H, 8-H_2), 3.70 (1H, bd, J=6, 2-H), 4.01 (1H, dd, J=6.0, 3.5, 18-H), 5.15 (1H, bt, J=7, 13-H), 5.72 (1H, d, J=8, 4- or 5-H), 5.79 (1H, d, J=8, 5- or 4-H), 6.72 (1H, bs, 9-H), 9.40 (1H, s, 19-H).

COMPOUND C (**9**).—Ms *m/z* (%) 360 (M^+-H_2O, 3), 343 (3), 300 (46), 218 (82), 189 (59), 176 (36), 109 (42), 82 (100), 69 (36); ^{1}H nmr δ ($CDCl_3$, 400 MHz) 0.79 (3H, d, J=7, 17-Me), 1.22, 1.24, 1.91 (each 3H, s) 15-, 16-Me, and Ac), 2.44 (1H, dd, J=20, 4, 8-H), 2.79 (1H, dm, J=20, 8-H), 2.85 (1H, m, 7-H), 3.08 (1H, dd, J=13, 10, 5-H), 3.17 (1H, bd, J=5, 2-H), 3.88 (1H, dd, J=5, 3, 18-H), 4.96 (2H, s, 20-H_2), 5.06 (1H, m, 4-H), 6.71 (1H, bs, 9-H), 9.50 (1H, s, 19-H).

FUKURINAL (**3**).—Ir ν max (CCl_4) 1730, 1695, 1635, 1230 cm^{-1}; ms *m/z* (%) 402 (M^+, 4), 342 (M^+-AcOH, 24), 282 (M^+-2AcOH, 18), 260 (M^+-2 AcOH-C_6H_{10}, 51), 200 (M^+-2 AcOH-C_6H_{10}, 39), 171 (33), 109 (36), 82 ($C_6H_{10}^+$, 100), 69 (15); ^{1}H nmr δ ($CDCl_3$, 400 MHz) 0.78 (3H, d, J=5.5, 17-Me), 1.61, 1.69 (each 3H, bs, 16-, 15-Me), 1.91, 2.07 (each 3H, s, Ac×2), 2.40 (1H, dd, J=20.9, 4.4, 8-H_b), 2.85 (1H, dm, J=20.9, 8-H_a), 3.02 (1H, m, 7-

H), 3.08 (1H, dd, J=14.3, 10.6, 5-H_a), 3.25 (1H, bd, J=5.1, 2-H), 4.85, 4.88 (each 1H, bs, 20-H_2), 4.92 (1H, dd, J=5.1, 3.6, 18-H), 5.06 (1H, m, 4-H), 5.15 (1H, bt, J=7, 13-H), 6.72 (1H, bs, 9-H), 9.50 (1H, s, 19-H).

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