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Amijitrienol and 14-Deoxyisoamijiol, Two New Diterpenoids from the Brown Seaweed *Dictyota linearis*

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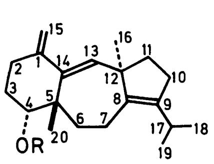
Synopsis. The structures of amijitrienol and 14-deoxyisoamijiol, two new diterpenoids isolated from the brown seaweed *Dictyota linearis*, have been established as **1** and **2** on the basis of spectral and chemical evidence.

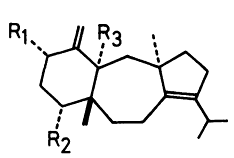
In previous papers, we have described the isolation of four diterpenoids of the dolastane class[1,2] and a unique member of the secodolastane class[3] from the brown seaweed *Dictyota linearis*. Our continuing search for the biologically active constituents of this alga has led to the isolation of two additional congeners, designated amijitrienol and 14-deoxyisoamijiol. In this note, a structural elucidation of these new compounds is presented. They were found to have a moderate antimicrobial activity against *Staphylococcus aureus* and *Mucor mucedo*.[4]

Amijitrienol (**1**), $C_{20}H_{30}O$, mp 129.0—129.5 °C, $[\alpha]_D^{18}$ +15.1° (*c* 0.09, EtOH), was isolated as fine needles in 0.0015% yield of fresh alga by conventional silica-gel column chromatography and preparative high-performance liquid chromatography. The IR, UV, and ^{1}H NMR spectra of **1** indicated the presence of one hydroxyl group [3440 cm^{-1}; δ=3.38 (1H, dd, J=3.0 and 3.0 Hz)], one conjugated diene [3080, 1640, and 890 cm^{-1}; 230 nm (ε=17000)], two tertiary methyl groups [δ=0.88 and 1.30 (3H each, s)], one isopropyl group [δ=0.93, 0.94 (3H each, d, J=6.8 Hz), and 2.64 (1H, qq, J=6.8 and 6.8 Hz)], and three olefinic protons [δ= 4.63 (1H, dd, J=2.6 and 2.6 Hz), 4.75 (1H, dd, J=2.6 and 2.1 Hz), and 5.81 (1H, s)]. In addition, the ^{13}C NMR data for **1** showed the presence of one fully-substituted double bond (δ=139.7 and 142.6), one tri-substituted double bond [δ=136.9 (s) and 138.8 (d)], and one exocyclic methylene group [δ=110.9 (t) and 150.5 (s)], together with two quaternary carbon atoms, one oxygen-bearing methine group, and six methylene groups. These facts suggested that **1** has a structure analogous to that of amijiol (**3**),[1] in which the allylic alcohol functionality in **3** is replaced by a C_{13}—C_{15} conjugated diene. This was confirmed by the chemical correlation of **1** with **3**. Thus, the acetylation of **1** with acetic anhydride and pyridine gave an acetate (**4**), which was found to be identical with the compound derived from **3** via the acetate (**5**)[1] by dehydration with phosphoryl chloride and pyridine.

14-Deoxyisoamijiol (**2**), $C_{20}H_{32}O$, mp 89.0—90.0 °C, $[\alpha]_D^{18}$−2.6° (*c* 0.09, EtOH), was obtained as fine needles in 0.0056% yield and displayed spectral data quite similar to that of 14-deoxyamijiol (**6**).[1] The 400 MHz ^{1}H NMR spectra of **2** and **6**, which were completely assigned by an extensive decoupling study and NOE measurements, were distinct from one another essentially only in the chemical shift of the methine proton on the oxygenated carbon atom [δ(**2**)—δ(**6**)=0.76 ppm]. This fact and the pertinent ^{13}C NMR data revealed that the hydroxyl group of **2** is attached to $C_{2\alpha}$ instead of $C_{4\alpha}$ in **6** and that the relationship of **6** to **2** corresponds to that of amijiol (**3**) to isoamijiol (**7**).[1] Consequently, 14-deoxyisoamijiol must be represented by structure **2**.



1 R=H
4 R=Ac



2 R_1=OH, R_2=R_3=H
3 R_1=H, R_2=R_3=OH
5 R_1=H, R_2=OAc, R_3=OH
6 R_1=R_3=H, R_2=OH
7 R_1=R_3=OH, R_2=H

Experimental

All the mps were determined on a Mitamura micromelting-point apparatus and are uncorrected. The IR and UV spectra were recorded on a JASCO model A-202 spectrophotometer and a Hitachi 340 spectrophotometer, respectively. The ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were taken on a Bruker WH-400 instrument in $CDCl_3$ solutions, with TMS as the internal standard. Mass spectra were recorded at 70 eV on a Finnigan MAT 312. A Union Gikken apparatus, model PM-101, was used for a measurement of the rotations. High-performance liquid chromatographic separation was performed on a Waters Associates HPLC model 6000A, with a TSK-GEL LS-410KG (ODS) column.

Isolation. Fresh alga (3.9 kg), collected in the Bay of Tosa in July 1982, was chopped up and extracted with methanol (10 l) for one week. The methanol solution was concentrated up to about 1.5 l and extracted with dichloromethane (0.5 l×3). The dichloromethane layer was washed with water, dried over Na_2SO_4, and evaporated to dryness. Then, the residue (42 g) was subjected to chromatography over silicic acid (800 g), eluting with hexane–ethyl acetate mixtures, ethyl acetate increasing from 10 to 50%. Elution with 20% ethyl acetate in hexane gave a fraction (506 mg) which was further purified by high-performance liquid chromatography (TSK-GEL LS-410KG, 80% MeOH in water) to obtain amijitrienol (**1**) and 14-deoxyisoamijiol (**2**).

Amijitrienol (1). The crude material was recrystallized from hexane to give white needles (59 mg); mp 129.0—129.5 °C, $[\alpha]_D^{18}$ 15.1° (*c* 0.09, EtOH); IR (nujol) 3440, 3080, 1640, and 890 cm^{-1}; UV (EtOH) 230 nm (ε=17000); ^{1}H NMR ($CDCl_3$) δ=0.88 and 1.30 (3H each, s, 20- and 16-H_3), 0.93 and 0.94 (3H each, d, J=6.8 Hz, 18- and 19-H_3), 2.64 (1H, qq, J=6.8 and 6.8 Hz, 17-H), 3.38 (1H, dd, J=3.0and 3.0 Hz, 4-H), 4.63

(1H, dd, J=2.6 and 2.6 Hz, 15-Ha), 4.75 (1H, dd, J=2.6 and 2.1 Hz, 15-Hb), and 5.81 (1H, s, 13-H); ^{13}C NMR ($CDCl_3$) δ=150.5 (C_1), 142.6 (C_8), 139.7 (C_9), 138.8 (C_{13}), 136.9 (C_{14}), 110.9 (C_{15}), 78.3 (C_4), 52.3 (C_{12}), 44.8 (C_5), 42.5 (C_{11}), 33.4 (C_2), 29.2 (C_3), 28.6 (C_6), 27.3 (C_{10}), 27.1 (C_{17}), 27.0 (C_{16}), 21.9 (C_7), 21.3 (C_{18}), 20.9 (C_{19}), and 20.5 (C_{20}); MS (70 eV) m/z 286 (M^+), 271 (M^+-CH_3), 253 (M^+−CH_3-H_2O), 243 (M^+−C_3H_7), and 225 (M^+−C_3H_7-H_2O). Found: m/z 286.2326. Calcd for $C_{20}H_{30}O$: M, 286.2297.

14-Deoxyisoamijiol (2). The crude substance was recrystallized from hexane to yield white needles (217 mg); mp 89.0—90.0 °C, $[\alpha]_D^{18}$−2.6° (c 0.09, EtOH); IR (nujol) 3260, 3080, 1640, and 890 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.64 and 1.11 (3H each, s, 20- and 16-H_3), 0.93 and 0.94 (3H each, d, J=7.0 Hz, 18- and 19-H_3), 1.08 (1H, ddd, J=13.1, 3.2, and 3.2 Hz, 4β-H), 1.33 (1H, ddd, J=14.6, 4.9, and 4.0 Hz, 6β-H), 1.45 (1H, dd, J=13.9 and 2.8 Hz, 13α-H), 1.54 (1H, dd, J=13.9 and 11.5 Hz, 13β-H), 1.58 (2H, m, 11-H_2), 1.75 (2H, m, 3-H_2), 1.86 (1H, ddd, J=14.6, 11.8, and 4.9 Hz, 6α-H), 1.91 (1H, ddd, J=13.1, 8.3, and 5.3 Hz, 4α-H), 2.13 (1H, ddddd, J=16.6, 4.9, 4.0, 1.5, and 1.5 Hz, 7α-H), 2.17 (2H, m, 10-H_2), 2.40 (1H, dddd, J=16.6, 11.8, 4.9, and 1.3 Hz, 7β-H), 2.61 (1H, qq, J=7.0 and 7.0 Hz, 17-H), 2.69 (1H, dddd, J=11.5, 2.8, 1.5, and 1.3 Hz, 14α-H), 4.28 (1H, dd, J=2.8 and 2.8 Hz, 2β-H), 4.67 (1H, dd, J=1.5 and 1.3 Hz, 15-Ha), and 4.97 (1H, dd, J=1.3 and 1.3 Hz, 15-Hb); ^{13}C NMR ($CDCl_3$) δ=153.8 (C_1), 140.2 (C_8), 139.0 (C_9), 109.8 (C_{15}), 74.3 (C_2), 50.1 (C_{12}), 42.1 (C_{13}), 41.2 (C_{11}), 41.1 (C_4), 40.5 (C_{14}), 39.4 (C_5), 36.6 (C_3), 30.2 (C_6), 27.4 (C_{10}), 26.8 (C_{17}), 24.1 (C_{16}), 21.9 (C_7), 21.1 (C_{18}), 20.9 (C_{19}), and 15.3 (C_{20}); MS (70 eV) m/z 288 (M^+), 273 (M^+−CH_3), 255 (M^+−CH_3-H_2O), 245 (M^+−C_3H_7), and 227 (M^+−C_3H_7-H_2O). Found: m/z 288.2459. Calcd for $C_{20}H_{32}O$: M, 288.2453.

Acetylation of 1. A solution of **1** (49 mg) in acetic anhydride (0.2 ml) and pyridine (0.8 ml) was allowed to stand at room temperature overnight and then worked up in the usual way. The product was subjected to chromatography using a Robar column (Merck, LiChroprep Si 60, size B) and 10% ether in hexane as the eluent to give an acetate (**4**) as a viscous oil (30 mg); IR ($CHCl_3$) 1738 and 1260 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.92 and 1.29 (3H each, s, 20- and 16-H_3), 0.92 and 0.94 (3H each, d, J=6.8 Hz, 18- and 19-H_3), 2.08 (3H, s, $COCH_3$), 2.63 (1H, qq, J=6.8 and 6.8 Hz, 17-H), 4.64 (1H, m, 15-Ha), 4.66 (1H, m, 15-Hb), 4.77 (1H, dd, J=3.0 and 2.0 Hz, 4-H), and 5.74 (1H, s, 13-H); ^{13}C NMR ($CDCl_3$) δ=170.9 ($\underline{C}OCH_3$), 150.3 (C_1), 142.7 (C_8), 139.7 (C_9), 137.1 (C_{13}), 136.7 (C_{14}), 111.0 (C_{15}), 80.1 (C_4), 52.2 (C_{12}), 43.3 (C_5), 42.5 (C_{11}), 32.8 (C_2), 29.8 (C_3), 29.4 (C_6), 27.2 (C_{10}), 27.0 (C_{17}), 26.9 (C_{16}), 21.8 (C_7), 21.4 ($CO\underline{C}H_3$ and C_{18}), 20.9 (C_{19}), and 20.5 (C_{20}); MS (70 eV) m/z 328 (M^+), 313 (M^+−CH_3), 285 (M^+−C_3H_7), 268 (M^+−AcOH), 253 (M^+−CH_3-AcOH), and 225 (M^+−C_3H_7-AcOH). Found: m/z 328.2404. Calcd for $C_{22}H_{32}O_2$: M, 328.2402.

Dehydration of 5. A mixture of **5** (80 mg) and $POCl_3$ (0.12 ml) in pyridine (0.6 ml) was stirred at room temperature for three days. The reaction mixture was worked up in the usual manner and the resulting product was chromatographed using a Robar column (LiChroprep Si 60, size B) and 10% ether in hexane as the solvent to yield a diene (30 mg) which was identified by TLC, IR, and ^{1}H NMR comparisons with **4**.

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References

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

4) Amijitrienol (**1**) and 14-deoxyisoamijiol (**2**) inhibited the growth of both *S. aureus* and *M. mucedo* at the concentration of 0.5 and 1.0 mg/disc respectively.