Crystal and molecular structure of 11α-methoxypuupehenol diacetate

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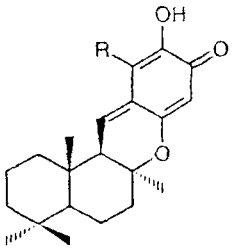
Puupehenone from the sea sponge *Dysidea sp.* was converted into 11α-methoxypuupehenol diacetate. The crystal and molecular structure of the title compound was established by X-ray diffraction analysis.

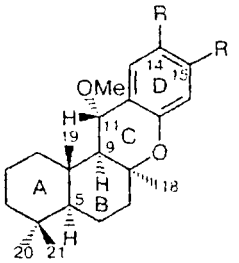
Key words: sea sponge, *Dysidea sp.*; 11α-methoxypuupehenol diacetate; crystal and molecular structure.

Puupehenone (**1**) was isolated for the first time from the sea sponge *Chondrosia chucalla*.[1] Its structure was established[1] based on the spectral characteristics and X-ray diffraction study of the ozonolysis product. The absolute stereochemistry of compoud **1** and biogenetically related metabolites[2–4] was established based on the chemical transformation of **1** into the known natural compound (−)-drimenol.[5]

Compound **1** and an insignificant amount of chloropuupehenone (**2**) were also isolated[6] from the Australian sea sponge *Dysidea sp.* It was demonstrated that compound **1** can undergo aromatization in alcoholic solutions.[7]



1: R = H
2: R = Cl



3a: R = OH
3b: R = OAc

Boiling of a solution of compound **1** in MeOH afforded methoxypuupehenol **3a**. With the aim of establishing the spatial structure of **3a**, its diacetate **3b** was studied by X-ray diffraction analysis.

The perspective view of molecule **3b** is shown in Fig. 1. The rings A and B of the isoprenoid portion of molecule **3b** are *trans*-fused and adopt a chair conformation. The conformations of these rings are distorted due to 1,3-diaxial interactions between the methyl groups and other substituents. The distortion of ring B is more pronounced. The endocyclic torsion angles at the C(5)—C(6) and C(8)—C(9) bonds are −62° and 42°, respectively. The C(5) and C(8) atoms deviate from the C(6)C(7)C(9)C(10) plane by −0.715 and 0.532 Å, respectively. The rings B and C are *cis*-fused. The epoxy ring adopts a C(8)α-envelope conformation. An analogous configuration of the fused rings was observed in ozonolysis product **1**.[1] The aromatic ring is planar. The deviations of the atoms from the plane of the ring were no more than twice the corresponding standard deviations. The C(9) atom deviates from the plane of the aromatic ring by 0.142(3) Å. The planar group consisting

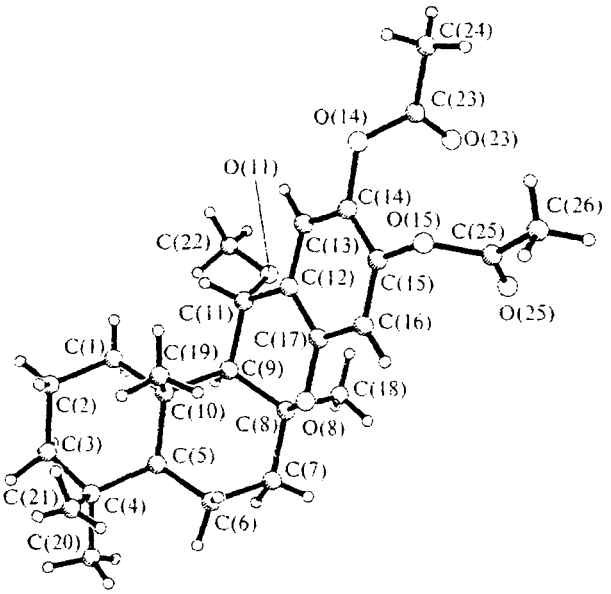


Fig. 1. Spatial structure of molecule **3b**.

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of the atoms of the rings C and D forms an angle of 130.6° with the mean plane of the A and B rings.

The acetoxy groups are located on one side of the plane of the aromatic ring, whereas the polycyclic system is located on the opposite side. This arrangement can be governed by the molecular packing in the crystal or by the effect of the spatially remote portion of the molecule on the direction of the addition of the acetyl groups. In the crystal, the molecules are linked to each other *via* the intermolecular C(24)—H...O(25)′ hydrogen bonds[8] (C...O, 3.33 Å; H...O, 2.40 Å; the position of the hydrogen atom was revealed from the difference electron density synthesis); the C—H bond length is 0.97 Å. An analogous direction of the addition of the acetyl groups was observed in isoavarol diacetate.[9] The inclination of the acetoxy groups to the plane of the aromatic ring is determined by the position, which is most suitable to conjugation between the lone electron pair and the orbital of the aromatic ring. The corresponding C(13)—C(14)—O(14)—C(23) and C(14)—C(15)—O(15)—C(25) dihedral angles are −108.6(4)° and −111.7(4)°, respectively. The orientation of the methoxy group is characterized by the C(9)—C(11)—O(11)—C(22) torsion angle of 96.0(4)°.

The data of ^{1}H NMR spectroscopy of compounds **3a** and **3b** agree with the results of X-ray diffraction analysis of diacetate **3b**. The spin-spin coupling constant is virtually absent for the H(11) and H(9) protons, which indicates that the dihedral angle between these protons is close to 90° and, consequently, the conformations of rings B and C in solutions are similar to those observed in the crystal (this angle is 93°).

Experimental

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WM-250 spectrometer with Me_4Si as the internal standard. The mass spectra were obtained on an LKB-9000S mass spectrometer with direct introduction of the sample into the ion source; the ionizing voltage was 70 eV. The optical rotation was measured on a Perkin—Elmer 141 polarimeter.

Extraction and chromatography. The sea sponge *Dysidea sp.* was collected in Australian coastal waters in 1989 in the course of the ninth trip of the "Academician Oparin" research ship. The lyophilized sponge (160 g) was extracted with CH_2Cl_2. The concentrated extract (0.8 g) was chromatographed on SiO_2 using a 10 : 1 CH_2Cl_2—EtOAc mixture and then on Sephadex LH-20 using a 3 : 1 CH_2Cl_2—$CHCl_3$ mixture as the solvent. TLC was carried out on Silufol plates using a 4 : 1 hexane—acetone solvent system. The fractions containing compound **1** were concentrated. In attempting to perform crystallization from hexane, an amorphous precipitate was obtained (the yield was 0.6 g).

Puupehenone (1), a bright-yellow amorphous compound. The spectral data are identical to those reported in the literature.[1] $[\alpha]_D$ +318° (*c* 0.55, CCl_4) (*cf.* Ref. 1: $[\alpha]_D$ +315° (*c* 1.64, CCl_4), lit. data[2]: $[\alpha]_D$ +297° (*c* 0.44, CCl_4), lit. data[5]: $[\alpha]_D$ +189° (*c* 1.08, CCl_4)).

Methoxypuupehenol (3a). A solution of compound **1** (43.2 mg, 0.15 mmol) in MeOH (30 mL) was refluxed for 24 h. After evaporation of the solvent, compound **3a** was obtained in a yield of 54 mg (100%), m.p. 136—138 °C (MeOH), $[\alpha]_D$ −41° (*c* 0.55, MeOH). Found (%): C, 73.20; H, 9.00. $C_{22}H_{32}O_4$. Calculated (%): C, 73.30; H, 8.95. UV (MeOH), λ_{max}/nm (ε): 215 (9076), 227 sh (5538), 300 (4707). ^{1}H NMR (MeOH-d_4), δ: 6.68 (s, 1 H, H(13)); 6.18 (s, 1 H, H(16)); 4.10 (s, 1 H, H(11)); 3.41 (s, 3 H, OCH_3); 1.55 (s, 1 H, H(9)); 1.19 (s, 3 H, C(18)H_3); 0.92 (s, 3 H, C(21)H_3); 0.83 (s, 3 H, C(20)H_3); 0.65 (s, 3 H, C(19)H_3); 1.00—1.20, 1.40—1.70, and 2.00 (m, 11 H, H(5), H(1), H(2), H(3), H(6), and H(7)). ^{13}C NMR (MeOH-d_4), δ: 148.6 (s); 147.5 (s); 140.1 (s); 117.1 (d); 115.3 (s); 104.6 (d); 75.8 (s); 75.1 (d); 56.2 (q); 56.3 (d); 54.9 (d); 43.0 (t); 42.0 (t); 41.1 (t); 38.1 (s); 34.2 (s); 34.2 (q); 27.9 (q); 22.5 (q); 19.5 (t); 19.5 (t); 15.0 (q). MS, *m/z*: 360 $[M]^+$.

11-Methoxypuupehenol diacetate (3b). A 1 : 1 Ac_2O—Py mixture (1 mL) was added to compound **3a** (36 mg, 0.1 mol). The reaction mixture was kept at ~20 °C for 3 h. After evaporation and crystallization from MeOH, compound **3b** was obtained in a yield of 44 mg (99%), m.p. 145—147 °C, $[\alpha]_D$ −52° (*c* 0.99, MeOH). Found (%): C, 70.16; H, 8.20. $C_{26}H_{36}O_6$. Calculated (%): C, 70.24; H, 8.16. UV (MeOH), λ_{max}/nm (ε): 220 (10666), 287 sh (4000). ^{1}H NMR ($CDCl_3$), δ: 6.79 (s, 1 H, H(13)); 6.32 (s, 1 H, H(16)); 4.09 (s, 1 H, H(11)); 3.47 (s, 3 H, OMe); 2.18 (s, 6 H, 2 OAc); 1.67 (s, 1 H, H(9)); 0.90—1.20, 1.40—1.70, and 1.90—2.15 (m, 11 H, H(5), H(1), H(2), H(3), H(6), H(7)); 1.21 (s, 3 H, C(18)H_3); 0.92 (s, 3 H, C(21)H_3); 0.83 (s, 3 H, C(20)H_3); 0.66 (s, 3 H, C(19)H_3). ^{13}C NMR ($CDCl_3$), δ: 168.4 (s); 167.7 (s); 151.9 (s); 142.2 (s); 135.3 (s); 124.2 (d); 121.8 (s); 111.7 (d); 75.8 (s);

Table 1. Atomic coordinates (×10^4) and equivalent isotropic thermal parameters (×10)

Atom	*x/a*	*y/b*	*z/c*	B_{eq}/Å^2
C(1)	−3858(4)	0	−1291(3)	62(1)
C(2)	−3401(5)	642(7)	−289(3)	91(1)
C(3)	−3331(5)	−880(7)	382(3)	96(1)
C(4)	−2500(5)	−2367(7)	211(3)	85(1)
C(5)	−2890(3)	−2939(6)	−837(2)	53(1)
C(6)	−2196(4)	−4482(6)	−1120(3)	63(1)
C(7)	−2904(4)	−5286(5)	−2018(3)	57(1)
C(8)	−3257(3)	−3995(5)	−2840(2)	42(1)
C(9)	−3761(3)	−2232(5)	−2554(2)	40(1)
C(10)	−3068(3)	−1435(5)	−1591(2)	43(1)
C(11)	−3944(3)	−910(5)	−3368(2)	41(1)
C(12)	−3024(3)	−1086(5)	−3972(2)	38(1)
C(13)	−3005(3)	117(5)	−4683(2)	43(1)
C(14)	−2156(3)	−42(5)	−5220(2)	44(1)
C(15)	−1328(3)	−1388(5)	−5055(2)	43(1)
C(16)	−1307(3)	−2592(5)	−4358(2)	45(1)
C(17)	−2160(3)	−2447(5)	−3802(2)	42(1)
C(18)	−4111(4)	−4880(6)	−3657(3)	64(1)
C(19)	−1866(4)	−603(6)	−1684(2)	58(1)
C(20)	−2672(6)	−3960(10)	833(3)	112(2)
C(21)	−1152(6)	−1890(10)	503(3)	123(2)
C(22)	−5988(4)	111(8)	−3800(3)	80(1)
C(23)	−2455(4)	890(6)	−6807(2)	62(1)
C(24)	−2075(5)	2260(7)	−7398(3)	86(1)
C(25)	−505(3)	−2780(6)	−6224(3)	53(1)
C(26)	450(4)	−2571(7)	−6753(3)	67(1)
O(8)	−2099(2)	−3663(3)	−3109(2)	47(1)
O(11)	−5125(2)	−1068(4)	−3980(2)	58(1)
O(14)	−2071(2)	1281(4)	−5887(2)	58(1)
O(15)	−451(2)	−1444(4)	−5594(2)	54(1)
O(23)	−2987(4)	−435(5)	−7072(2)	109(1)
O(25)	−1191(3)	−3978(5)	−6256(2)	100(1)

73.0 (d); 56.4 (q); 55.1 (d); 54.0 (d); 41.9 (t); 40.7 (t); 39.9 (t); 37.0 (s); 33.7 (q); 33.3 (s); 27.3 (q); 21.9 (q); 20.6 (2 q); 18.5 (t); 18.4 (t); 14.6 (q). MS, *m/z*: 444 $[M]^+$.

Crystallographic data for compound 3b: $C_{26}H_{36}O_6$, M = 444.57; a = 11.330(3), b = 7.555(2), c = 14.643(2) Å; β = 103.24(2)°; monoclinic system, space group $P2_1$; V = 1220.1 Å^3; Z = 2; d_{calc} = 1.21 g cm^{-3}; F(000) = 240; μ_{Mo} = 0.8 cm^{-1}.

The crystals were grown from a solution in EtOH. The X-ray data were collected on an automated Enraf-Nonius CAD-4 diffractometer (graphite monochromator, Mo-Kα radiation, λ = 0.71073 Å) at ~23 °C using the ω-θ scanning technique to θ = 28°. A total of 3149 independent reflections were measured of which 1841 reflections with $I > 3\sigma(I)$ were used in the refinement. Corrections for the Lorentz and polarization factors were applied. The structure was solved by the direct method and refined anisotropically by the full-matrix least-squares method to R = 0.046 (the hydrogen atoms were introduced in geometrically calculated positions). All calculations were carried out using the SDP-PLUS program package.[10]

The coordinates of the nonhydrogen atoms and their equivalent isotropic thermal parameters are given in Table 1. The bond lengths and bond angles in molecule **3b** are close to the corresponding standard values except for the short C(2)—C(3) and C(6)—C(7) bonds (1.503(5) and 1.503(4) Å, respectively) and the angles, which are increased due to 1,3-diaxial interactions between the methyl groups and other atoms. The maximum increase in the bond angle is observed for C(4)—C(5)—C(10) (to 117.1(2)°).

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