Stereochemistry Structure of Odonicin

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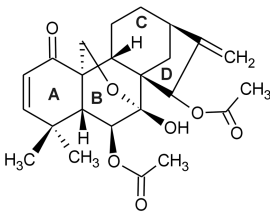
Ent-kaurene diterpenoids have various biological activities, such as antitumor, antibacterial, anti-HIV activities etc.[1-3] The plant of the genus *Isodon* used in Chinese traditional medicine[4] is a major source of compounds of this structural class.[5] Our investigations on the bitter diterpenoids constituents of the genus *Isodon* led to the first isolation of odonicin (**1**) from the leaves and tender branches of *Isodon henryi* obtained from Taibai Mountain, Shaanxi Province, P. R. China.[6]



(**1**)

Odonicin, an *ent*-kaurene type diterpenoid, was reported in 1973[7] as a new compound isolated from *Isodon japonicus.* Up to now, no direct evidence has been reported for the configuration, conformation and crystal structure of compound **1**. Herein, we present the stereochemistry characters of this compound on the basis of X-ray diffraction analysis.

The chemical structure of odonicin is 6β,15β-diacetoxy-7,20-epoxy-7β-hydroxy-*ent*-kaur-2,16-dien-1-one. The structure's character is presented clearly in Figure 1 as determined by X-ray diffraction analysis. The molecule of (**1**) consists of three six-membered rings A, B, C and one five-membered ring D. The bond lengths O2-C1, C1-C2 and C2-C3 are 1.214(3), 1.455(5) and 1.326(4) Å. The bond angles of O2-C1-C10, C2-C1-C10, C1-C2-C3, C2-C3-C4 and C3-C4-C5 are 120.7(3)°, 118.1(2)°, 122.2(3)°, 122.8(3)° and 107.5(2)°, respectively. These values indicate that the C1, C2 and C3 are in sp^2 hybrid, the C1, C2, C3, C4, C10 are in a common plane, and the C5 rises from the common plane. In addition, a conjugate system of α,β-unsaturated ketone exists in ring A, and ring A approximates a boat conformation. Ring B, fused with ring A in anti-form, is in a boat conformation due to the presence of 7,20-epoxy bond. The acetoxyl group at C6 and hydroxyl at C7 are in β-orientations. Ring C fuses with ring B in *cis*-form and adopts a boat conformation. Ring D is in an envelope conformation, the C14 α-oriented from the common plane of C8, C15, C16 and C13. An acetoxyl group is at C15 in β-orientation. The bond angles of 124.8(3)° (C17-C16-C15), 127.8(3)° (C17-C16-C13), 107.3(2)° (C15-C16-C13) and the bond length of 1.319(5) Å (C16-C17) show the C16 and C17 are sp^2 hybrid and an exo-methylene attaches at C16. The bond angle of 97.4(2)° (C15-C8-C14) and the bond angles at C16 diverge the normal bond angles of Csp^3 and Csp^2, which leads to the torsion angles at C8 and C16 and a bigger tensile force in ring D. Previous studies on *ent*-kaurene type diterpenoids indicated their various biological activities[8,9] can be attributed to the chemical activity of ring D and exo-methylene, which opens ring D and shows the addition reaction of C=C when it interacts with a biological substance.[10] The structure character of (**1**) suggests its biological activity.

In the crystal packing of compound **1**, molecules arrange as illustrated in Figure 2. The crystal of **1** is a monoclinic crystal system. Space group: $P2_1$. Accurate lattice constants: a = 9.965(1) Å, b = 11.212(1) Å, c = 10.636(3) Å, α= 90°, β = 113.50°, γ = 90°. F(000): 460. Cell volume: 1089.8(2) $Å^3$, Z=2. Extinction coefficient: 0.024(3). Two intermolecular hydrogen bonds are present between the hydroxyl H atom at C7 and the carbonyl O atom of the acetoxyl group at C15, the hydroxyl O atom at C7 and the methyl H atom of

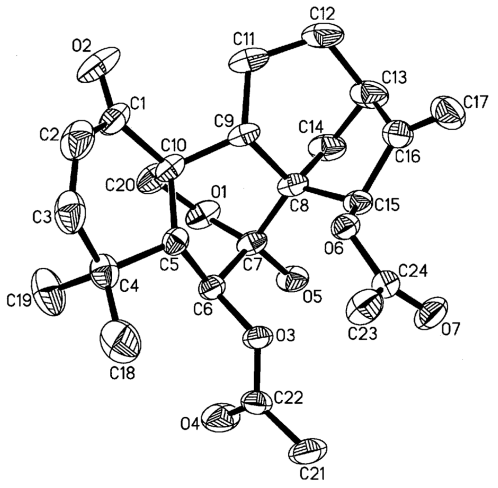


Figure 1. Molecular structure of odonicin. H atoms have been omitted for clarity.

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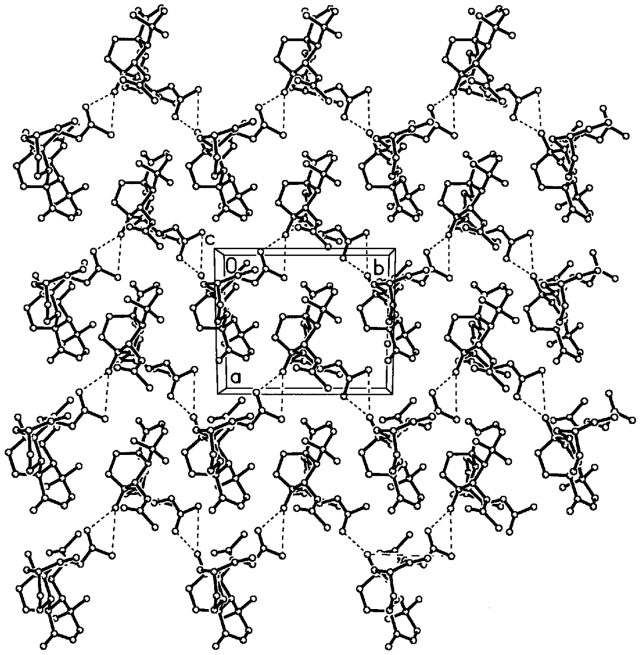

Figure 2. Crystal packing of odonicin.

the acetoxyl group at C15, with H···O separations of 2.861(3) and 3.298(3) Å, respectively. The molecules arrange in a one-dimension structure along the b axis in the crystal resulting from the intermolecular hydrogen bonds.

Experimental Section

General Methods. The ^{13}C NMR spectrum of compound **1** was recorded on a Bruker Avance-DMX500 instrument. Chemical shift values δ are given in ppm using TMS as the internal standard. IR spectrum was recorded in KBr pellet on a 170SX FT-IR instrument. X-ray diffraction analysis was performed on a Siemens P4 four-circle diffractometer.

Extraction and isolation. The dried powdered leaves and new branches of *Isodon henryi* (5.0 kg) were extracted with 95% EtOH (15 L × 3) at room temperature for 7 days. After removal of the solvent in vacuo, the residue was suspended in H_2O and extracted with petroleum ether (3 L × 3) and EtOAc (3 L × 3), respectively. The EtOAc extract (122 g) was subjected to column chromatography on silica gel (2 kg, 200-300 mesh) and eluting with gradient mixtures of $CHCl_3$ and Me_2CO ($CHCl_3$/Me_2CO: from 10 : 0 to 0 : 10) to afford the crude compound (**1**). Final purification was accomplished by silica column chromatography to yield (**1**) (113 mg, 0.0023%). Colorless prism crystals were obtained from a solution of the compound in methanol by slow evaporation at room temperature.

Odonicin (1). $C_{24}H_{30}O_7$, IR ν (cm^{-1}): 3447, 2962, 2839, 2867, 1730, 1663, 1377, 1257, 1230, 1143, 1062. ^{13}C NMR ($CDCl_3$) δ (ppm): 197.0 (C-1), 127.9 (C-2), 159.3 (C-3), 35.5 (C-4), 50.8 (C-5), 74.7 (C-6), 96.4 (C-7), 51.3 (C-8), 42.4 (C-9), 46.5 (C-10), 17.5 (C-11), 31.7 (C-12), 35.3 (C-13), 26.0 (C-14), 74.0 (C-15), 157.3 (C-16), 109.4 (C-17), 29.6 (C-18), 24.7 (C-19), 65.3 (C-20), 173.4, 170.2, 21.0, 21.6 (2 × AcO-). Data collection and structure determinations of X-ray diffraction analysis are listed in Table 1. Some selected bond lengths and angles are listed in Table 2. Crystallographic data have been deposited with the Cambridge Crystallographic Data Center. CCDC deposition number is 220128.

Table 1. Data collection and structure refinement for odonicin*

Empirical formula	$C_{24}H_{30}O_7$
Formula weight	430.48
Temperature	295(2) K
Wavelength	0.71073 Å
Density (calculated)	1.312 Mg/m^3
Absorption coefficient	0.096 mm^{-1}
Crystal size	0.54 × 0.46 × 0.46 mm
θ range for data collection	2.09° to 28.49°
Limiting indices	$0 \le h \le 13$, $0 \le k \le 15$, $-14 \le l \le 13$
Reflections collected	3164
Independent reflections	2898 (R_{int} = 0.0109)
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2898 / 2 / 289
Goodness-of-fit on F^2	0.940
Final R indices [$I > 2\sigma(I)$]	R1=0.0399, wR2=0.0877
R indices (all data)	R1=0.0589, wR2=0.0945
Absolute structure parameter	1.2(11)
Largest diff. peak and hole	0.179 and -0.145 e $Å^{-3}$

*$(\Delta/\sigma)_{max}$ = 0.00, w = $1/[\sigma^2(F_o^2) + (0.0534P)^2]$, where P = $(F_o^2 + 2F_c^2)/3$. 25 Reflection determined crystal cell ($2.89 < \theta < 14.96$), crystal structure was obtained by direct method. The H atom of O5 was synthesized by residual quantity fourier, and data for other H atoms were obtained from theoretical calculations. Siemens SHELXTL 5.10 program was used for all calculation.

Table 2. Selected geometric parameters (Å, °) for odonicin

O2-C1	1.214(3)	C13-C14	1.534(4)
C1-C2	1.455(5)	C13-H13	0.9800
C1-C10	1.524(3)	C15-C16	1.509(3)
C2-C3	1.326(4)	C16-C17	1.319(5)
C2-H2	0.9300	C8-C14	1.544(3)
C3-C4	1.501(4)	C8-C15	1.534(4)
C3-H3	0.9300	C17-H17A	0.9300
C4-C18	1.527(5)	C17-H17B	0.9300
C13-C16	1.524(5)		
O2-C1-C2	121.2(3)	C7-C8-C14	110.9(2)
O2-C1-C10	120.7(3)	C15-C8-C9	110.7(2)
C2-C1-C10	118.1(2)	C16-C13-C14	102.1(2)
C3-C2-C1	122.2(3)	C13-C14-C8	101.1(2)
C3-C2-H2	118.9	C16-C15-C8	103.0(2)
C1-C2-H2	118.9	C17-C16-C15	124.8(3)
C2-C3-C4	122.8(3)	C17-C16-C13	127.8(3)
C2-C3-H3	118.6	C15-C16-C13	107.3(2)
C4-C3-H3	118.6	C16-C17-H17A	120.0
C15-C8-C7	117.62(18)	C16-C17-H17B	120.0
C15-C8-C14	97.4(2)	H17A-C17-H17B	120.0

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