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Crystal Structure of ent-7a, 18-Diacetoxykaur-16-ene (Epicandicandioldiacetate)

The title compound (C₂₄H₃₆O₄) crystallizes in the orthorhombic space group P2₁2₁2₁, with a=6.250(1) Å, b=13.676(1) Å, c=25.419(2) Å, V=2172.7(1) Å³, Z=4, D_x=1.19 g.cm⁻³. The structure was solved by direct methods and refined by full-matrix least-squares method (R=0.076). The title molecule is an *ent*-kaurene diterpene containing two acetoxy groups at positions C7 and C18, The ring junction A-B is in *trans*, while B-C is in *cis*. The rings A and B have chair conformations, while ring C has a twist conformation but the conformation of ring D is nearer to an envelope.

Keywords: *ent*-kaurene, diterpene, epicandicandioldiacetate, *Sideritis sipylea* Boiss, crystal structure, diacetoxykaur-16-ene

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1. Introduction

During the last decade, *ent*-kaurene diterpenes have been studied in the identification of new-HIV and antitumor agents (GUSTAFSON et al., 1991), biological-activity research (LOBITZ et al., 1997) and microbiological transformation reactions (HANSON & WILLIS, 1992).

Epicandicandiol, which is an important diterpene in phytochemistry, is used in the microbiological transformation reactions of some diterpenoids by *Gibbrella Fujikuroi* (FRAGA et al., 1994; HANSON & WILLIS, 1992; DIAZ et al., 1989). Although there are a lot of reports about the spectroscopic studies of *ent*-kaurenes, only a very limited number of reports on the crystallographic researches of them are observed in the literature.

Sideritis sipylea Boiss is distributed in western and southern Anatolia. The extract of aerial parts of this plant with petroleum (40-60 °C) was chromatographed [silica gel (Merck, 70-230 mesh)] and several diterpenes were obtained. Between these epicandicandiol was eluted with hexane-diethylether-methanol (3:6:1) mixture. The title compound was synthesized by pyridine-Ac₂O treatment of epicandicandiol. It was re-crystallized from light-petroleum, m.p. 124 °C, [α]_D²²=-10.8 (c=1.0 CHCl₃)

2. Experimental

All X-ray measurements were made at 298 K on an Enraf Nonius CAD-4 diffractometer with graphite monochromated CuK_α radiation (λ=1.54184 Å) operating in ω/2θ scanning mode using a single crystal suitable for data collection. Accurate lattice parameters were

determined from least-squares refinement of the setting angles of 25 well-centered reflections in the range $23^\circ \leq \theta \leq 43^\circ$. During data collection, three standard reflections periodically observed showed no significant intensity variation. The ranges of h, k, l are $0 \leq h \leq 7$, $-17 \leq k \leq 0$, $0 \leq l \leq 31$. 2554 unique reflections were measured. The final cycle of full-matrix least-squares refinement was based on 1605 observed reflections ($I > 3\sigma(I)$) and 253 variable of parameters. The refinement was performed based on (F) against all reflections. Corrections for Lorentz-polarization factors and absorption were applied to the intensity values. Table 1 shows the crystal and experimental data.

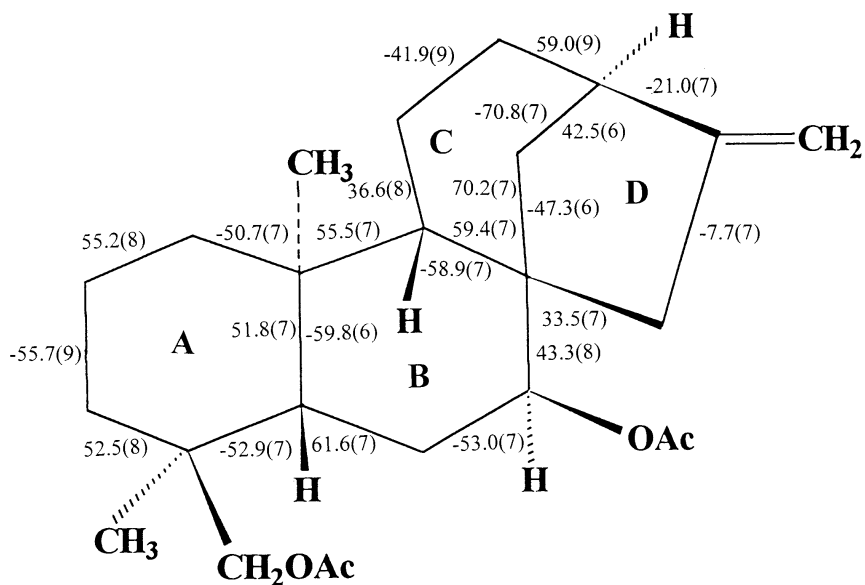


Fig. 1: Chemical structure of the title compound with the endocyclic torsion angles ($^\circ$).

Table 1: Crystal data for the title compound

Crystal morphology	colorless, rod-shaped
Crystal dimensions (mm)	0.20 x 0.25 x 0.30
Chemical formula	$C_{24}H_{36}O_4$
Molecular weight (g/mol)	388.55
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Lattice parameters	
a	6.250(1) Å
b	13.676(1) Å
c	25.419(2) Å
Volume(Å ³)	2172.7(1)
Number of formula units Z	4
Calculated density D_x (g.cm ⁻³)	1.19

Absorption coefficient (cm ⁻¹)	0.59
Absorption corrections (T _{min} , T _{max})	0.872, 0.998
2θ _{max}	148.7°
Overall data measured	2583
Unique data measured	2554 (R _{int} =0.025)
Observed data	1605 (I>3σ(I))
R	0.076
w	1/[σ ² (F _o)+(0.02 F _o) ² +1]
wR	0.077
No. of parameters refined	253
Program system	MoLEN (FAIR, 1990)

Table 2: Final atomic coordinates for non-hydrogen atoms and equivalent isotropic thermal parameters (Å²)

Atom	X	Y	z	B _{eq}
O1	0.647(1)	0.4791(6)	0.3109(3)	13.4(2)
O2	0.7544(8)	0.5748(4)	0.2475(2)	5.1(1)
O3	0.721(1)	0.2645(4)	0.1748(2)	9.4(2)
O4	0.8569(8)	0.3926(3)	0.1330(2)	4.5(1)
C1	0.736(1)	0.7231(4)	0.0875(3)	4.3(1)
C2	0.639(1)	0.7897(5)	0.1284(3)	5.3(2)
C3	0.630(1)	0.7425(5)	0.1818(3)	4.9(2)
C4	0.511(1)	0.6448(5)	0.1821(3)	4.3(1)
C5	0.608(1)	0.5799(4)	0.1393(2)	3.7(1)
C6	0.514(1)	0.4757(5)	0.1360(3)	4.5(2)
C7	0.655(1)	0.4058(5)	0.1038(2)	4.3(1)
C8	0.710(1)	0.4437(5)	0.0499(2)	3.8(1)
C9	0.771(1)	0.5534(4)	0.0518(2)	3.6(1)
C10	0.624(1)	0.6229(4)	0.0829(2)	3.7(1)
C11	0.820(1)	0.5884(5)	-0.0071(2)	4.5(2)
C12	0.684(1)	0.5457(5)	-0.0498(3)	5.4(2)
C13	0.644(1)	0.4367(5)	-0.0427(3)	5.3(2)
C14	0.533(1)	0.4215(5)	0.0105(2)	4.6(2)
C15	0.894(1)	0.3831(5)	0.0259(3)	5.1(2)
C16	0.860(1)	0.3873(5)	-0.0324(3)	5.2(2)
C17	1.000(2)	0.3560(6)	-0.0691(3)	7.3(2)
C18	0.534(1)	0.5993(6)	0.2361(3)	5.1(2)
C19	0.265(1)	0.6608(7)	0.1771(3)	6.1(2)
C20	0.408(1)	0.6396(5)	0.0570(3)	4.7(2)
C21	0.789(1)	0.5157(6)	0.2866(3)	6.5(2)
C22	1.020(1)	0.5020(7)	0.2991(3)	8.0(2)
C23	0.870(2)	0.3172(5)	0.1655(3)	5.7(2)
C24	1.089(1)	0.3029(6)	0.1854(3)	6.8(2)

$$B_{eq} = 8/3 \cdot \pi^2 [U_{11}(aa)^2 + U_{22}(bb)^2 + U_{33}(cc)^2 + 2U_{12}aa^*bb^* \cos\gamma + 2U_{13}aa^*cc^* \cos\beta - 2U_{23}bb^*cc^* \cos\alpha]$$

3. Structure analysis

The structure was solved by direct methods. (SHELDRICK, 1990 (SHELXS86)), expanded using Fourier techniques (FAIR, 1990 (MoLEN)), and refined on (F) by full-matrix least-squares methods. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were assigned based on expected geometry and a riding model was used during the refinement process. The final atomic parameters are listed in Table 2, and the molecular geometries for the non-H atoms are given in Tables 3 and 4, respectively. The chemical structure of the title compound with the endocyclic torsion angles are represented in Fig. 1. An ORTEP drawing of the molecular structure with atom numbering is shown in Fig. 2.

4. Discussion

The physical and spectroscopic properties of the title compound were identical with those reported in the literature (GONZÁLEZ et al., 1973; FRAGA et al., 1987) The structure analysis of epicandicandiol-diacetate (Fig. 2) was undertaken in order to understand the effects of the two acetoxy groups at positions 7 and 18 on the geometry of the kaurene skeleton, and to compare the obtained results with those of previously reported diterpenes. The endocyclic torsion angles (Fig. 1) have opposite signs except of C8-C9 bond with respect to the corresponding ones in linearol (HÖKELEK et al., 1999).

Table 3: Bond lengths (Å)

O4-C7	1.475(8)	C10-C20	1.519(9)
O4-C23	1.324(8)	C2-C1	1.51(1)
C7-C14	1.506(9)	C2-C3	1.502(9)
C7-C6	1.537(9)	C23-O3	1.20(1)
O2-C18	1.448(9)	C23-C24	1.47(1)
O2-C21	1.30(1)	C11-C12	1.50(1)
C9-C8	1.550(9)	C12-C13	1.52(1)
C9-C10	1.541(9)	C14-C13	1.53(1)
C9-C11	1.601(8)	C4-C3	1.53(1)
C5-C10	1.552(8)	C4-C19	1.55(1)
C5-C4	1.530(9)	C15-C16	1.50(1)
C5-C6	1.546(9)	C13-C16	1.53(1)
C8-C15	1.54(1)	C16-C17	1.35(1)
C8-C14	1.519(9)	C21-O1	1.19(1)
C10-C1	1.544(9)	C21-C22	1.49(1)
C18-C4	1.514(9)		

The ring junction A-B is in *trans* while B-C is in *cis* configuration. The rings A and B have chair conformations, while ring C has a twist conformation but the conformation of ring D is nearer to an envelope. Ring C is especially distorted. The puckering parameter of ring D, the angle between the planes C14-C13-C16-C15 and C14-C8-C15 is 41.3(5)°. The corresponding puckering parameter was 40.6(3)° in *ent-3b*, **7a**-dihydroxy-18-acetoxykaur-16-ene (linearol) (HÖKELEK et al., 1999). The close intramolecular distances; C19...C20 3.195(6), C14...C20 3.302(5), O4...H51 2.129 and O2...H51 2.762 Å may be effective on the conformation of the kaurene skeleton, as discussed by Karle, for the structure of (-)-kaur-15-en-19-al (KARLE, 1972). The Flack absolute structure parameter (FLACK, 1983) was refined;

expected values are 0 for the correct and +1 for the inverted absolute structure. The refined value is $-0.24(63)$, (SHELXL97 (SHELDRICK, 1997)). Since the large e.s.d. means that the assignment is not unambiguous, the absolute structure can not be determined reliably.

Table 4: Bond angles ($^{\circ}$)

C7-O4-C23	117.4(6)	C7-C8-C14	111.4(5)
O4-C7-C8	107.8(5)	C9-C8-C15	110.4(5)
O4-C7-C6	107.4(5)	C9-C8-C14	113.2(5)
C8-C7-C6	113.7(5)	C4-C8-C14	109.1(5)
C18-O2-C21	117.0(6)	C9-C10-C5	106.2(5)
C8-C9-C10	117.7(5)	C9-C10-C1	108.4(5)
C8-C9-C11	107.8(5)	C9-C10-C20	113.6(5)
C10-C9-C11	114.1(5)	C5-C10-C1	107.2(5)
C10-C5-C4	117.5(5)	C5-C10-C20	113.7(5)
C10-C5-C6	108.8(5)	C1-C10-C20	107.6(5)
C4-C5-C6	114.8(5)	C1-C2-C3	112.2(6)
C7-C8-C9	111.1(5)	C9-C11-C12	117.1(6)
C7-C8-C15	110.1(5)	C11-C12-C13	112.8(6)
C10-C1-C2	113.8(6)	C5-C4-C18	111.6(6)
O2-C18-C4	111.5(5)	C5-C4-C3	108.0(5)
O4-C23-O3	123.1(8)	C5-C4-C19	114.7(6)
O4-C23-C24	111.9(7)	C18-C4-C3	108.5(6)
O3-C23-C24	124.9(7)	C18-C4-C19	103.0(6)
C3-C4-C19	110.8(6)	C8-C15-C16	105.2(6)
C7-C6-C5	112.5(5)	C8-C14-C13	103.0(6)
O2-C21-O1	122.4(8)	C12-C13-C14	108.1(6)
O2-C21-C22	113.6(7)	C12-C13-C16	108.1(7)
O1-C21-C22	123.9(8)	C14-C13-C16	100.8(6)
C2-C3-C4	113.5(6)	C15-C16-C13	108.1(6)
C15-C16-C17	125.3(8)	C13-C16-C17	126.5(7)

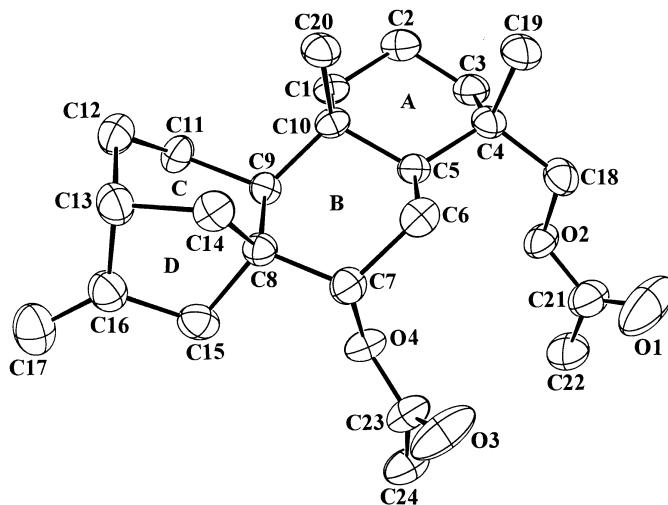


Fig. 2: An ORTEP drawing of the title compound with 50% probability ellipsoids and the numbering system.

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