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ent-7*α*,18-Hydroxykaur-16-ene ethanol solvate

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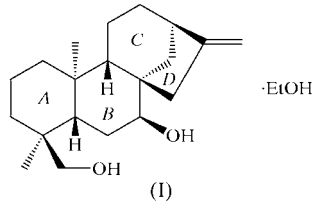
The *ent*-kaurene diterpene in the title compound, 7-epicandicandiol ethanol solvate, $C_{20}H_{32}O_2\cdot C_2H_6O$, was isolated from the aerial parts of *Sideritis ozturkii* Aytaç & Aksoy. The molecule has the usual conformation and stereochemistry found in related *ent*-kaurene derivatives. The methyl-substituted ring junction has a *trans* arrangement and the other junction is *cis*. The six-membered rings have chair or slightly distorted chair conformations and the five-membered ring has an envelope conformation. Intermolecular hydrogen bonds link the 7-epicandicandiol and ethanol molecules into two-dimensional networks, part of which comprise co-operative O—H···O—H···O—H··· chains.

Comment

The genus *Sideritis* L., of which 46 species are found in Turkey (Huber-Morath, 1982; Davis *et al.*, 1988; Aytaç & Aksoy, 2000; Duman, 2000), is recognized as a rich source of biologically active diterpenoids and flavonoids. Our previous chemical studies of the aerial parts of a local endemic species, *Sideritis ozturkii* Aytaç & Aksoy, led to the isolation of *ent*-kaurene-type diterpenoids and flavonoids, as well as phenylethanoid glycosides. Among these, two diterpenes were identified on the basis of their spectroscopic data (MS, and one- and two-dimensional NMR) as the known compounds linearol and 7-epicandicandiol (Şahin *et al.*, 2004, 2005). The crystal structure of linearol has been reported previously (Ergin *et al.*, 1993; Hökelek *et al.*, 1999), although in the latter report the inverse enantiomer was employed for the structure refinement model and the chemical diagram shows the incorrect stereochemistry at atom C4. The crystal structure of 7-epicandicandiol, (I), reported here, was determined in order to confirm the stereochemistry and molecular structure of the compound.

The molecular structure of compound (I) is shown in Fig. 1. The compound crystallizes from ethanol as the 1:1 ethanol solvate. All bond lengths and angles fall within normal ranges. The absolute configuration has not been determined, but was assigned to correspond with that usually depicted for



(I)

7-epicandicandiol and related *ent*-kaurenes. The crystal structures of 57 kaurene derivatives are reported in the Cambridge Structural Database (CSD; Release 5.27 with January 2006 updates; Allen, 2002). Of these, only the structure of (4*α*)-kaur-16-en-18-carbonyl 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranoside (Mora *et al.*, 2004) represents a definitive absolute configuration determination because of the known configuration of the *α*-D-glucopyranoside substituent. It is assumed that this structure establishes the absolute configuration of the core of this class of compounds. Although the configuration at the glucopyranoside-substituted C atom is opposite to that of the corresponding C atom in (I) and the hydroxy group at the 7-position is absent, the configurations of the remainder of the stereogenic centres correspond with those hitherto depicted for *ent*-kaurenes and also with those in (I).

The reported crystal structures of compounds most similar to (I) are those of epicandicandiol diacetate (*ent*-7*α*,18-diacetoxykaur-16-ene), which was synthesized directly from epicandicandiol (Hökelek *et al.*, 2001), methyl *ent*-7*α*-hydroxykaur-16-en-19-oate (Le Quesne *et al.*, 1985; Baynham *et al.*, 1988) and (−)-*ent*-3*β*,7*α*-dihydroxy-18-acetoxykaur-16-ene (linearol; Ergin *et al.*, 1993; Hökelek *et al.*, 1999). The ring conformations in each of these structures are very similar to those observed in the structure of (I). The ring junction *A*–*B* in (I) is *trans*, while *B*–*C* is *cis* (see scheme). Rings *A* and *B* have

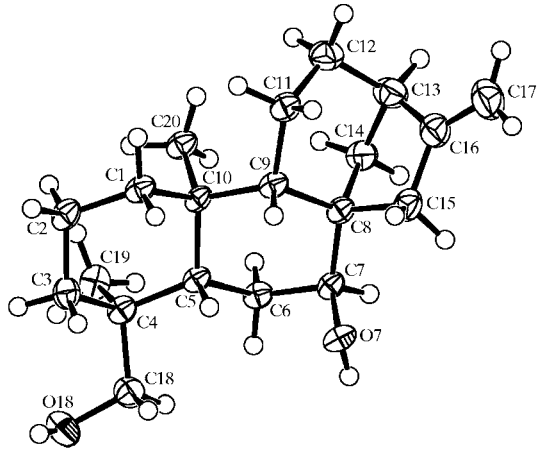


Figure 1
A view of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by circles of arbitrary size.

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almost normal chair conformations, with ring *B* being the more distorted, as shown by the puckering parameter, θ (Cremer & Pople, 1975), which has values of 176.7 (3) and 167.3 (3)° for the atom sequences C1–C5/C10 and C5–C10, respectively. The hydroxymethyl substituent at C4 in ring *A* lies in an equatorial position, while the hydroxy substituent at C7 in ring *B* adopts an axial position. The conformation of ring *C* is that of a slightly more twisted chair, as a result of atoms C8, C13 and C14 also being part of the five-membered ring. For ring *C*, the puckering parameter *Q* is 0.631 (3) Å, θ is 23.7 (3)° and φ_2 is 287.8 (8)° for the atom sequence C8/C9/C11–C14. The five-membered ring, *D*, has an envelope conformation, with atom C14 as the envelope flap and a value for the φ_2 puckering parameter of 29.4 (4)° for the atom sequence C8/C14/C13/C16/C15. Atom C14 lies 0.687 (3) Å from the plane defined by the remaining four atoms of the ring.

It has been noted previously (Karle, 1972) that steric crowding of the methyl substituent at the *A*–*B* ring junction by other substituents in axial or pseudo-axial positions, namely atoms C12, C14 and C19 in (I), causes convex buckling of the molecular plane so as to allow these substituents more room. Similar to the observations of Karle and the corresponding intramolecular distances quoted for the above-mentioned related compounds, the buckling has relieved the crowding at C20 in (I) and there are no intramolecular distances involving C20 that are less than 3.2 Å [C19···C20 = 3.214 (4) Å].

The H atom of the hydroxy substituent on the central six-membered ring, *B*, forms an intermolecular hydrogen bond with the O atom of the solvent ethanol molecule (Table 1). In turn, the hydroxy H atom of the ethanol molecule forms an intermolecular hydrogen bond with the O atom of the hydroxymethyl substituent in ring *A* of a different neighbouring 7-epicandicandiol molecule. These two interactions link the ethanol and 7-epicandicandiol molecules in an alternating fashion into extended chains which run parallel to the [100] direction and can be described by a binary graph-set motif (Bernstein *et al.*, 1995) of $C_2^2(10)$. The hydroxy H atom of the hydroxymethyl substituent forms its own intermolecular hydrogen bond with the hydroxy O atom on ring *B* of another neighbouring molecule. This interaction links the 7-epicandicandiol molecules into extended chains which also run parallel to the [100] direction and can be described by a graph-set motif of $C(8)$. The combination of all hydrogen-bonding interactions links all the moieties in the structure into two-dimensional networks which lie parallel to the (001) plane. In addition, the three structurally different hydroxy groups form a co-operative O—H···O—H···O—H··· chain which runs parallel to the [010] direction (Fig. 2) and can be described by a ternary graph-set motif of $C_3^3(6)$.

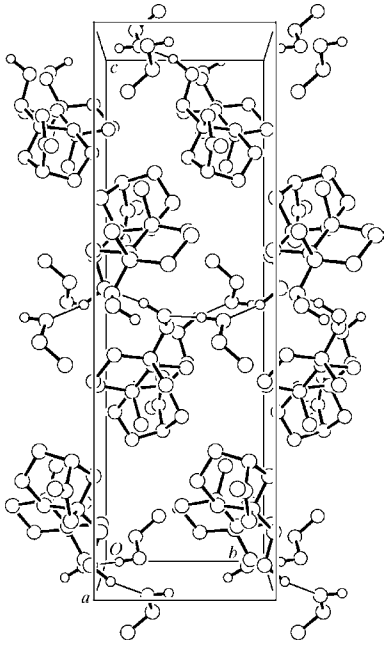

Figure 2
The crystal packing in (I), viewed along the *a* axis, showing the co-operative O—H···O—H···O—H··· chain. Most of the H atoms have been omitted for clarity. Hydrogen bonds are represented by thin lines.

Experimental

The title compound was isolated from *Sideritis ozturkii* Aytaç & Aksoy as described by Şahin *et al.* (2004, 2005). Suitable crystals were obtained by slow evaporation of a solution of the compound in ethanol (m.p. 316 K).

Crystal data

$C_{20}H_{32}O_2\cdot C_2H_6O$
M_r = 350.54
Orthorhombic, $P2_12_12_1$
a = 12.3391 (2) Å
b = 7.1780 (1) Å
c = 22.8065 (4) Å
V = 2019.97 (6) Å^3
Z = 4
D_x = 1.153 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3806 reflections
θ = 2.0–25.0°
μ = 0.07 mm^{-1}
T = 160 (1) K
Needle, colourless
0.30 × 0.12 × 0.12 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans with κ offsets
20732 measured reflections
2049 independent reflections
1714 reflections with $I > 2\sigma(I)$
R_{int} = 0.062
θ_{max} = 25.0°
$h = -14 \rightarrow 14$
$k = -8 \rightarrow 8$
$l = -27 \rightarrow 27$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.112
S = 1.03
2047 reflections
241 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0544P)^2 + 0.8216P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.50 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O7—H7···O23	0.82 (4)	1.96 (4)	2.767 (3)	169 (4)
O18—H18···O7^{i}	0.84 (4)	1.92 (4)	2.757 (3)	173 (4)
O23—H23···O18^{ii}	0.82 (5)	1.92 (5)	2.726 (3)	166 (4)

Symmetry codes: (i) $x+\frac{1}{2}, -y+\frac{1}{2}, -z+1$; (ii) $x-\frac{1}{2}, -y+\frac{3}{2}, -z+1$.

The hydroxy H atoms were located in a difference Fourier map and their positions were refined freely along with individual isotropic displacement parameters. The methyl H atoms were constrained to an ideal geometry (C—H = 0.98 Å), with U_{iso}(H) = 1.5U_{eq}(C), but were allowed to rotate freely about the C—C bonds. All other H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms [C—H = 0.99–1.00 Å and U_{iso}(H) = 1.2U_{eq}(C)]. As there are no significant anomalous dispersion effects with this compound, Friedel opposites were merged prior to the final cycles of refinement. The enantiomer used in the refinement model was chosen so as to correspond with that usually depicted for 7-epicandicandiol, although there does not appear to have been a definitive determination of the absolute configuration of this compound. Two low-angle reflections were omitted from the final cycles of refinement because their observed intensities were much lower than the calculated values, as a result of being partially obscured by the beam stop.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *DENZO* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG3006). Services for accessing these data are described at the back of the journal.

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