

An *ent*-kaurane diterpenoid from *Isodon japonica*Zhi-An He, Ji-Xia Zhang and
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Key indicators

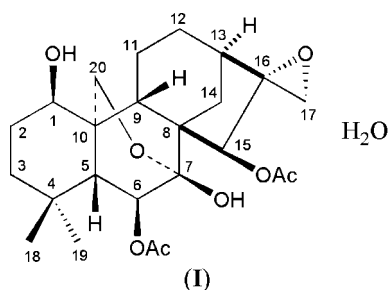
Single-crystal X-ray study
 $T = 294$ K
Mean $\sigma(\text{C}-\text{C}) = 0.004$ Å
 R factor = 0.039
 wR factor = 0.087
Data-to-parameter ratio = 9.7For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.

The title compound, $1\beta,7\beta$ -dihydroxy- $6\beta,15\beta$ -diacetoxy- $16\alpha,17:7\alpha,20$ -diepoxy-*ent*-kaurane or Maoyecrystal B, $\text{C}_{24}\text{H}_{34}\text{O}_8 \cdot \text{H}_2\text{O}$, crystallizes with one molecule of water of crystallization. It is a natural diterpenoid composed of four fused rings with the expected *cis* and *trans* junctions. Molecules are linked together by $\text{O}-\text{H} \cdots \text{O}$ hydrogen bonds.

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Comment

The title compound, (I), is a natural *ent*-kaurane diterpenoid isolated from the medicinal plant *Isodon japonica*. This plant has been used as antibacterial, inflammation-diminishing and stomachic agents. The diterpenoid has been reported previously (Zhang *et al.*, 2002), but its structure, determined by spectroscopic methods, seems questionable. In order to establish the structure unambiguously, especially the stereochemistry of the oxirane, a crystal structure analysis has been undertaken.



An ORTEP-3 plot (Farrugia, 1997) of the molecule is shown in Fig. 1. The X-ray crystallographic analysis of (I) shows that the oxirane has $16\alpha,17$ -epoxy substituents, not $16\beta,17$ as reported previously from the spectroscopic study (Zhang *et al.*, 2002). In addition, $7\alpha,20$ -epoxy substituents are observed, and two hydroxyl groups together with two acetoxy groups adopt β -orientations at C1, C7, C6 and C15, respectively. There is a *trans* junction between ring A (C1–C5/C10) and ring B (C5–C10); *cis* junctions are present between ring B and ring C (C8/C9/C11–C14), and ring C and ring D (C8/C13–C16).

The bond lengths and angles of (I) are within the expected ranges (Allen *et al.*, 1987), with average values (Å) $\text{Csp}^3-\text{Csp}^3$ (excluding C16–C17) = 1.535 (3), $\text{Csp}^3-\text{Csp}^3$ (in oxirane) = 1.448 (4), $\text{Csp}^3-\text{Csp}^2$ = 1.484 (4), $\text{C}=\text{O}$ = 1.203 (3), Csp^3-O = 1.436 (4), Csp^2-O = 1.340 (3). Ring A has a chair conformation, with an average torsion angle of 55.4 (3)°. Rings B and C both adopt slightly twisted boat conformations. Ring D adopts an envelope conformation; the flap atom, C14, lies 0.690 (3) Å from the plane defined by atoms C8, C15, C16 and C13. In addition, the six-membered rings O1/C20/C10/C5–C7 and O1/C7–C10/C20 both adopt boat conformations.

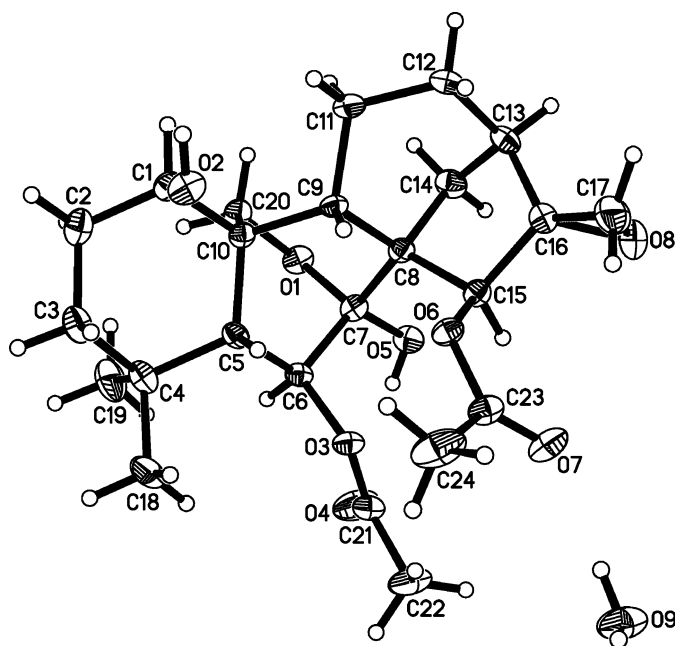


Figure 1
A view of the molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level. Only one component is shown for the H atoms of each disordered acetyl group.

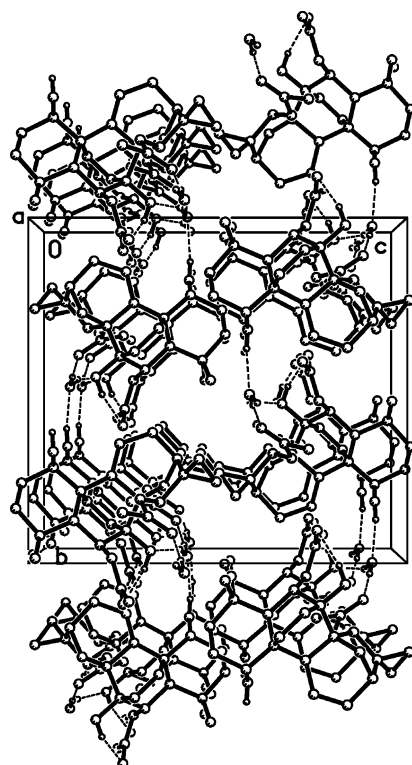


Figure 2
The crystal packing of (I), viewed along the *a* axis. O—H...O hydrogen bonds are shown as dashed lines; H atoms not involved in these interactions have been omitted.

It was not possible to determine the absolute configuration of (I) by anomalous dispersion effects, but the negative optical rotation showed this compound to be in the *ent*-kaurane series

as reported in the genus *Isodon* (Sun *et al.*, 2001), rather than in the kaurane series.

In the crystal structure, the molecules stack along the *a* axis and are linked by O—H...O hydrogen bonds (Table 1 and Fig. 2).

Experimental

The dried and crushed leaves of *Isodon japonica* (7.5 kg, collected from the Taihang Mountain, Henan Province, China) were extracted three times with Me₂CO/H₂O (7:3 *v/v*) at room temperature over a period of five days. The extract was filtered and the solvent was removed under reduced pressure. The residue was then partitioned between water and AcOEt. After removal of the solvent, the AcOEt residue was separated by repeated silica gel (200–300 mesh) column chromatography and recrystallization from MeOH/CHCl₃ (5:1), giving 23 mg of compound (I) (m.p. 474–476 K. Optical rotation: $[\alpha]_D^{20} -64.4^\circ$ (c 0.90, MeOH). Crystals suitable for X-ray analysis were obtained by slow evaporation of a solution of (I) in MeOH/H₂O (0.95:0.05) at room temperature.

Crystal data

C₂₄H₃₄O₈·H₂O
M_r = 468.53
 Orthorhombic, *P*2₁2₁2₁
a = 9.492 (2) Å
b = 14.909 (4) Å
c = 16.354 (4) Å
V = 2314.2 (8) Å³

Z = 4
D_x = 1.345 Mg m⁻³
 Mo *K*α radiation
 μ = 0.10 mm⁻¹
T = 294 (2) K
 Prism, colourless
 0.68 × 0.68 × 0.44 mm

Data collection

Siemens *P4* diffractometer
 ω scans
 Absorption correction: none
 3354 measured reflections
 3003 independent reflections
 2210 reflections with *I* > 2σ(*I*)

R_{int} = 0.015
 θ_{\max} = 27.5°
 3 standard reflections
 every 97 reflections
 intensity decay: 2.4%

Refinement

Refinement on *F*²
R [*F*² > 2σ(*F*²)] = 0.039
wR (*F*²) = 0.087
S = 0.96
 3003 reflections
 311 parameters
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0466P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$
 $\Delta\rho_{\max} = 0.20 \text{ e \AA}^{-3}$
 $\Delta\rho_{\min} = -0.15 \text{ e \AA}^{-3}$
 Extinction correction: *SHELXL97*
 Extinction coefficient: 0.0094 (10)

Table 1

Hydrogen-bond geometry (Å, °).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
O2—H2O...O9 ⁱ	0.82	2.03	2.842 (3)	170
O5—H5O...O4	0.82	2.15	2.879 (3)	147
O9—H0B...O5 ⁱⁱ	0.82 (1)	2.37 (3)	3.135 (3)	156 (6)
O9—H0A...O7	0.83 (1)	2.04 (1)	2.864 (3)	176 (4)

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

For each acetyl group the H atoms of the methyl group are disordered over two sites with site occupancy factors of 0.5. The water H atoms were located in a difference Fourier map and refined freely.

All other H atoms were included in calculated positions and refined as riding, with C—H = 0.96–0.98 Å and O—H = 0.82 Å; $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C},\text{O})$. In the absence of significant anomalous scattering effects, Friedel pairs were averaged. The choice of enantiomer was based on a comparison of the optical rotation with that of related compounds with known stereochemistry.

Data collection: *XSCANS* (Siemens, 1994); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Sheldrick, 1997b); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997a); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXTL*.

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