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Sipeimine, a steroidal alkaloid from *Fritillaria roylei* Hooker

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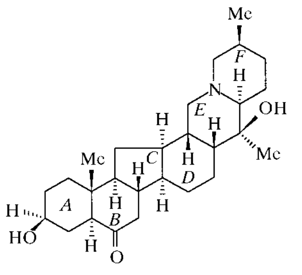
In the title compound, 3,20-dihydroxycevan-6-one, $C_{27}H_{43}NO_3$, all the six-membered rings have normal chair conformations except ring *D*, which exists in a twist-chair conformation. The five-membered ring *C* adopts an envelope conformation. An O—H$\cdots$O hydrogen bond connects the molecules into spirals, which run along the *b*-axis direction.

Comment

The title compound, (I), was first isolated from *Fritillaria imperialis* L. (Liliaceae). It has since been extracted from several other species of *Fritillaria* (Xu *et al.*, 1990; Hu *et al.*, 1993) and also named imperialine and kashmirine. The structure and relative stereochemistry have been established by spectroscopy. In the course of systematic screening for anti-cough agents, sipeimine was isolated from *Fritillaria roylei* Hooker. The present study reports the crystal structure of sipeimine. The relative stereochemistry and conformation of all the rings in the molecule and the hydrogen-bonding scheme are now clearly defined.



(I)

The molecule (Fig. 1) is composed of five six-membered rings and one five-membered ring. The stereochemistry of the ring junctures are *A*/*B trans*, *B*/*C trans*, *C*/*D cis*, *D*/*E cis* and *E*/*F trans*. The configurations at the other chiral centres are as follows: C3—OH and C20—Me equatorial; C10—Me, C20—OH and C22—Me axial. Molecular dimensions are unexceptional. The cyclohexane rings *A*, *B*, *E* and *F* are found to have normal chair conformations with mean torsion-angle values of 55 (4), 55 (5), 57 (5) and 54.9 (16)°, respectively (the torsion angle of the normal chair form of cyclohexane is 56°). Ring *D* exists in a twist chair form owing to the *cis* fusion with ring *C* and ring *E*. This is also indicated by the smaller torsion angles C13—C12—C14—C15 of 30.6 (3)° and C12—C14—C15—C16 of −44.3 (4)°. The five-membered ring *C* adopts an envelope

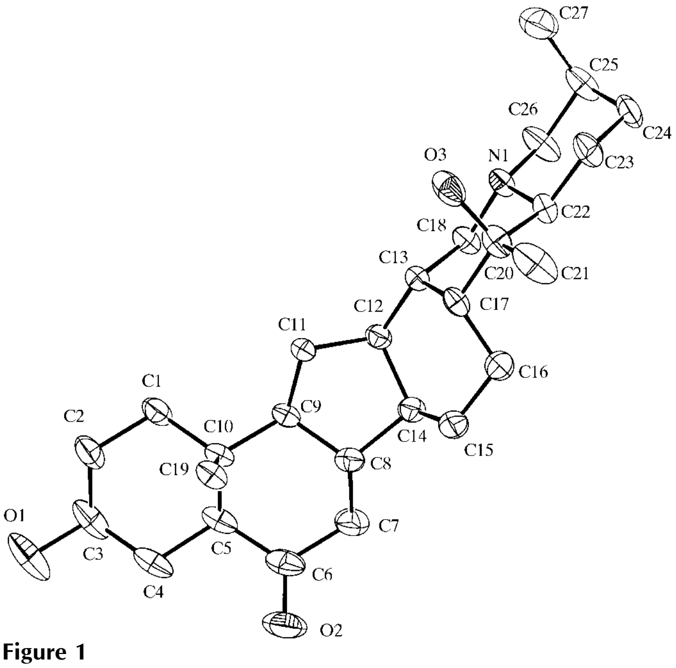


Figure 1
The molecular structure and atomic numbering scheme for (I). Displacement ellipsoids are drawn at the 30% probability level.

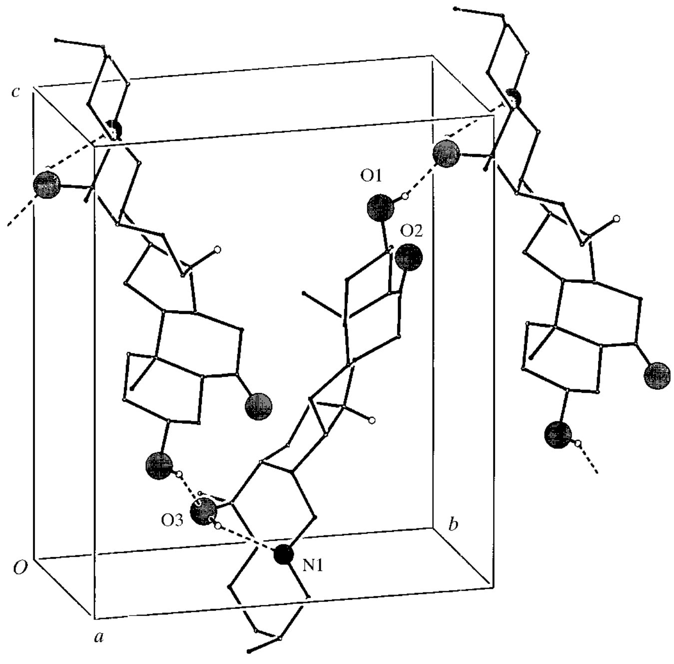


Figure 2
Crystal packing of (I) shown in a projection along the crystallographic *a* axis. Intermolecular hydrogen bonds are shown as dashed lines.

conformation with C11 displaced by 0.683 (4) Å from the mean plane of the remaining four atoms. The model also reveals that the skeleton is twisted strongly at the *D* ring because of the presence of *cis* H atoms H12, H14 and H13, H17; this results in an interplanar angle of 79.9 (1)° between the planes of the *A*/*B*/*C* and *E*/*F* ring atoms.

Details of hydrogen bonding are in Table 1. Molecules are linked into spirals along the *b* direction (Fig. 2). There is also an intramolecular O—H···N hydrogen bond.

Experimental

Dried bulbs of *Fritillaria roylei* Hooker (1 kg) was ground to a fine powder and mixed with 5% sodium carbonate solution and dried at room temperature. The powder was macerated with CH_2Cl_2 for 3 d, filtered and the solution extracted with 1% hydrochloric acid. The pH of the solution was adjusted to 9 with potassium carbonate solution and extracted with diethyl ether. The solution was condensed under reduced pressure to give a diethyl ether extract, which was separated on an aluminium oxide chromatography column using an acetyl acetate/methanol/concentrated ammonia solution (20:1:1) as eluent to afford sipeimine (30 mg). The product was dissolved in methanol and chloroform (3:2) and stored at room temperature. Transparent prism crystals were obtained after 3 d.

Crystal data

$C_{27}H_{43}NO_3$
$M_r = 429.62$
Monoclinic, $P2_1$
$a = 6.6185$ (5) Å
$b = 12.3948$ (8) Å
$c = 14.5069$ (10) Å
$\beta = 90.8220$ (10)°
$V = 1189.95$ (14) Å^3
$Z = 2$

$D_x = 1.199$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3905 reflections
$\theta = 1.40$–26.01°
$\mu = 0.076$ mm^{-1}
$T = 293$ (2) K
Prism, colourless
0.52 × 0.35 × 0.20 mm

Data collection

Bruker SMART/CCD diffractometer
ω scans
7280 measured reflections
2455 independent reflections
1789 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.032$
$\theta_{\rm max} = 26.01°$
$h = -8 \rightarrow 8$
$k = -15 \rightarrow 13$
$l = -16 \rightarrow 17$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.110$
$S = 0.992$
2455 reflections
285 parameters

H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0662P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.16$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.18$ e Å^{-3}

H atoms were visible in difference maps and were allowed for as riding atoms with O—H = 0.82 Å and C—H = 0.96– Å. With no atoms having significant anomalous dispersion contributions, Friedel reflections were merged before the final refinement and the relative stereochemistry is shown in the Scheme and Figures.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SMART* and *SAINT* (Bruker, 1998); data reduction: *XPREP* in *SHELXTL* (Sheldrick, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *XP* (Bruker, 1998); software used to prepare material for publication: *SHELXTL* (Sheldrick, 1997).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DE1149). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (2001). C**57**, 170–171 Ren-Wang Jiang *et al.* • $C_{27}H_{43}NO_3$ **171**