Acta Crystallographica Section E
**Structure Reports Online**
ISSN 1600-5368

# Redetermination of 14-deoxyandrographolide

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**Key indicators**

Single-crystal X-ray study
$T$ = 296 K
Mean $\sigma$(C–C) = 0.004 Å
$R$ factor = 0.042
$wR$ factor = 0.112
Data-to-parameter ratio = 9.9

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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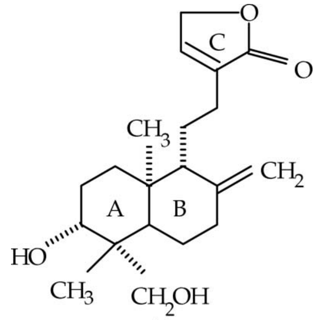
Received 16 June 2005
Accepted 22 July 2005
Online 30 July 2005

The title compound [systematic name: *ent*-3$\beta$-hydroxy-8(17),13(14)-labdadiene-16,15-olide], $C_{20}H_{30}O_4$, contains two *trans* fused six-membered rings, with a lactone ring at the end of an equatorial side chain. The six-membered rings are in chair conformations and the lactone ring is planar. There is an infinite chain of both inter- and intramolecular O—H···O hydrogen bonds along the $b$ axis. The present study is a confirmation of the results of previous structure determinations of 14-deoxyandrographolide by Medforth, Chang, Chen, Olmstead & Smith [*J. Chem. Soc. Perkin Trans. 2* (1990), pp. 1011–1016] and Rajnikant, Gupta, Singh, Lal, Gupta & Varghese [*Mol. Cryst. Liq. Cryst. Sect. C* (1996), **6**, 227–233].

## Comment

The title compound, (I), has been isolated from the leaves of *Andrographis paniculata* Nees (Acanthaceae), which is an annual herb common in Sri Lanka and India. It is extensively used in the Ayurvedic system of medicine in Sri Lanka and India to treat fevers, dysentry, general debility and certain forms of dyspepsia, and also as a stomachic, an anthelmintic and a tonic. A preparation of (I) with pepper is used in the treatment of malarial fever (Spek *et al.*, 1987). Spectoscopic analysis of 14-deoxyandrographolide (Pramanick *et al.*, 2005) affords proof of the stereochemistry at C3, C4 and C9. The present X-ray structure analysis confirms the results of the previous structure determinations of this compound by Medforth *et al.* (1990) and Rajnikant *et al.* (1996), but the present structure is determined with better data [1813, $F_o > 4\sigma(F_o)$], which resulted in a lower reliability factor and more precise molecular geometry.




(I)

The molecule (Fig. 1) has a bicyclic nucleus, to which an $\alpha,\beta$-unsaturated $\gamma$-lactone system is attached through a side chain. Substituents on ring A are a hydroxyl group, a hydroxymethyl group and a methyl group with a second methyl group at the A/B ring junction. Ring B also has an exocyclic methylene group. The hydroxyl group at C3 is equatorial, an $\alpha$ configuration, the C4 hydroxymethyl group is axial and the side

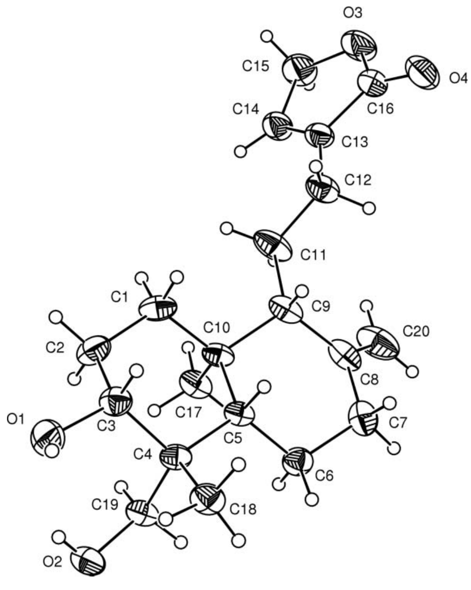



**Figure 1**
The structure of the title compound, showing 30% probability displacement ellipsoids and the atom numbering.

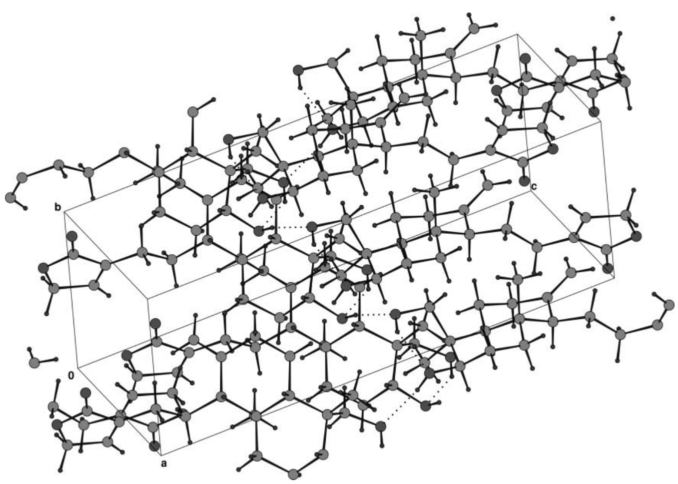



**Figure 2**
The crystal packing of (I), with hydrogen bonds drawn as dotted lines.

chain at C9 is equatorial. Ring A adopts a chair conformation, while ring B is a slightly distorted chair. The ring-puckering parameters for rings *A* and *B* (Cremer & Pople, 1975) are given in Table 3. The five-membered lactone ring is planar, the maximum deviation of ring *C* atoms from the mean plane describing them being 0.002 (3) Å. The OH group at C3 is equatorial, with a C1—C2—C3—O1 torsion angle of 175.7 (2)°. The C18 methyl at C4 is equatorial with C19 axial; torsion angles are C2—C3—C4—C18 = 169.1 (2)°, C10—C5—C4—C18 = −163.5 (2)°, C2—C3—C4—C19 = −72.1 (3)° and C10—C5—C4—C19 = 76.2 (2)°. The side chain at C9 is equatorial, with torsion angles C7—C8—C9—C11 = 176.5 (2)° and C5—C10—C9—C11 = −170.9 (2)°. The two O—H groups on ring *A* are involved in an intramolecular O2 — H2*O*2···O1 hydrogen bond and an intermolecular O1—H1*O*1···O2($x+2, y-\frac{1}{2}, -z+1$) hydrogen bond (Table 2), which links the molecules in infinite chains along the *b* axis (Fig. 2). A similar hydrogen-bonding scheme has been reported for the related compound andrographolide (Spek *et al.*, 1987).

## Experimental

Dry powdered leaves of Andrographis paniculata were successively extracted (Soxhlet) with petroleum ether (333–353 K), chloroform and methanol. Chromatographic separation of the methanol extract resulted in the isolation 14-deoxyandrographolide. Crystals were obtained from a solution of the compound in MeOH by slow evaporation at room temperature.

*Crystal data*

$C_{20}H_{30}O_4$
$M_r$ = 334.44
Monoclinic, $P2_1$
$a$ = 6.744 (2) Å
$b$ = 6.988 (2) Å
$c$ = 19.377 (3) Å
$\beta$ = 93.19 (3)°
$V$ = 911.8 (4) Å$^3$
$Z$ = 2
$D_x$ = 1.218 Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 867 reflections
$\theta$ = 5.2–23.6°
$\mu$ = 0.08 mm$^{-1}$
$T$ = 296 (2) K
Cylinder, colourless
0.23 × 0.22 × 0.11 mm

*Data collection*

Bruker AXS CCD diffractometer
$\varphi$ and $\omega$ scans
Absorption correction: multi-scan (*SHELXTL-NT*; Bruker, 1999)
$T_{min}$ = 0.984, $T_{max}$ = 0.991
9476 measured reflections
2189 independent reflections
1813 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.037
$\theta_{max}$ = 28.2°
$h = -8 \rightarrow 8$
$k = -9 \rightarrow 9$
$l = -25 \rightarrow 25$

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.112
$S$ = 1.09
2189 reflections
222 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0663P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.16 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.15 e Å$^{-3}$

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| C3—O1 | 1.435 (3) | C15—O3 | 1.438 (4) |
| C8—C20 | 1.332 (4) | C16—O4 | 1.204 (3) |
| C13—C14 | 1.324 (3) | C16—O3 | 1.346 (3) |
| C13—C16 | 1.473 (3) | C19—O2 | 1.424 (3) |
| C14—C15 | 1.482 (4) | | |
| O1—C3—C2 | 107.5 (2) | C14—C13—C16 | 107.3 (2) |
| C2—C3—C4 | 112.8 (2) | C13—C14—C15 | 109.9 (2) |
| C3—C4—C18 | 107.75 (18) | O3—C16—C13 | 109.2 (2) |
| C19—C4—C5 | 112.29 (18) | C16—O3—C15 | 109.07 (19) |
| C7—C8—C9 | 114.6 (2) | | |
| C1—C2—C3—O1 | 175.7 (2) | C18—C4—C5—C10 | −163.51 (18) |
| C2—C3—C4—C19 | −72.1 (3) | C7—C8—C9—C11 | 176.53 (18) |
| C2—C3—C4—C18 | 169.10 (19) | C11—C9—C10—C5 | −170.9 (2) |
| C19—C4—C5—C10 | 76.2 (2) | | |

**Table 2**
Hydrogen-bond geometry (Å, °).

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O2—H2*O*2···O1$^i$ | 0.82 | 1.98 | 2.675 (2) | 142 |
| O1—H1*O*1···O2$^i$ | 0.82 | 1.94 | 2.740 (2) | 166 |

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

**Table 3**
Ring-puckering parameters (Å, °) for the three rings.

| Ring | $q_2$ | $q_3$ | $Q_T$ | $\theta$ |
|---|---|---|---|---|
| A (C1–C5/C10) | 0.082 (3) | −0.531 (2) | 0.537 (3) | 171.3 (3) |
| B (C5–C10) | 0.126 (2) | −0.575 (3) | 0.589 (3) | 167.6 (2) |

All H atoms bound to carbon were refined using a riding model, with C—H = 0.98 Å and $U_{iso}(H) = 1.2U_{eq}(C)$ for methine, C—H = 0.97 Å and $U_{iso}(H) = 1.2U_{eq}(C)$ for methylene, C—H = 0.93 Å and $U_{iso}(H) = 1.2U_{eq}(C)$ for aromatic, C—H = 0.96 Å and $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl, and C—H = 0.93 Å and $U_{iso} = 1.2_{eq}(C)$ for ethylenic $CH_2$. For the hydroxyl H atom, O—H = 0.82 Å and $U_{iso} = 1.5U_{eq}(O)$. In the absence of a significant anomalous scattering, Friedel pairs were merged, and the absolute configuration was assigned by reference to the known chirality of related compounds.

Data collection: *SMART* (Bruker, 1999); cell refinement: *SAINT* (Bruker, 1999); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1999); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1983).

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