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14-Deoxy-11,12-didehydro-3,19-isopropylidene-andrographolide

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The title compound, (*E*)-3-[2-(3,3,6a,10*b*-tetramethyl-8-methyleneperhydronaphtho[2,1-*d*][1,3]dioxin-7-yl)vinyl]furan-2(5*H*)-one, $C_{23}H_{32}O_4$, an andrographolide analogue, was semi-synthesized from 14-deoxy-11,12-didehydroandrographolide. All the six-membered rings in the structure adopt chair conformations. The crystal structure is stabilized by C—H$\cdots$O interactions, which form a two-dimensional network parallel to the *ab* plane

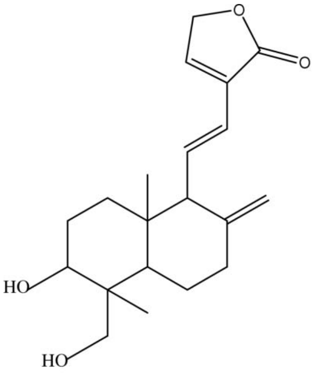
Key indicators

Single-crystal X-ray study
T = 297 K
Mean σ(C–C) = 0.003 Å
R factor = 0.043
wR factor = 0.107
Data-to-parameter ratio = 13.9

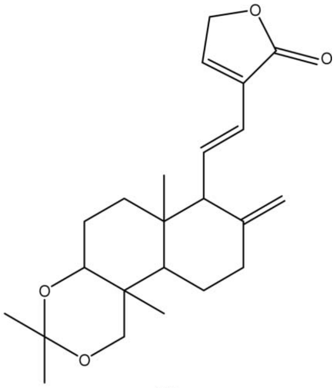
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

Andrographis paniculata Nees (Acanthaceae) is a very popular herb commonly used in Indian Ayurvedic and Chinese traditional medicine for the treatment of a variety of illnesses. Extracts of this plant have been shown to possess anti-inflammatory (Shen *et al.*, 2002), antiviral (Chang *et al.*, 1991; Calabrese *et al.*, 2000), immunostimulatory (Puri *et al.*, 1993; See *et al.*, 2002), hypoglycaemic (Zhang & Tan, 2000), hypotensive (Zhang & Tan, 1996) and anticancer (Siripong *et al.*, 1992; Stanslas *et al.*, 2001; Kumar *et al.*, 2004) activities. The main labdane type diterpenoid constituents of this plant are andrographolide, neoandrographolide, 14-deoxyandrographolide and 14-deoxy-11,12-didehydroandrographolide.



(I)



(II)

During the course of developing andrographolide analogues with significant pharmacological activities, the title compound, (II), was semi-synthesized by reacting compound (I) with 2,2-dimethoxypropane under reflux. The X-ray crystal structure analysis of (II) was undertaken in order to establish its molecular structure and stereochemistry.

A molecular view of (II) is shown in Fig. 1. Bond lengths and angles display normal values (Allen *et al.*, 1987), comparable with related structures (Smeets *et al.*, 1987; Spek *et al.*, 1987; Fujita *et al.*, 1984). The five-membered lactone ring is planar, with a maximum deviation of 0.014 (2) Å for atom

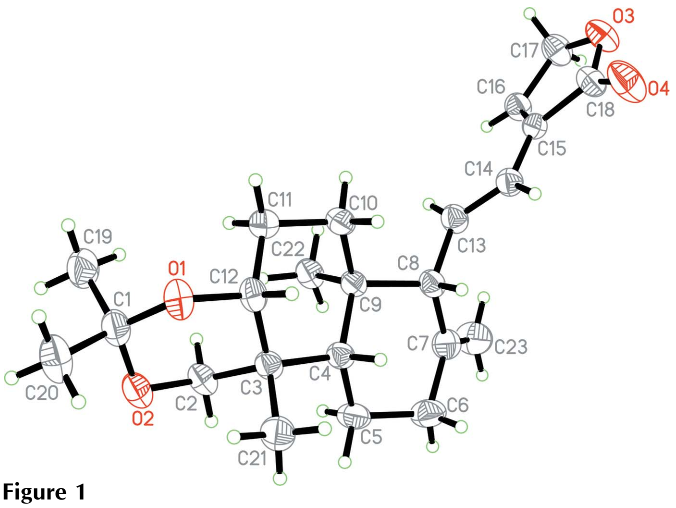


Figure 1
The structure of (II), showing 30% probability displacement ellipsoids and the atomic numbering.

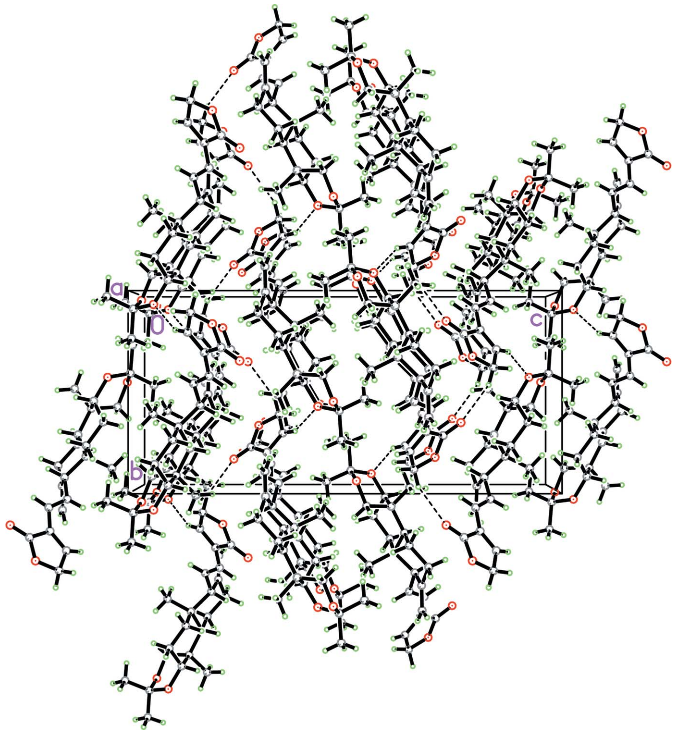


Figure 2
The crystal packing of (II), viewed along the *a* axis. Hydrogen bonds are shown as dashed lines.

C15. The orientation of the five-membered ring with respect to the fused ring system is illustrated by the torsion angles C9—C8—C13—C14 [126.2 (2)°], C8—C13—C14—C15 [172.5 (2)°] and C13—C14—C15—C18 [171.7 (2)°]; the corresponding torsion angles for neoandrographolide monohydrate [164.3 (5), −171.8 (5) and 83.3 (7)°; Smeets *et al.*, 1987] and andrographolide [170.6 (2), 158.2 (2) and 175.9 (2)°; Spek *et al.*, 1987] indicate different orientations.

The six-membered rings adopt chair conformations; the Cremer & Pople (1975) puckering parameters Q, θ and φ are 0.531 (2) Å, 12.3 (2)° and 204.3 (10)°, respectively, for the C3–C4/C9–C12 ring, 0.590 (2) Å, 170.3 (2)° and 148.1 (12)°, respectively, for the C4–C9 ring, and 0.515 (2) Å, 164.5 (2)° and 18.7 (8)°, respectively, for the O1/C1/O2/C2–C3/C12 ring.

The crystal structure is stabilized by C—H···O interactions (Table 1), which form a two-dimensional network parallel to the *ab* plane (Fig. 2).

Experimental

A mixture of 14-deoxy-11,12-didehydroandrographolide (100 mg, 0.3 mmol), 2,2-dimethoxypropane (312 mg, 3.0 mmol) and a catalytic amount of pyridinium *p*-toulenesulfonate in benzene/dimethyl sulfoxide (5.0 ml/0.5 ml) was refluxed for 1 h. After completion of the reaction (checked by thin-layer chromatography), the reaction mixture was cooled to room temperature. The remaining catalyst was quenched with excess triethylamine (a few drops). The reaction mixture was diluted with benzene and washed with water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The final residue was purified by silica gel column chromatography with dichloromethane/methanol (98:2 *v*/*v*) as an eluting solvent system. After slow evaporation of the solvent, compound (II) (90 mg, 62%) formed as colourless crystals.

Crystal data

$C_{23}H_{32}O_4$
$M_r = 372.49$
Orthorhombic, $P2_12_12_1$
$a = 9.1528$ (2) Å
$b = 10.3440$ (2) Å
$c = 22.0663$ (4) Å
$V = 2089.16$ (7) Å^3
$Z = 4$
$D_x = 1.184$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 7069 reflections
$\theta = 1.9$–30.0°
$\mu = 0.08$ mm^{-1}
$T = 297$ (2) K
Rod, colourless
0.54 × 0.21 × 0.21 mm

Data collection

Bruker SMART APEX2 CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2005)
$T_{min} = 0.825$, $T_{max} = 0.984$
27503 measured reflections

3452 independent reflections
2173 reflections with $I > 2\sigma(I)$
$R_{int} = 0.034$
$\theta_{max} = 30.0°$
$h = -12 \rightarrow 12$
$k = -14 \rightarrow 14$
$l = -31 \rightarrow 31$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.043$
$wR(F^2) = 0.107$
$S = 1.01$
3452 reflections
248 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0499P)^2 + 0.0866P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.12$ e Å^{-3}
$\Delta\rho_{min} = -0.13$ e Å^{-3}

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C16—H16···O1^{i}	0.93	2.42	3.273 (2)	153
C17—H17*A*···O4^{ii}	0.97	2.40	3.302 (3)	155

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

H atoms were placed in calculated positions, with C—H distances in the range 0.93–0.98 Å. The U_{iso} values were constrained to be $1.5U_{eq}$ of the carrier atom for methyl H atoms and $1.2U_{eq}$ for the remaining H atoms. Owing to the absence of any significant anom-

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alous dispersion in the molecules, Friedel pairs were merged before the final refinement.

Data collection: *APEX2* (Bruker, 2005); cell refinement: *APEX2*; data reduction: *SAINT* (Bruker, 2005); program(s) used to solve structure: *SHELXTL* (Sheldrick, 1998); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2003).

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