organic papers

Cimicidol-3-one: a cycloartenol triterpenoid from the rhizomes of *Cimicifuga racemosa*

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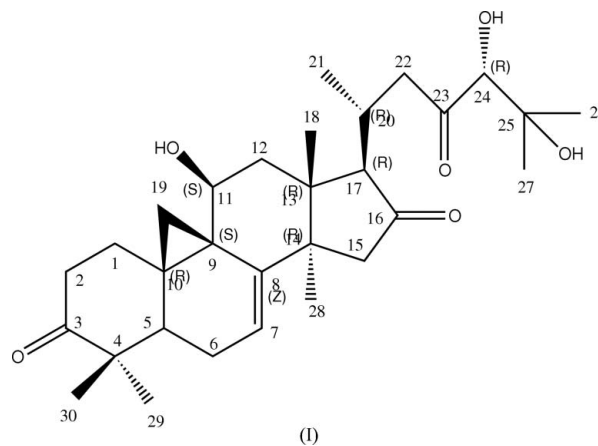
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The title compound [systematic name: (20R,24R)-11β,24,25-trihydroxy-9,19-cyclolanost-7-ene-3,16,23-trione], $C_{30}H_{44}O_6$, is a cycloartenol triterpenoid which was isolated from the rhizomes of *Cimicifuga racemosa*. The molecule contains three six-membered rings adopting chair and distorted boat conformations, a five-membered ring exhibiting an envelope conformation and a three-membered ring. The molecules are linked by three hydrogen bonds, forming a two-dimensional structure parallel to the (001) plane.

Comment

Cimicifuga racemosa (*L.*) Nutt. (black cohosh, black snake-root) is a herb indigenous to North America and Europe. In the middle of the 20th century it was introduced to several countries in western Europe and has gained increasing importance for the treatment of menopausal complaints (*e.g.* hot flushes, depression) and dysmenorrhea (Kristian *et al.*, 2001). Our investigation of the bioactive constituents of the rhizomes of *C. racemosa* led to the isolation of cimicidol-3-one, (I). The structure of (I) was elucidated by spectroscopic analysis, including two-dimensional NMR, and was confirmed by single-crystal X-ray diffraction analysis, the results of which are presented here.

(I)

The molecular structure of (I) and the atom-numbering scheme are shown in Fig. 1. The molecule contains three six-membered rings (*A*, atoms C1–C5/C10; *B*, C5–C10; and *C*, C8/C9/C11–C14), a five-membered ring (*D*, C13–C17) and a three-membered ring (C9/C10–C19). Ring *A* adopts a chair conformation, while rings *B* and *C* adopt distorted boat conformations as a result of the C7═C8 double bond. Ring *D* exhibits an envelope conformation. All rings are *trans* fused.

In the crystal structure of (1), The molecules are connected by three hydrogen bonds, forming a two-dimensional structure parallel to the (001) plane.
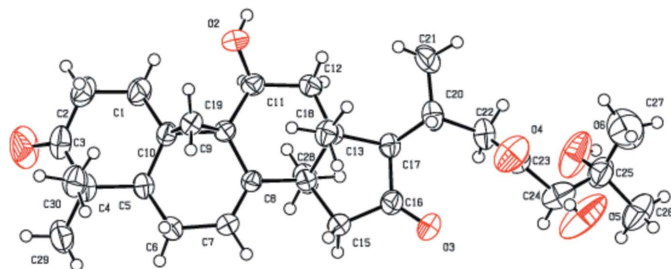
Figure 1
View of the molecule of (I) showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. Note that the chirality was not determined.

Experimental

The ethanol extract was purchased from Jiahe Phytochem Co., Ltd, Shanxi province, People's Republic of China. The extract (1 kg) was suspended in water and then partitioned successively with petroleum ether, ethyl acetate and *n*-BuOH (4× 3000 ml). The ethyl acetate extract (336 g) was divided into 8 fractions (Fr. 1–Fr. 8) by chromatography on a silica gel column (2 kg, 160–200 mesh) eluted with chloroform–methanol (gradients 20:1–1:1). Fr. 5 (18 g) was rechromatographed over silica gel (300 g, 200–300 mesh) and eluted with petroleum ether-acetone (7:1–1:1) to afford the pure title compound (I) (m.p. 471–473 K). Suitable crystals were obtained by slow evaporation of a methanol solution at room temperature. ^{13}C NMR (125 MHz, pyridine-d$_5$, δ, p.p.m.): 218.2 (C16), 215.4 (C3), 213.7 (C23), 147.1 (C8), 115.1 (C7), 84.0 (C24), 72.4 (C25), 62.8 (C11), 61.3 (C17), 49.6 (C15), 48.9 (C4), 47.5 (C22), 46.9 (C12), 46.0 (C14), 45.3 (C5), 44.3 (C13), 37.0 (C2), 28.9 (C1), 28.9 (C10), 28.2 (C9), 27.9 (C27), 27.5 (C28), 27.4 (C29), 27.3 (C20), 25.7 (C26), 22.7 (C30), 22.1 (C6), 20.2 (C21), 20.2 (C18), 18.0 (C19).

Crystal data

C$_{30}$H$_{44}$O$_6$	$D_x = 1.207$ Mg m^{-3}
$M_r = 500.65$	Mo $K\alpha$ radiation
Monoclinic, $P2_1$	Cell parameters from 29
$a = 8.809$ (1) Å	reflections
$b = 9.236$ (2) Å	$\theta = 3.4$–14.7°
$c = 16.944$ (3) Å	$\mu = 0.08$ mm^{-1}
$\beta = 91.88$ (1)°	$T = 296$ (2) K
$V = 1377.9$ (4) Å^3	Prism, colourless
$Z = 2$	$0.52 \times 0.50 \times 0.44$ mm

Data collection

Siemens P4 diffractometer	$\theta_{max} = 27.5$°
ω scans	$h = 0 \rightarrow 11$
Absorption correction: none	$k = 0 \rightarrow 12$
3702 measured reflections	$l = -22 \rightarrow 22$
3368 independent reflections	3 standard reflections
2585 reflections with $I > 2\sigma(I)$	every 97 reflections
$R_{int} = 0.017$	intensity decay: 5.7%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0926P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.050$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.137$	$(\Delta/\sigma)_{max} < 0.001$
$S = 0.98$	$\Delta\rho_{max} = 0.35$ e Å^{-3}
3368 reflections	$\Delta\rho_{min} = -0.21$ e Å^{-3}
336 parameters	Extinction correction: *SHELXL*
H-atom parameters constrained	Extinction coefficient: 0.010 (3)

Table 1
Selected geometric parameters (Å, °).

O1—C3	1.202 (4)	O5—C24	1.446 (5)
O2—C11	1.433 (4)	O6—C25	1.432 (5)
O3—C16	1.209 (3)	C7—C8	1.327 (3)
O4—C23	1.206 (4)		
C3—C2—C1	110.3 (3)	C12—C13—C14	107.7 (2)
O1—C3—C2	122.1 (3)	C18—C13—C14	111.0 (2)
C2—C3—C4	115.6 (3)	C8—C14—C15	116.2 (2)
C7—C8—C9	121.4 (2)	O3—C16—C17	126.3 (2)
C8—C9—C19	116.8 (2)	C17—C16—C15	110.5 (2)
C19—C9—C10	58.65 (18)	O4—C23—C24	117.8 (4)
C19—C9—C11	117.8 (2)	C23—C24—C25	116.8 (3)
C19—C10—C1	119.5 (3)	O6—C25—C27	108.0 (5)
O2—C11—C9	108.4 (2)	C27—C25—C26	112.0 (4)
C12—C11—C9	116.3 (2)		
C1—C2—C3—O1	−124.5 (4)	C14—C15—C16—O3	−176.1 (3)
O1—C3—C4—C5	128.0 (4)	C14—C15—C16—C17	6.7 (4)
C2—C3—C4—C5	−52.8 (4)	C16—C17—C20—C21	−178.3 (3)
C6—C7—C8—C9	5.9 (5)	C16—C17—C20—C22	58.8 (3)
C7—C8—C9—C10	−19.1 (4)	C21—C20—C22—C23	123.4 (3)
C11—C9—C10—C19	−106.4 (3)	C20—C22—C23—C24	158.6 (3)
C19—C9—C10—C1	109.5 (3)	O4—C23—C24—O5	2.3 (5)
C11—C9—C10—C1	3.0 (4)	C22—C23—C24—O5	−179.2 (3)
O2—C11—C12—C13	123.9 (3)	O5—C24—C25—O6	177.5 (3)
C11—C12—C13—C14	46.1 (4)	O5—C24—C25—C27	−65.6 (5)
C7—C8—C14—C13	−145.4 (3)	C23—C24—C25—C27	55.4 (5)

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

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
O2—H2O⋯O3^i	0.82	2.03	2.830 (3)	165
O5—H5O⋯O4	0.82	2.06	2.555 (4)	119
O6—H6O⋯O2^{ii}	0.82	2.12	2.908 (4)	161

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

All H atoms were positioned geometrically (C—H distances of 0.93–0.98 Å, O—H distances of 0.82 Å) and refined as riding, with U_{iso}(H) = 1.2U_{eq}(C). In the absence of significant anomalous dispersion effects, Friedel pairs were averaged. The absolute configuration could, however, be assigned by reference to a chiral molecule of known absolute configuration (Mamoru *et al.*, 1995).

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

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