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Amarisolide monohydrate, a 2-(β-glucosyl)neoclerodane

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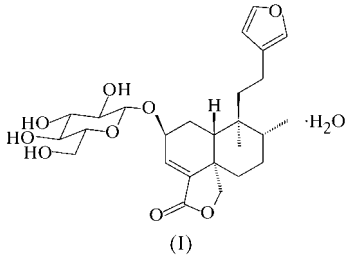
The absolute configuration of the neoclerodane glycoside amarisolide, presented here as the monohydrate, $C_{26}H_{36}O_9\cdot H_2O$, has been determined by association with the known configuration of the glucose moiety. Its structure was established as 2β-(*O*-β-D-glucopyranosyl)neocleroda-3,13(16),14-trien-15,16-epoxy-18,19-olide. Extensive hydrogen bonding among the hydroxyl groups of the sugar moiety forms layers which are interconnected by water molecules.

Comment

In the course of our phytochemical investigation of the *Salvia* genus (Maldonado *et al.*, 1992; Ortega *et al.*, 1995), we have investigated *S. amarissima* Ort. (family Labiatae, section *Uricae*, subgenus *Calosphace*). From an acetone extract of the aerial parts of this plant, we isolated the new diterpenoid glycoside amarisolide monohydrate, (I), this being the first report of the occurrence of this type of glycoside in a *Salvia* species.



(I)

A spectroscopic study of the title compound (Fig. 1) revealed it to be a glucosyl derivative of a *trans*-neoclerodane diterpene, and led to the establishment of its relative configuration (Maldonado *et al.*, 1996). We here confirm that finding and report the absolute configuration of this compound.

Although the absolute configuration could not be determined from the diffraction data alone, it was established by the known configuration of the β-D-glucose moiety attached at C2 and shows that the molecule is comprised of a tricyclic skeleton with the six-membered rings *trans*-fused [$\tau_{1,10,5,4}$ = −39.4 (3)° and $\tau_{9,10,5,6}$ = 61.8 (3)°]. The six-membered sugar ring exhibits torsion angles in the range −63.1 (3) to 61.8 (3)°, which are close to the ideal value of 56° for the chair conformation (Bucourt & Hainaut, 1965). The deviations may result from the extensive hydrogen-bonding network involving the sugar hydroxyl groups. The cyclohexene and cyclohexane rings exhibit conformations intermediate between half-chair and sofa for the former and a slightly distorted chair for the latter [Cremer & Pople (1975) parameters: φ = 344.1 (5)°, θ = 52.3 (4)° and Q_T = 0.531 (3) Å, and φ = 349 (3)°, θ = 6.5 (4)° and Q_T = 0.577 (4) Å, respectively]. The five-membered lactone ring adopts an envelope conformation [φ = 288.7 (6)° and q_2 = 0.401 (4) Å] with C5 as a flap. Both methyl groups are α-oriented, while the sugar moiety at C2 and the fully extended [$\tau_{9,11,12,13}$ = −170.8 (3)°] side chain are β-oriented.

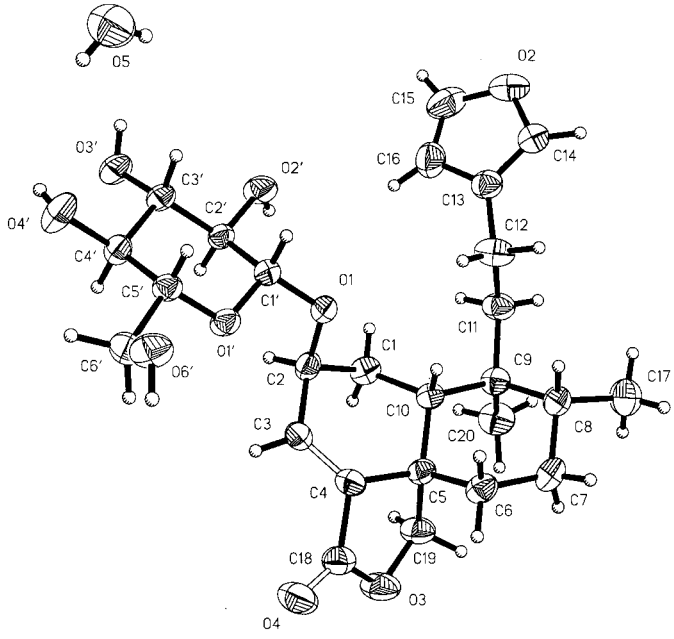


Figure 1
Displacement ellipsoid plot of (I). Ellipsoids are shown at 50% probability while H atoms are represented by spheres of arbitrary size.

The packing scheme may be described as follows: layers of glycoside molecules approximately parallel to the [503] plane are formed by hydrogen bonding among the hydroxyl groups O3′—H3′*A*, O4′—H4′*A* and O6′—H6′ of the sugar moiety with the corresponding O atoms O2′, O6′ and O4′, respectively, of symmetry-related molecules. Water molecules interconnect these layers with three hydrogen bonds acting as donors towards the lactone carbonyl O4 atom and the hydroxyl O3′ atom, while the water O5 atom acts as acceptor for the H atom from the hydroxyl O2′—H2′*A* group (Table 1).

Experimental

The dried and finely powdered aerial parts of *S. amarissima* were extracted with acetone at room temperature. The extract was subjected to a partition between methanol and hexane. The methanolic extract was fractionated over a celite column using mixtures of hexane–ethyl acetate–acetone of increasing polarity. The fractions eluted with 9:1 (*A*) and 4:1 (*B*) ethyl acetate–acetone contained the title compound. Fractions *A* and *B* were combined, decoloured with activated charcoal and crystallized from methanol–water to obtain the title compound (m.p. 393–405 K). The anhydrous form melts at 479–481 K.

Crystal data

$C_{26}H_{36}O_9\cdot H_2O$
M_r = 510.56
Monoclinic, *C*2
a = 16.997 (2) Å
b = 8.441 (1) Å
c = 17.763 (1) Å
β = 92.57 (1)°
V = 2545.9 (4) Å^3
Z = 4
D_x = 1.332 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 41 reflections
θ = 5.0–12.5°
μ = 0.10 mm^{-1}
T = 293 (2) K
Prism, colourless
0.60 × 0.50 × 0.20 mm

Data collection

Siemens *P*4/PC diffractometer
$\omega/2\theta$ scans
8034 measured reflections
7373 independent reflections
4762 reflections with $I > 2\sigma(I)$
R_{int} = 0.037
θ_{max} = 30.0°
$h = 0 \rightarrow 23$
$k = 0 \rightarrow 11$
$l = -24 \rightarrow 24$
3 standard reflections
every 97 reflections
intensity decay: 3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.062
$wR(F^2)$ = 0.143
S = 1.03
7373 reflections
439 parameters
Only coordinates of H atoms refined
$w = 1/[\sigma^2(F_o^2) + (0.0463P)^2 + 0.1240P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.017
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.0076 (7)

H atoms of the hydroxyl groups in the sugar moiety, as well as those of the water molecule, were refined with restraints to give an O—H bond distance in the range 0.85±0.003 Å. The isotropic displacement parameters of the H atoms were given as $U_{iso} = 1.2U_{eq}$ of the parent atom. Diffraction data were collected for one quarter of the sphere plus several hundred Friedel opposites. Since the refinement of the Flack parameter [−0.4 (12); Flack, 1983] was not useful in assigning the absolute configuration, it was instead assigned by internal reference based on the stereochemistry of the sugar moiety. Amarisolide was resistant to hydrolysis under acidic or basic conditions.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2′—H2′*A*···O5^{i}	0.80 (4)	1.91 (4)	2.688 (4)	166 (4)
O3′—H3′*A*···O4′^{ii}	0.85 (3)	1.87 (4)	2.721 (4)	178 (4)
O4′—H4′*A*···O6′^{ii}	0.74 (4)	2.17 (4)	2.769 (3)	139 (5)
O6′—H6′···O2′^{iii}	0.86 (4)	1.90 (4)	2.741 (3)	166 (4)
O5—H5*A*···O3′^{iv}	0.73 (4)	2.14 (4)	2.854 (4)	165 (6)
O5—H5*B*···O4^{v}	0.72 (4)	2.13 (4)	2.826 (4)	162 (6)

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

Nevertheless, the aglycone was obtained by fungal action of Fusarium moniliforme, which is known to use the sugar moieties of glucosides as a carbon source (García *et al.*, 1979). The absolute configuration was therefore assigned to agree with the known chirality of the glucosyl moiety at C2.

Data collection: *XSCANS* (Siemens, 1993); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL*/*PC* (Sheldrick, 1990); software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1187). Services for accessing these data are described at the back of the journal.

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