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Asperuloside monohydrate

Anthony Linden,[a]* Ihsan Çalis,[b] Markus Neuburger[c] and Otto Sticher[d]

[a]Institute of Organic Chemistry, University of Zurich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland, [b]Department of Pharmacognosy, Faculty of Pharmacy, Hacettepe University, TR-06100 Ankara, Turkey, [c]Institute of Inorganic Chemistry, University of Basel, Spitalstrasse 51, CH-4056 Basel, Switzerland, and [d]Department of Applied Biosciences, Institute of Pharmaceutical Sciences, Swiss Federal Institute of Technology (ETH) Zurich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland
Correspondence e-mail: alinden@oci.unizh.ch

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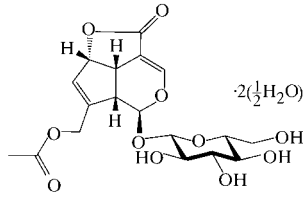
The title compound, [2a*S*-(2aα,4aα,5α,7bα)]-5-(β-D-glucopyranosyloxy)-2a,4a,5,7b-tetrahydro-1-oxo-1*H*-2,6-dioxacyclopent[*cd*]inden-4-ylmethyl acetate monohydrate, $C_{18}H_{22}O_{11}\cdot H_2O$, was extracted from the Turkish plant *Putoria calabrica* (L. fil.) DC. The three fused rings have envelope or distorted envelope conformations and form a bowl in which ring strain causes distortion of some bond angles and significant pyramidalization of two of the Csp^2 atoms. The ring junction H atoms are all *cis* to one another and the glycosidic linkage is in the β axial position. The structure incorporates two symmetry-independent water molecules, each of which is located on a twofold axis. Intermolecular hydrogen bonds involving all the hydroxy groups and water molecules link the molecules into a complex three-dimensional framework.

Comment

As a part of our phytochemical research on the plants of the flora of Turkey, we investigated *Putoria calabrica* (L. fil.) DC (*Rubiaceae*) (Ehrendorfer, 1982) and isolated several iridoid glucosides. Among them, two compounds were separated as a mixture from which the major component, the title compound, (I), was crystallized. The spectroscopic data (^{1}H and ^{13}C NMR) of this component correspond well with those reported for the known iridoid glucoside asperuloside (Bobbitt & Segebarth, 1969; Bailleul *et al.*, 1977). A chromatographic comparison with an authentic sample of asperuloside confirmed the identity of (I) and its crystal structure was determined in order to confirm the stereochemistry. The spectroscopic data obtained for the minor component of the mixed fraction are similar to those of asperuloside, but there are subtle differences. A further analysis of this latter compound is in progress.

Compound (I) crystallizes as a monohydrate, but there are actually two symmetry-independent water molecules in the structure, each of which sits on a twofold axis. The three fused rings in (I) form a bowl with C10 at the base (Fig. 1). The H atoms at the ring junctions C10, C11 and C14 all lie on the outside surface of the bowl and *cis* to one another. The conformation of the lactone ring lies between an envelope with C10 as the flap and a half-chair twisted on C10—C11. The puckering parameter (Cremer & Pople, 1975) φ_2 is 240.3 (5)°. Values of 234 and 252° would correspond with an ideal half-chair and an envelope conformation, respectively. Atom C10 is −0.321 (7) Å from the plane defined by O9, C9 and C15, while C11 is only 0.165 (7) Å from this plane. The cyclopentene ring has an envelope conformation [φ_2 = 357.3 (6)°] with C10, the envelope flap, lying 0.387 (4) Å from the plane defined by C11, C12, C13 and C14. The maximum deviation of these latter four atoms from their mean plane is 0.0059 (15) Å for C12. This conformation is dictated by the steric requirements of the C12═C13 bond.



(I)

The best description for the conformation of the fused six-membered ring is also an envelope (Boeyens, 1978), as the puckering parameters θ and φ_2 are 123.8 (2) and 290.6 (3)°, respectively. Atom C14 forms the envelope flap and lies 0.636 (3) Å from the plane defined by C7, O7, C8, C9 and C10. The maximum deviation of these latter five atoms from their mean plane is 0.0437 (15) Å for C9. The fused six-membered ring can be thought of as a pseudo-sugar ring in which the glycosidic bridging atom, O1, is in the β axial position. Considering this ring, the torsion angles about the glycosidic linkage, O7—C7—O1—C1 and C14—C7—O1—C1, correspond with the −synclinal (−*sc*) and +antiperiplanar (+*ap*) conformations, respectively, which defines the A1 conformer (de Hoog *et al.*, 1969).

The glucoside ring has a normal chair conformation with a puckering parameter θ of 7.9 (2)°, and the hydroxymethyl substituent adopts the *gauche–trans* conformation with respect to O5 and C4, respectively. The torsion angles about the glycosidic linkage, O5—C1—O1—C7 and C2—C1—O1—C7, define the E1 conformer and deviate only very slightly from the most stable −*sc* and +*ap* conformations.

The structure of only one other asperuloside derivative has been reported (Böjthe-Horváth *et al.*, 1982). That derivative, (II), possesses a 1-(4-hydroxyphenyl)propionyl substituent at C2 of the glucoside ring, but is otherwise identical to compound (I). The overall conformations of the fused three-ring systems of (I) and (II) are very similar, as are the orientations of the glucoside ring with respect to the fused rings. However, while the acetyl substituent at C13 in (I) is folded

back under the base of the fused rings and lies nearly parallel to the mean C13—C14—C7—O1 vector, the corresponding substituent in (II) lies virtually perpendicular to this direction and tends to head away from the glucoside ring. This difference is presumably dictated by the different crystal packing requirements introduced by the 1-(4-hydroxyphenyl)propionyl substituent in (II).

The bond lengths in (I) are normal. The O9—C11 bond in the lactone ring is not significantly elongated, unlike the corresponding bond in (II), which was found to be 1.505 (5) Å. The strain of the fused-ring system is highlighted by distortions of some bond angles from normal values. In particular, the angles C10—C9—C15 and C12—C13—C14 are about 10° smaller than normally observed about Csp^2 atoms, while the C9—C10—C11, C10—C11—C12 and C10—C14—C13 angles are also up to 10° smaller than normal (Table 1). Conversely, the C7—C14—C13 angle is about 10° larger than normal. Similar trends are found in the structure of (II). Although C9 has sp^2 hybridization, it is significantly pryamidalized. The sum of the bond angles about C9 is only 355.0 (3)° and this atom lies 0.184 (3) Å from the plane defined by C8, C10 and C15. In (II), this pyramidalization is slightly more severe, with the sum of the angles about the corresponding atom being 353.6°. To a lesser extent, C13 is also slightly pyramidalized and lies 0.073 (3) Å from the plane defined by C12, C14 and C16.

Each hydroxy group in (I) acts as a donor for intermolecular hydrogen bonds (Table 2). The four acceptor atoms are all in different neighbouring molecules and consist of two hydroxy O atoms, the carbonyl O atom of the acetyl substituent and one water molecule (O12). Because this water molecule sits on a twofold axis, it accepts a hydrogen bond from each of two symmetry-related asperuloside molecules. The other water molecule does not accept any hydrogen bonds. Each water molecule acts as a donor for two hydrogen bonds: one donates to the methylhydroxy O atom on the glucoside ring of each of two symmetry-related asperuloside molecules, while the other water molecule donates to the carbonyl O atom of the lactone ring, also in each of two symmetry-related asperuloside molecules. The combination of all these hydrogen-bonding interactions links the molecules into an infinite three-dimensional framework (Fig. 2).

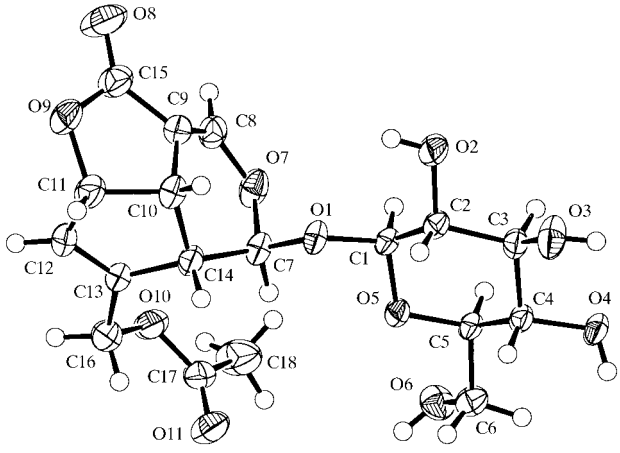


Figure 1
The molecular structure of (I) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by circles of arbitrary size. The water molecules have been omitted.

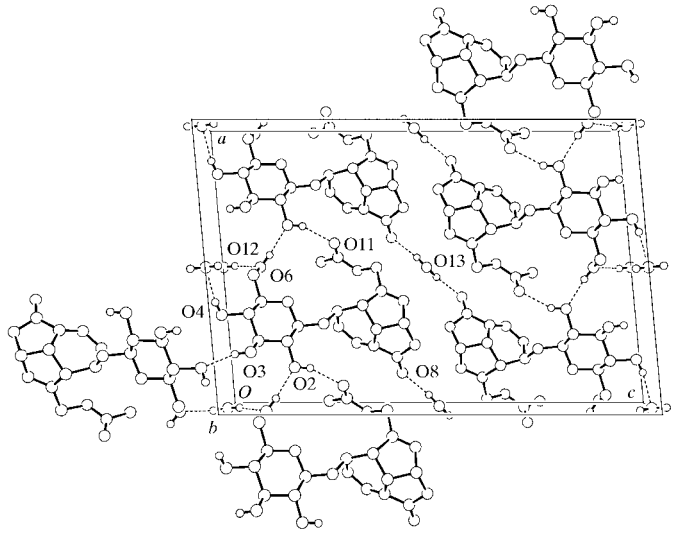


Figure 2
The crystal packing of (I) viewed down the *b* axis showing the network of hydrogen bonds (dashed lines). H atoms not involved in hydrogen bonding have been omitted for clarity.

Experimental

The plant material of *Putoria calabrica* (L. fil.) DC was collected from Antakya, Turkey, in June 1999. The voucher specimen has been deposited at the herbarium of the Faculty of Pharmacy, Hacettepe University, Ankara. The whole dried plant material was extracted with MeOH at 323 K. The water soluble part of the methanolic extract was fractionated over polyamide yielding several fractions. The fractions rich in iridoids were further subjected to column chromatography on silica gel using CH_2Cl_2/MeOH/H_2O (90:10:1 → 85:15:1.5) as eluants. This produced additional fractions containing two compounds, of which (I) was the major component that subsequently crystallized as a pure compound from the solution. Recrystallization from ethyl acetate yielded needle-shaped crystals (m.p. 404–405 K).

Crystal data

$C_{18}H_{22}O_{11}\cdot H_2O$	D_x = 1.470 Mg m^{-3}
M_r = 432.38	Mo $K\alpha$ radiation
Monoclinic, *C*2	Cell parameters from 13 638 reflections
a = 15.1250 (4) Å	θ = 1–30°
b = 5.67020 (10) Å	μ = 0.125 mm^{-1}
c = 22.8781 (5) Å	*T* = 291 (2) K
β = 95.3753 (13)°	Needle, colourless
V = 1953.44 (8) Å^3	0.35 × 0.10 × 0.10 mm
Z = 4	

Data collection

Nonius KappaCCD area-detector diffractometer	R_{int} = 0.032
φ and ω scans with θ offsets	θ_{max} = 30.01°
10 609 measured reflections	*h* = −21 → 21
3091 independent reflections	*k* = −7 → 7
2393 reflections with $I > 2\sigma(I)$	*l* = −31 → 31

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0544P)^2 + 0.1452P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.041$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.101$	$\Delta\rho_{max} = 0.23$ e Å^{-3}
$S = 1.028$	$\Delta\rho_{min} = -0.19$ e Å^{-3}
3091 reflections	Extinction correction: *SHELXL*97 (Sheldrick, 1997)
284 parameters	Extinction coefficient: 0.0043 (9)
H atoms treated by a mixture of independent and constrained refinement	

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.416 (2)	O7—C8	1.353 (3)
O1—C7	1.406 (3)	O9—C11	1.466 (3)
O5—C1	1.414 (2)	O9—C15	1.362 (3)
O5—C5	1.439 (2)	C8—C9	1.326 (3)
O7—C7	1.437 (3)	C12—C13	1.334 (3)
C8—C9—C10	123.83 (19)	O9—C11—C12	112.9 (2)
C8—C9—C15	122.1 (2)	C10—C11—C12	101.89 (17)
C10—C9—C15	109.06 (19)	C13—C12—C11	112.80 (19)
C9—C10—C11	98.99 (17)	C12—C13—C14	110.7 (2)
C9—C10—C14	108.63 (19)	C7—C14—C10	109.70 (17)
C11—C10—C14	106.69 (16)	C7—C14—C13	119.6 (2)
O9—C11—C10	105.84 (16)	C10—C14—C13	101.77 (16)
C1—O1—C7—O7	−71.2 (2)	C7—O1—C1—C2	178.07 (16)
C1—O1—C7—C14	165.98 (16)	O5—C5—C6—O6	73.4 (2)
C7—O1—C1—O5	−63.4 (2)	C4—C5—C6—O6	−167.47 (16)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O11^{i}	0.82	1.98	2.752 (2)	156
O3—H3···O4^{ii}	0.82	2.08	2.800 (2)	147
O4—H4···O12^{iii}	0.82	2.03	2.8347 (18)	169
O6—H6···O2^{iv}	0.82	1.90	2.717 (2)	174
O12—H12···O6	0.85 (3)	1.88 (3)	2.729 (2)	173 (3)
O13—H13···O8^{v}	0.895 (19)	1.98 (2)	2.863 (3)	169 (5)

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

Reflection 004 was omitted from the final refinement because of suspected severe extinction effects. The methyl and hydroxy H atoms were constrained to an ideal geometry with $U_{iso}(H) = 1.5U_{eq}$(parent atom), but were allowed to rotate freely about the C—C or O—C bonds. The two unique water H atoms were located from a difference Fourier map and their positions were refined with $U_{iso}(H) = 1.5U_{eq}(O)$. An O—H bond-length restraint of 0.82 (2) Å was applied in the case of the water molecule involving O13. All other H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms with $U_{iso}(H) = 1.2U_{eq}(C)$. The data set included 2213 pairs of Friedel-related reflections, which gave a coverage of 72% of the total possible number of Friedel pairs with $\theta < \theta_{max}$. Due to the lack of anomalous scatterers, the absolute configuration could not be established reliably, as illustrated by the value of −0.6 (10) obtained for the Flack *x* parameter (Flack, 1983) derived during a structure-factor calculation using a data set in which all Friedel-related reflections were treated as independent. The absolute structure was therefore set in accordance with the known configuration of the glucoside moiety. As there was no significant anomalous dispersion, the final refinement cycles were carried out using a data set in which the Friedel-related reflections had been merged.

Data collection: *KappaCCD Server Software* (Nonius, 1999); cell refinement: *DENZO-SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN*; program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1376). Services for accessing these data are described at the back of the journal.

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