metal-organic compounds

Absolute configuration of strictosidinic acid

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The absolute configuration of strictosidinic acid, (2S,3R,4S)-3-ethenyl-2-(β-D-glucopyranosyloxy)-4-{[(1S)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl]methyl}-3,4-dihydro-2H-pyran-5-carboxylate, was determined from its sodium chloride trihydrate, poly[[diaqua((2S,3R,4S)-3-ethenyl-2-(β-D-glucopyranosyloxy)-4-{[(1S)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]-indol-2-ium-1-yl]methyl}-3,4-dihydro-2H-pyran-5-carboxylate)sodium] chloride monohydrate], {[Na(C$_{26}$H$_{32}$N$_2$O$_9$)-(H$_2$O)$_2$]Cl·H$_2$O}$_n$. The strictosidinic acid molecule participates in intermolecular hydrogen bonds of the O—H···O and O—H···Cl types. The solid-state conformation was observed as a zwitterion, based on a charged pyridine N atom and a carboxylate group, the latter mediating the packing through coordination with the sodium cation.

Comment

Palicourea coriacea (Rubiaceae), popularly known as Douradinha, is a typical plant of the Brazilian savanna (Cerrado), whose tea is popularly used in folk medicine for the treatment of kidney stones and kidney and urethra inflammation, as well as having an effective diuretic action. Previous studies of this genus have yielded triterpenes (Bolzani *et al.*, 1992), alkaloids (do Nascimento *et al.*, 2006), fluoroacetate (Kemmerling, 1996), coumarins (El-Seedi, 1999) and macrocyclic peptides (Bokesch *et al.*, 2001), many of them possessing interesting biological properties, such as anti-HIV (Bokesch *et al.*, 2001) and anticancer activities (Hartwell, 1971). As part of our continued interest in plants from the Brazilian Cerrado (Lião *et al.*, 2001), we have investigated the leaves of *P. coriacea*. Strictosidinic acid, an alkaloid that has important biological properties, was isolated and its structure has been elucidated based on NMR and IR spectroscopic data, and its absolute structure was determined by X-ray crystallographic analysis.

The strictosidinic acid molecule is composed of a tryptoline moiety bonded to a pyran ring bonded to a β-glucose group.

This molecule crystallized as a sodium chloride trihydrate, (I), with three water molecules, a coordinated sodium cation and a chloride counter-ion. The indole group of the tryptoline moiety shares a double bond [C2=C10 = 1.371 (6) Å] with the six-membered heterocyclic pyridinium ring (N13/C1/C2/C10/C11/C12), which adopts a half-chair conformation with the protonated N13 atom as the flap atom [puckering parameters: Q = 0.513 (4) Å, θ = 49.7 (5)° and φ = 349.6 (7)°; Cremer & Pople, 1975; Spek, 2009]. The pyran ring (C20/C19/O18/C17/C16/C15) includes a C=C double bond [C16=C17 = 1.341 (6) Å] which allows for a half-chair conformation with C20 as the flap atom [puckering parameters: Q = 0.501 (5) Å, θ = 125.1 (5)° and φ = 198.6 (6)°]. This pyran ring is substituted with a carboxylate group (C21/O22/O23) in the 5-position (on C16), which is coordinated to the sodium cation through the O22 carbonyl group. Atom O23 transfers its proton to amine atom N13 and is a strong hydrogen-bond acceptor from both N13 and the O1S water molecule (Table 1), which is also coordinated to the sodium cation. The C21=O22 bond is lengthened to 1.248 (5) Å and C21—O23 is shortened to 1.274 (5) Å, indicating that electron delocalization increases in this group. Given that the C15—C16—C21—O23 torsion angle is 9.8 (6)°, there is no resonance between the carboxylate group and the pyran ring C=C double bond, which is reflected in the elongation of the C16—C21 single bond to 1.501 (6) Å, compared with the expected formal bond distance. The N13—C1 and N13—C12 single bonds of 1.509 (6) and 1.501 (6) Å, respectively, indicate that the N13 atom is sp³-hybridized. The β-glucose group shows a chair conformation [puckering parameters: Q = 0.574 (5) Å, θ = 6.0 (5)° and φ = 300 (4)°], with O32 as the pivot atom.

(I)
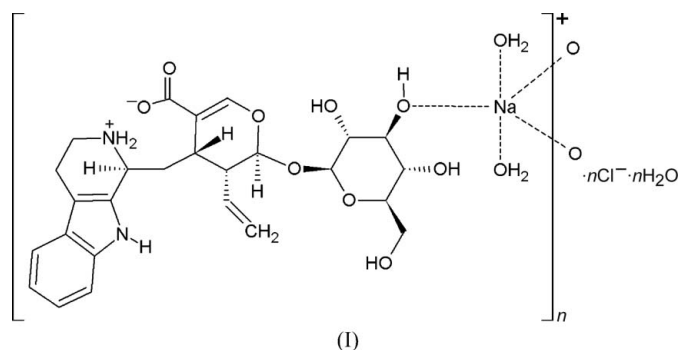
A search of the Cambridge Structural Database (CSD, Version 5.23, May 2011 update; Allen, 2002) gave two structures with a chiral tryptoline moiety not substituted in the C12 and N13 positions, namely 1(S)-(α-D-arabinofuranosyl)-1,2,3,4-tetrahydro-β-carboline (CSD refcode DOJBIN; Piper *et al.*, 1985) and 1-[2-(pyrrolidin-1-yl)phenyl]-2,3,4,9-tetrahydro-1H-β-carboline (HOPNOQ; Zhang *et al.*, 2009). In general, the bond lengths are comparable within standard uncertainty, the exceptions (see Table 1) being N3—C2 which is shorter in (I) by 0.036 Å compared to DOJBIN, N13—C1 which is longer in (I) by 0.032 and 0.026 Å, respectively, compared to DOJBIN and HOPNOQ, and N13—C12 which is longer in (I) by 0.03 Å compared to HOPNOQ. These elon-
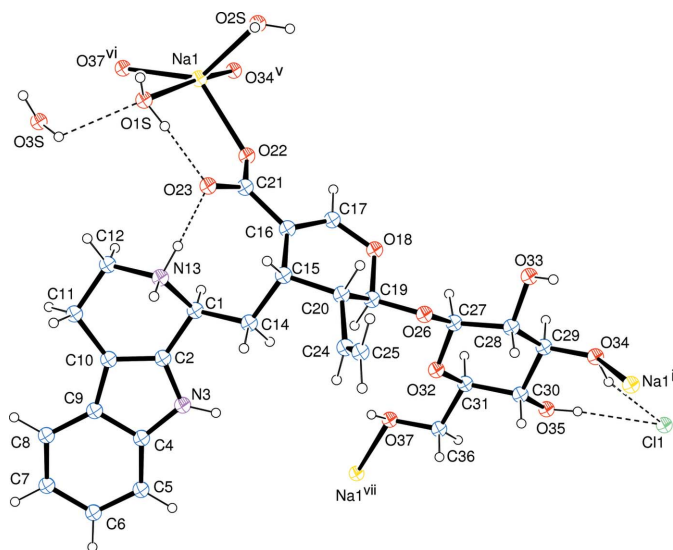
Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. Dashed lines indicate intramolecular interactions. [Symmetry codes: (i) $x + \frac{1}{2}$, $-y + \frac{3}{2}$, $-z + 1$; (v) $x - \frac{1}{2}$, $-y + \frac{3}{2}$, $-z + 1$; (vi) $-x + \frac{1}{2}$, $-y + 2$, $z - \frac{1}{2}$; (vii) $-x + \frac{1}{2}$, $-y + 2$, $z + \frac{1}{2}$.]

gated N13—C bonds might be ascribed to the lowered charge density in these bonds due to the quaternary N atom.

Because the natural extract contained salt, this allowed the establishment of the absolute configuration of (I) (Flack & Bernardinelli, 1999, 2000); we determined the chiral centers as follows: C1 *S*, C15 *S*, C19 *S*, C20 *R*, C27 *S*, C28 *R*, C29 *S*, C30 *R* and C31 *R*.

The sodium cation is involved in the packing stabilization mediating the intermolecular interactions, being five-coordinated by the hydroxy O34^{vi} atom, the methoxy O37^{v} atom, the carboxylate O22 atom and the O1*S* and O2*S* water molecules (symmetry codes as in Fig. 1). In the crystal, there are classical intermolecular interactions (*a*) where the strictosidinic acid molecule acts as a donor (O33—H33···O22^{i}) and (*b*) involving the coordinated O2*S* water molecule (O2*S*—H2*SB*···O35^{i}). There are also nonclassical intermolecular hydrogen-bond interactions, *viz*. O34—H34···Cl1, O35—H35···Cl1 and O37—H37···Cl1^{iv} (Table 2). The O3*S* water molecule is involved in intermolecular interactions both as a donor, *viz*. in O3*S*—H3*SA*···O1*S* and O3*S*—H3*SB*···O26^{iii}, and as an acceptor, *viz*. in O2*S*—H2*SA*···O3*S*^{ii} (symmetry codes as in Table 2). All these intermolecular interactions create a three-dimensional polymeric chain.

Experimental

The air-dried and powdered leaves (362 g) of *P. coriacea* were successively extracted with EtOH (1.5 l for 48 h). The resulting extract was filtered and concentrated under reduced pressure to give 41.3 g of residue to which was added a 10% HOAc solution (250 ml) and the suspension was kept at 278 K overnight. The suspension was filtered and the acidic aqueous phase was partitioned with CH₂Cl₂. The resulting aqueous layer was basified (pH 8–9) with saturated

NaHCO₃ solution, and was then extracted with CH₂Cl₂. The combined organic layers were treated with Na₂SO₄ and filtered, affording a CH₂Cl₂ basic fraction. Strictosidinic acid (29 mg) was obtained from a crude methanolic extract of the leaves after repeated fractionation using column chromatography (CHCl₃/MeOH gradient eluent system) followed by preparative thin-layer chromatography on silica gel (organic phase: *n*-butanol/HOAc/H₂O 4:1:5 *v*/*v*/*v*). Crystals suitable for single-crystal X-ray diffraction studies were obtained as yellow blocks by recrystallization from chloroform and methanol (1:1 *v*/*v*) (m.p. 482–485 K).

Crystal data

[Na(C₂₆H₃₂N₂O₉)(H₂O)₂]Cl·H₂O	$V = 2904.3$ (3) Å^3
$M_r = 629.02$	$Z = 4$
Orthorhombic, $P2_12_12_1$	Cu $K\alpha$ radiation
$a = 7.6419$ (4) Å	$\mu = 1.89$ mm^{-1}
$b = 16.2205$ (8) Å	$T = 100$ K
$c = 23.4299$ (12) Å	$0.2 \times 0.15 \times 0.1$ mm

Data collection

Bruker SMART APEX DUO diffractometer	22917 measured reflections
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)	5062 independent reflections
	4390 reflections with $I > 2\sigma(I)$
$T_{min} = 0.706$, $T_{max} = 0.835$	$R_{int} = 0.078$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.063$	H atoms treated by a mixture of
$wR(F^2) = 0.159$	independent and constrained
$S = 1.14$	refinement
5062 reflections	$\Delta\rho_{max} = 0.53$ e Å^{-3}
402 parameters	$\Delta\rho_{min} = -0.26$ e Å^{-3}
6 restraints	Absolute structure: Flack (1983), 2134 Friedel pairs
	Flack parameter: 0.04 (3)

All water H atoms were located in a difference Fourier map, and refined with restraints on bond distances using O—H = 0.84 (2) Å.

Table 1
Exceptional tryptoline moiety bond lengths (Å).

Bond	(I)	DOJBIN	HOPNOQ
N3—C2	1.353 (6)	1.389 (4)	1.374 (3)
N13—C1	1.509 (6)	1.477 (4)	1.483 (3)
N13—C12	1.501 (6)	1.487 (5)	1.471 (3)

CSD refcodes: DOJBIN (Piper *et al.*, 1985) and HOPNOQ (Zhang *et al.*, 2009).

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

D—H···A	D—H	H···A	D···A	D—H···A
O1*S*—H1*SB*···Cl1^{i}	0.84 (2)	2.35 (2)	3.192 (4)	177 (6)
O1*S*—H1*SA*···O23	0.85 (2)	1.85 (2)	2.694 (5)	176 (7)
O2*S*—H2*SA*···O3*S*^{ii}	0.84 (2)	1.90 (3)	2.726 (6)	165 (7)
O2*S*—H2*SB*···O35^{i}	0.83 (2)	2.00 (3)	2.816 (5)	167 (6)
O3*S*—H3*SA*···O1*S*	0.85 (2)	2.33 (8)	2.801 (6)	115 (7)
O3*S*—H3*SB*···O26^{iii}	0.85 (2)	2.50 (4)	3.276 (5)	152 (7)
O33—H33···O22^{i}	0.84	1.95	2.711 (4)	151
O34—H34···Cl1	0.84	2.42	3.217 (3)	158
O35—H35···Cl1	0.84	2.30	3.134 (3)	172
O37—H37···Cl1^{iv}	0.84	2.43	3.209 (4)	154
N3—H3···Cl1^{iv}	0.88	2.44	3.314 (4)	173
N13—H13*B*···O23	0.92	1.69	2.576 (5)	160

Symmetry codes: (i) $x + \frac{1}{2}, -y + \frac{3}{2}, -z + 1$; (ii) $-x + 1, y - \frac{1}{2}, -z + \frac{1}{2}$; (iii) $-x + \frac{3}{2}, -y + 2, z - \frac{1}{2}$; (iv) $-x + 1, y + \frac{1}{2}, -z + \frac{3}{2}$.

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The remaining H atoms were positioned geometrically (aromatic C—H = 0.95 Å, methine C—H = 1.00 Å, alkyl C—H = 0.99 Å, ethylene C—H = 0.95 Å, N^+—H = 0.92 Å, aromatic N—H = 0.88 Å and hydroxy O—H = 0.84 Å) and refined using a riding model, with $U_{iso}(H) = 1.2U_{eq}(C, N, O_{water})$ and $1.5U_{eq}(O_{hydroxy})$. Hydroxy groups were allowed to rotate in order to fit the difference electron-density map.

Data collection: *APEX2* (Bruker, 2007); cell refinement: *SAINT* (Bruker, 2007); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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