organic papers

Amygdalin trihydrate

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Extensive hydrogen bonding is present in the crystal structure of the title compound [systematic name: (R)-1-cyano-1-(phenylmethyl)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside], $C_{20}H_{27}NO_{11}\cdot 3H_2O$, involving all of the hydroxy groups. The water molecules are also involved in the hydrogen bonding; in particular, one of them acts as a bridge between the endocyclic O atoms of the two sugar residues. The overall conformation of the disaccharide is described by the *exo*-anomeric conformations, $\varphi''_H = 26°$ and $\varphi'_H = 38°$, together with an antiperiplanar extended conformation of the constituent sugar residues, with $\psi'' = 155°$.

Comment

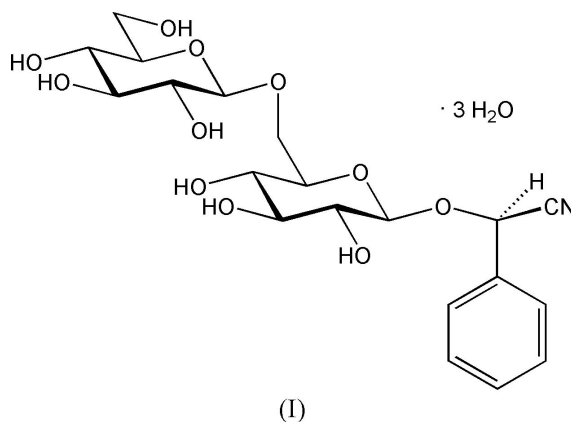Amygdalin is a cyanogenic glycoside found in the kernels of, for example, apples, almonds and peaches (Jones, 1998). More than 2500 plant species have been identified as containing cyanogenic compounds (Moller *et al.*, 1999). The title compound is a diglycosyl glycoside from which cytotoxic hydrogen cyanide can be released, leading to acute cyanide poisoning. This (R)-1-cyano-1-(phenylmethyl)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside, (I), has been studied in solution by NMR spectroscopy (Ribeiro, 1990) and recently also in the solid state as a function of temperature (Widmalm *et al.*, 2003). It was found that the phenyl ring exhibited thermally activated dynamics about the *para* axis, whereas the glucosyl residues remained static. We present here the crystal structure of amygdalin trihydrate, and analyze a number of important degrees of freedom with respect to its torsion angles and the possibility of forming a complex hydrogen-bonding network due to the presence of three ordered water molecules per amygdalin molecule.
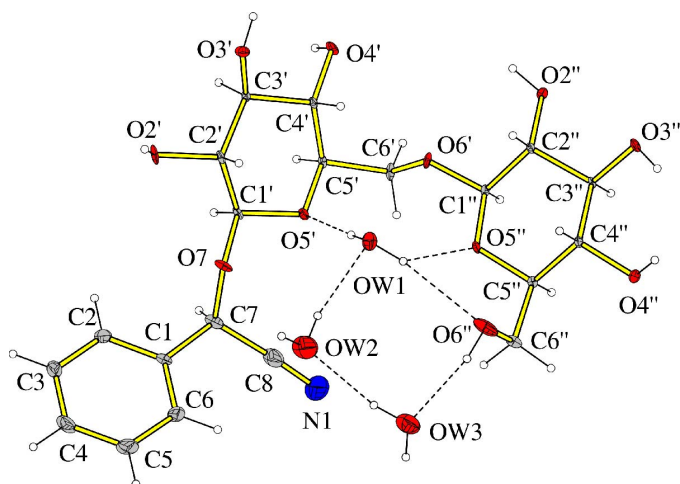

(I)

The conformation of an oligosaccharide is described by the torsion angles φ and ψ at the glycosidic linkage between the

Figure 1
Molecular structure of (I), showing 50% probability displacement ellipsoids. Hydrogen-bond contacts are shown as dashed lines.

constituent monosaccharides. The φ and ψ angles for the present compound are defined by φ'' ($O5''-C1''-O6'-C6'$), φ' ($O5'-C1'-O7-C7$), ψ'' ($C1''-O6'-C6'-C5'$) and ψ' ($C1'-O7-C7-C1$). Selected torsion angles are shown in Table 1.

The additional major degree of freedom in a hexopyranosyl residue is the conformational preference of the hydroxy-methyl group. In amygdalin this is described by the torsion angles ω'' ($O5''-C5''-C6''-O6''$) and ω' ($O5'-C5'-C6'-O6'$), the latter being part of the ($1\rightarrow6$) linkage. The two ω torsion angles both correspond to the *gg* conformation (Fig. 1), which is one of the two found to be significantly populated in solution. The two φ_H torsion angles are in the vicinity of the *exo*-anomeric conformation ($\varphi_H \simeq 50°$), as indicated by the torsion angles φ''_H ($H1''-C1''-O6'-C6'$) and φ'_H ($H1'-C1'-O7-C7$) (Table 1). For the β-($1\rightarrow6$) linkage the value of ψ'' leads to an extended antiperiplanar conformation, also found in solutions of similar compounds, on the basis of NMR spectroscopic and computer simulation studies (Lycknert *et al.*, 2004).

The torsion angle at the glycosidic linkage to the aglycone, ψ', results in spatial proximity of atoms H1$'$ and H7 and, in oligosaccharide terminology, a *syn* conformation. For the aglyconic part, the torsion angle χ (C2—C1—C7—O7) describes the orientation of the phenyl group. The latter is planar within less than 0.01 (1) Å, with atom C7 deviating by 0.023 (2) Å from the least-squares plane defined by the phenyl ring. The plane defined by atoms C1, C7 and C8 is inclined by 14.0 (2)° to the phenyl ring plane. Atom N1 is displaced by 0.060 (4) Å from the C1/C7/C8 plane.

The Cremer & Pople (1975) parameters for the two sugar rings are $Q = 0.5915$ (11) Å, $\theta = 3.85$ (11)° and $\varphi = 221.4$ (15)° for the O5$''$ $\rightarrow$ C5$''$ direction, and $Q = 0.5607$ (10) Å, $\theta = 12.68$ (10)° and $\varphi = 345.5$ (6)° for the O5$'$ $\rightarrow$ C5$'$ direction. Both of the sugar residues have the anticipated chair conformation, *i.e.* $^4C_1$.

All hydroxy groups act as donors in intermolecular hydrogen bonds. The O3$''$ hydroxy group is also involved in an intramolecular hydrogen bond to O4$''$. All hydroxy groups, except O4$'$, also act, at least once, as hydrogen-bond acceptors. Furthermore, atoms O4$''$ and O2$'$ are dual hydrogen-bond acceptors. The three water molecules (OW1, OW2 and OW3) act as dual hydrogen-bond donors. In fact, OW1 provides donor H atoms for three hydrogen bonds, *viz.* one simple and one bifurcated. Two of the water molecules are single acceptors and one (OW1) is a dual hydrogen-bond acceptor. Interestingly, OW1 mediates the intramolecular hydrogen bonding between O5$'$ and O5$''$. A view of the hydrogen-bond pattern around the three water molecules is shown in Fig. 1. In addition, atom N1 is an acceptor in the hydrogen-bond pattern. The sugar residues pack in the *ab* plane and the phenyl rings are involved in π–π interactions *via* a T-shaped edge-to-face arrangement (Meyer *et al.*, 2003). The angle between the least-squares planes of the phenyl rings at (x, y, z) and ($2 - x, \frac{1}{2} + y, 2 - z$) is 77.02 (4)°. The distance between the centers of gravity of these rings is 4.930 (1) Å, comparable to that in the crystal structure of edge-to-face oriented benzene (5.025 Å). A diagram of the packing, viewed along the *a* axis, is shown in Fig. 2. C—H$\cdots\pi$ interactions are present (Table 2), similar to the aromatic interaction described above. Although weak, the C—H$\cdots\pi$ interactions play important structure-stabilizing roles, in particular for carbohydrate–protein complexes.

Experimental

Amygdalin [or (*R*)-1-cyano-1-(phenylmethyl)-β-D-glucopyranosyl-($1\rightarrow6$)-β-D-glucopyranoside] was obtained from C. A. F. Kahlbaum GmbH, Berlin, Germany. The compound was crystallized by slow evaporation of a mixture of water, ethanol and acetonitrile (1:1:1) at ambient temperature, yielding needles which were mounted with epoxy glue on to glass fibres. The scattering power of the crystals was weak; thus it was decided to collect data with synchrotron radiation at beamline I711 at the Swedish synchrotron radiation facility MAXLAB, Lund, Sweden.

Crystal data

$C_{20}H_{33}NO_{14}$	Synchrotron radiation
$M_r = 511.47$	$\lambda = 0.891$ Å
Monoclinic, $P2_1$	Cell parameters from 999
$a = 9.4794$ (11) Å	reflections
$b = 7.9025$ (9) Å	$\theta = 3.0$–$29.0°$
$c = 16.2016$ (19) Å	$\mu = 0.12$ mm^{-1}
$\beta = 94.089$ (3)°	$T = 110$ (2) K
$V = 1210.6$ (2) Å^3	Plate, colorless
$Z = 2$	$0.20 \times 0.10 \times 0.02$ mm
$D_x = 1.403$ Mg m^{-3}	

Data collection

Bruker SMART 1K area-detector diffractometer	5454 independent reflections
ω scans at different φ and 2θ	5010 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2002)	$R_{int} = 0.031$
	$\theta_{max} = 45.9°$
$T_{min} = 0.98$, $T_{max} = 1.00$	$h = -15 \rightarrow 14$
20604 measured reflections	$k = -10 \rightarrow 12$
	$l = -16 \rightarrow 25$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0714P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.037$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.097$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.04$	$\Delta\rho_{max} = 0.50$ e Å^{-3}
5454 reflections	$\Delta\rho_{min} = -0.55$ e Å^{-3}
343 parameters	Extinction correction: *SHELXL97*
H atoms treated by a mixture of independent and constrained refinement	Extinction coefficient: 0.051 (3)

Table 1
Selected torsion angles (°).

C2—C1—C7—O7	69.87 (16)	C6′—O6′—C1″—O5″	−94.69 (11)
C1—C7—O7—C1′	−145.08 (11)	O5″—C5″—C6″—O6″	−61.27 (13)
O7—C7—C8—N1	172 (3)	H1″—C1″—O6′—C6′	25.7
C7—O7—C1′—O5′	−83.22 (12)	H1′—C1′—O7—C7	37.8
O5′—C5′—C6′—O6′	−74.07 (12)	C1′—O7—C7—H7	−28.1
C5′—C6′—O6′—C1″	154.93 (10)		

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

Cg is the centroid of the phenyl ring.

D—H···A	D—H	H···A	D···A	D—H···A
O2′—H2X···O2″^{i}	0.84	1.88	2.701 (1)	166
O3′—H3X···OW1	0.84	2.02	2.813 (2)	157
O4′—H4X···O3′^{ii}	0.84	2.00	2.817 (1)	164
O2″—H2Y···O3″^{iii}	0.84	1.85	2.690 (1)	175
O3″—H3Y···O4″	0.84	2.40	2.835 (1)	113
O3″—H3Y···O2^{iv}	0.84	2.51	3.346 (1)	176
O4″—H4Y···O2^{iv}	0.84	1.99	2.823 (1)	174
O6″—H62C···OW3^v	0.84	1.96	2.774 (1)	162
OW1—H1W1···O5′^{ii}	0.82 (2)	2.14 (2)	2.958 (2)	173 (2)
OW1—H2W1···O5″^{ii}	0.84 (2)	2.26 (2)	2.904 (1)	133 (2)
OW1—H2W1···O6″^{ii}	0.84 (2)	2.36 (2)	3.126 (2)	151 (2)
OW2—H1W2···OW1	0.81 (3)	2.07 (3)	2.864 (2)	165 (3)
OW2—H2W2···O4″^{iii}	0.82 (2)	2.04 (2)	2.860 (2)	174 (2)
OW3—H1W3···OW2	0.83 (2)	1.95 (2)	2.760 (2)	164 (2)
OW3—H2W3···N1^{vi}	0.83 (2)	2.28 (2)	3.094 (2)	167 (2)
C5—H5···Cg^{vii}	0.95	2.71	3.590 (2)	155
C5″—H5″···Cg^{viii}	1.00	2.83	3.640 (2)	138

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

H atoms were positioned geometrically and allowed to ride on their parent atoms, with CH, CH$_2$ and aromatic C—H bonds set equal to 1.00, 0.99 and 0.95 Å, respectively, and U_{iso}(H) = 1.2U_{eq}(C) and 1.5U_{eq}(O). A 'rigid-bond' restraint was applied to U^{ij} values (Rollett, 1970). The Flack (1983) parameter was inconclusive, but the absolute configuration was set by the *a priori* knowledge that the sample is a known natural product. In the absence of significant anomalous scattering effects, the 5001 Friedel pairs were merged.
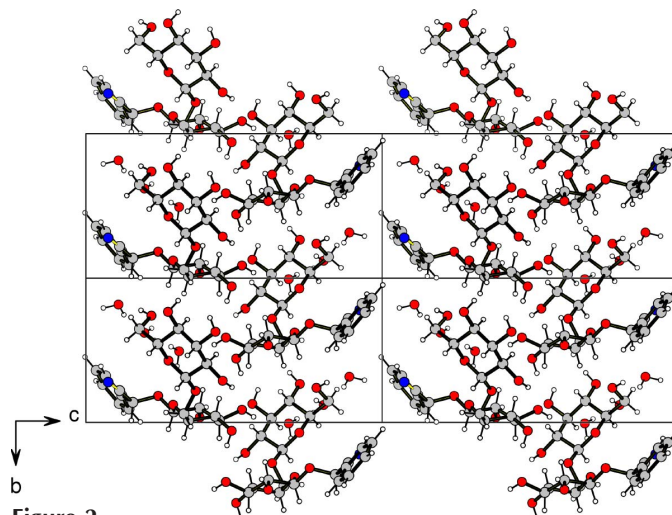

Figure 2
Packing view along the *a* axis, showing the contents of slightly more than four unit cells.

Data collection: *SMART* (Siemens, 1998); cell refinement: *SMART*; data reduction: *SAINT* (Siemens, 1998); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *DIAMOND* (Bergerhoff, 1996); software used to prepare material for publication: *PLATON* (Spek, 2003).

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