ware (Enraf-Nonius, 1989) with local modifications. Cell refinement: *SET*4 (de Boer & Duisenberg, 1984). Data reduction: *HELENA* (Spek, 1990*a*). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *SHELX*76 (Sheldrick, 1976). Molecular graphics: *PLATON*93 (Spek, 1990*b*). Software used to prepare material for publication: *PLATON*93.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: AB1112). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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1-Deoxynojirimycin Hydrochloride

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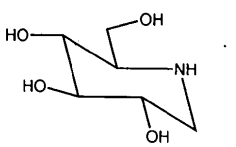
Abstract

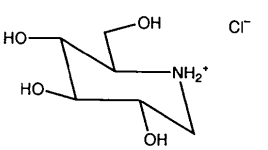
The structure of the hydrochloride salt of 1-deoxynojirimycin [(1*R*,3*R*,4*R*,5*S*)-3,4,5-trihydroxy-2-(hydroxymethyl)piperidinium chloride, $C_6H_{14}NO_4^+.Cl^-$] is reported. The cation has an almost undistorted $^4C_1$ conformation. The crystal structure is built up from alternating layers of cations and anions interconnected by a three-dimensional network of hydrogen bonds. Each chloride ion is coordinated through four hydrogen bonds and there are also two intercationic hydrogen bonds.

Comment

1-Deoxynojirimycin [1,5-dideoxy-1,5-imino-glucitol (I)] is a strong competitive inhibitor of α- and β-glucosidases (Legler, 1990). It has been isolated from various strains of *Bacillus* (Schmidt, Frommer, Müller & Truscheit, 1979), from plants of the genus *Morus* (Yagi, Kouno, Aoyagi & Murai, 1976) and from the root bark of the mulberry tree (Daigo, Inamori & Takemoto, 1986). It has been synthesized by a variety of routes (*e.g.* Paulsen, Sangster



(I)



(II)

& Heyns, 1967; Inouye, Tsuruoka, Ito & Niida, 1968; Vasella & Voeffray, 1982; Bernotas & Ganem, 1985; Beaupere, Stasik, Uzan & Demailly, 1989; Fleet, Carpenter, Petursson & Ramsden, 1990; Ermert & Vasella, 1991). As a result of its inhibitory potential and its stability in water, it has been used in glycobiology (Winchester & Fleet, 1992) for such purposes as altering the processing of N-linked glycoproteins (Elbein, 1987) or inhibition of syncytium formation of HIV-infected cells (Gruters *et al.*, 1987). The mechanism of inhibition exerted by (I) is still unclear. It is neither a transition-state analogue (Dale, Ensley, Kern, Sastry & Byers, 1985) nor, presumably, a substrate analogue. The X-ray structure of the complex between (I) and the glucoamylase from *Aspergillus awamori* var. X100 has been published recently (Harris, Aleshin, Firsow & Honzatko, 1993). The resolution of the study (2.4 Å) did not permit the determination of the conformation of the inhibitor at the active site. According to NMR studies (Ermert & Vasella, 1991) the conformation of (I) and the hydrochloride (II) in aqueous solution is $^4C_1$. The X-ray structure determination of the hydrochloride (II), reported here, complements the existing structural information.

A view of the cation showing the atom-numbering scheme is shown in Fig. 1. The absolute configuration of (II) was assigned to agree with that of its known precursor, D-glucose, and was further confirmed by the X-ray analysis.

The bond lengths and angles within the cation exhibit normal values, although the C(1)—N(5)—C(5) angle has opened to 113.5 (1)°. The ring conformation is $^4C_1$ and the torsion angles around the piperidine ring show that the

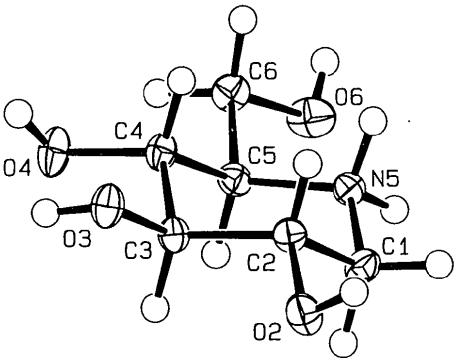


Fig. 1. View of the cation of (II) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by spheres of arbitrary size.

ring conformation is quite close to a perfect chair. Only two other structures containing the hydroxymethylpiperidine moiety have been reported: the nojirimycin bisulfite dihydrate adduct (Kodama, Tsuruoka, Niwa & Inouye, 1985) and 4-*O*-α-D-glucopyranosyl-*N*-methylmoranoline dihydrate (Ezure, Yoshikuni, Ojima, Sugiyama, Hirotsu & Higuchi, 1987). These structures also exhibit very regular and virtually undistorted piperidine rings. The C—N bond lengths in 4-*O*-α-D-glucopyranosyl-*N*-methylmoranoline are slightly shorter than those observed for (II), since the latter compound has a positive charge at the N atom.

The orientation of the C(6)—O(6) bond is *gauche-trans* in the crystal, whereas the *gauche-gauche* conformation is predominant in solution (Bock & Pedersen, 1988; Ermert & Vasella, 1991). The preference for the *gauche-trans* conformation in the solid state is not due to intramolecular hydrogen bonds, of which none were found, but arises from the crystal packing, which is dominated by a complex three-dimensional network of interionic hydrogen bonds.

Fig. 2 presents a packing diagram in which the hydrogen bonds are emphasized. Each hydroxyl group of the cation acts as a hydrogen-bond donor. Two of the hydroxyl groups also act as hydrogen-bond acceptors, thereby forming intercationic hydrogen bonds. These two intercationic hydrogen bonds join the same two cations and link the cations into infinite one-dimensional zigzag chains which run parallel to the *a* axis. Each chloride anion is hydrogen bonded to four different cations in an asymmetric fashion. Two of the hydroxyl H atoms and both H atoms of the $-NH_2^+$ group act as donors to chloride anions. All of the hydrogen-bonding interactions combine to form a three-dimensional network. Fig. 2 also shows that the packing of the anions and cations forms a layered structure with alternating layers of cations and anions lying parallel to the *ac* plane.

Note added in proof. After this work had been accepted for publication, the structure of the free base, 1-deoxynojirimycin, was reported (Hempel, Camerman, Mastropaolo & Camerman, 1993). The conformation of the hydrochloride salt is very similar to that of the free base, including the O(6)—C(6)—C(5)—C(4) torsion angle.

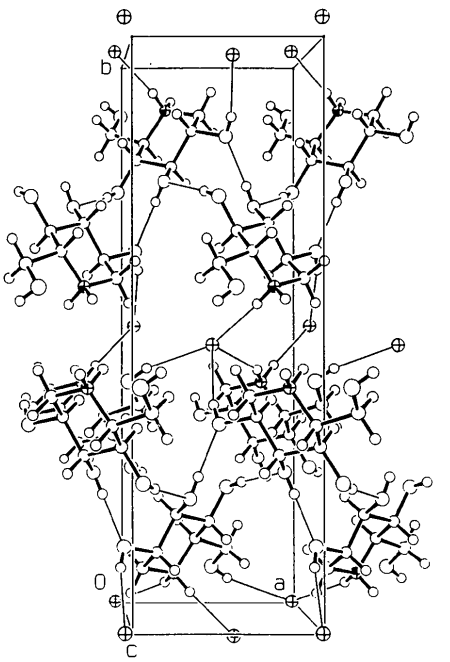


Fig. 2. The packing of (II) in the unit cell viewed down **c** showing the hydrogen-bonding interactions.

Experimental

The title compound (II) was prepared from the readily available (Hoos, Naughton & Vasella, 1993; Overkleeft, Wiltenburg & Pandit, 1993) 5-amino-5-deoxy-2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactam (Nippon Shinyaku Co., Ltd, 1980) by reduction (Ermert & Vasella, 1991; Overkleeft, Wiltenburg & Pandit, 1993) followed by hydrogenolysis in acetic acid and conversion of the resulting hydroacetate to (II) (Ermert & Vasella, 1991). Crystals suitable for X-ray analysis were obtained from methanol/ethyl acetate after purification of crude (II) by reversed-phase HPLC with H_2O as eluant. The crystals deteriorated rapidly after removal from the mother liquor at room temperature, presumably losing HCl. However, the crystals remained stable under a nitrogen gas stream at 173 K for the duration of the data collection.

Crystal data

$C_6H_{14}NO_4^+.Cl^-$
M_r = 199.63
Orthorhombic
$P2_12_12_1$
a = 6.648 (3) Å
b = 20.473 (5) Å
c = 6.400 (3) Å
V = 871.1 (5) Å^3
Z = 4
D_x = 1.522 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 25 reflections
θ = 19.5-20°
μ = 0.412 mm^{-1}
T = 173 (1) K
Prism
0.50 × 0.45 × 0.15 mm
Colourless

Data collection

Rigaku AFC-5*R* diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical (*DIFABS*; Walker & Stuart, 1983)
T_{min} = 0.87, T_{max} = 1.18
3650 measured reflections
2526 independent reflections
2340 observed reflections [$I > 3\sigma(I)$]
R_{int} = 0.029
θ_{max} = 30°
$h = -9 \rightarrow 9$
$k = -28 \rightarrow 28$
$l = -9 \rightarrow 9$
3 standard reflections monitored every 150 reflections
intensity variation: insignificant

Refinement

Refinement on *F*
R = 0.0233
wR = 0.0250
S = 1.583
2340 reflections
165 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o) + (0.005F_o)^2]$
$(\Delta/\sigma)_{max}$ = 0.0003
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	*y*	*z*	U_{eq}
Cl(1)	0.94566 (4)	0.01701 (1)	0.25789 (5)	0.02231 (8)
O(2)	0.4547 (2)	0.35143 (4)	−0.0119 (2)	0.0244 (3)
O(3)	0.7959 (1)	0.27121 (5)	−0.0283 (2)	0.0226 (3)
O(4)	1.0311 (2)	0.26318 (5)	0.3529 (2)	0.0257 (3)
O(6)	0.9929 (1)	0.42103 (5)	0.7763 (2)	0.0288 (3)
N(5)	0.7508 (2)	0.41684 (5)	0.4328 (2)	0.0178 (3)
C(1)	0.5710 (2)	0.40169 (6)	0.3016 (2)	0.0203 (3)
C(2)	0.6326 (2)	0.36609 (6)	0.1038 (2)	0.0178 (3)
C(3)	0.7414 (2)	0.30373 (6)	0.1602 (2)	0.0176 (3)
C(4)	0.9280 (2)	0.32076 (6)	0.2890 (2)	0.0180 (3)
C(5)	0.8728 (2)	0.35762 (6)	0.4889 (2)	0.0178 (3)
C(6)	1.0573 (2)	0.38011 (6)	0.6084 (2)	0.0217 (3)

Table 2. *Selected geometric parameters* (Å, °)

O(2)—C(2)	1.427 (2)	C(1)—C(2)	1.517 (2)
O(3)—C(3)	1.425 (2)	C(2)—C(3)	1.511 (2)
O(4)—C(4)	1.424 (1)	C(3)—C(4)	1.529 (2)
O(6)—C(6)	1.428 (2)	C(4)—C(5)	1.530 (2)
N(5)—C(1)	1.493 (2)	C(5)—C(6)	1.517 (2)
N(5)—C(5)	1.502 (2)		
C(1)—N(5)—C(5)	113.5 (1)	O(4)—C(4)—C(3)	110.9 (1)
N(5)—C(1)—C(2)	110.7 (1)	O(4)—C(4)—C(5)	106.5 (1)
O(2)—C(2)—C(1)	108.1 (1)	C(3)—C(4)—C(5)	111.6 (1)
O(2)—C(2)—C(3)	110.1 (1)	N(5)—C(5)—C(4)	109.1 (1)
C(1)—C(2)—C(3)	109.6 (1)	N(5)—C(5)—C(6)	108.2 (1)
O(3)—C(3)—C(2)	108.3 (1)	C(4)—C(5)—C(6)	112.2 (1)
O(3)—C(3)—C(4)	110.9 (1)	O(6)—C(6)—C(5)	108.4 (1)
C(2)—C(3)—C(4)	108.93 (9)		
C(1)—C(2)—C(3)—C(4)	−59.7 (1)	C(5)—N(5)—C(1)—C(2)	−56.4 (1)
C(2)—C(3)—C(4)—C(5)	59.1 (1)	N(5)—C(1)—C(2)—C(3)	58.5 (1)
C(3)—C(4)—C(5)—N(5)	−55.0 (1)	O(6)—C(6)—C(5)—C(4)	172.5 (1)
C(4)—C(5)—N(5)—C(1)	53.8 (1)	O(6)—C(6)—C(5)—N(5)	52.1 (1)

Table 3. *Hydrogen-bond geometry* (Å, °)

D—H···A	D—H	H···A	D···A	D—H···A
O(2)—H(21)···Cl(1^{i})	0.82 (2)	2.32 (2)	3.120 (1)	165 (2)
O(3)—H(31)···O(2^{ii})	0.80 (2)	1.95 (2)	2.736 (2)	169 (2)
O(4)—H(41)···O(3^{ii})	0.86 (2)	1.97 (2)	2.813 (2)	169 (2)
N(5)—H(51)···Cl(1^{iii})	0.96 (2)	2.30 (2)	3.141 (1)	145 (1)
N(5)—H(52)···Cl(1^{iv})	0.91 (2)	2.22 (2)	3.125 (1)	171 (2)
O(6)—H(61)···Cl(1^{v})	0.80 (2)	2.55 (3)	3.274 (2)	150 (2)

H(21^{ii})···Cl(1)···H(51^{v})	85.5 (6)
H(21^{ii})···Cl(1)···H(52^{vi})	115.7 (6)
H(21^{ii})···Cl(1)···H(61^{iii})	67.0 (7)
H(51^{v})···Cl(1)···H(52^{vi})	85.4 (6)
H(51^{v})···Cl(1)···H(61^{iii})	132.5 (6)
H(52^{vi})···Cl(1)···H(61^{iii})	140.9 (7)

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

The data collection was extended to include the measurement of the intensities of the Friedel opposites of all reflections in the unique octant. Friedel pairs were not averaged during the data reduction. The absolute configuration was determined using the program *CRYSTALS* (Watkin, Carruthers & Betteridge, 1985) to refine the final atomic coordinates together with the enantiopole parameter (Flack, 1983). The refined value of the enantiopole parameter was 0.00 (5), thus confirming that the atomic coordinates represented the correct enantiomorph. Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1991). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN PROCESS* (Molecular Structure Corporation, 1989). Program(s) used to solve structure: *SHELXS86 PATTERSON* (Sheldrick, 1990). Program(s) used to refine structure: *TEXSAN LS*. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *TEXSAN FINISH*.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71824 (19 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: SH1087]

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Crystal Studies of Musk Compounds. VII.† Molecular Structures of 1-*tert*-Butyl-2,4,6-trimethyl-3,5-dinitrobenzene, $C_{13}H_{18}N_2O_4$ (2), and 1-Bromo-3,5-dimethyl-2,4,6-trinitrobenzene, $C_8H_6BrN_3O_6$ (4)

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Abstract

The crystal structures of the title compounds (both non-musks) have been determined by X-ray diffraction. The angles between the nitro groups and the phenyl ring [75.1 (3)–86.6 (3)° for (2) and 67.8 (3)–80.1 (3)° for (4)] are compared with the values found in two strong musk compounds [(1) and (3)]. The phenyl ring in (4) is essentially planar; in (2), significant distortions from planarity are observed.

† This work forms part of a thesis by De Ridder (1992).

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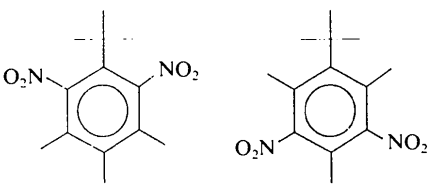
Comment

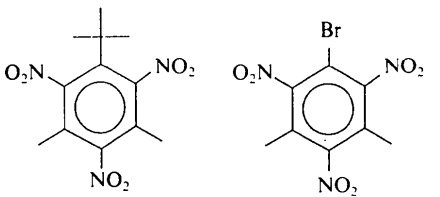
In the first paper of this series (De Ridder, Goubitz & Schenk, 1990), the molecular structure of Musk Ambrette was described. This compound belongs to the class of nitrobenzene musks of which Musk Tibetene (1) and Musk Xylene (3) are two other examples.

In 1977, Beets introduced the pseudo-*meta* and pseudo-*ortho* musks enabling the classification of the nitrobenzene compounds: the prefix pseudo is based on two postulates in which he stated that a nitro group is able to play two different roles, depending on its position in the total structure (Beets, 1957, 1977). According to the first postulate, a nitro group in a sterically unhindered position, permitting its coplanarity with the benzene ring, may act, in the absence of more effective candidates, as a functional group analogous to an acetyl group. The second postulate states that a nitro group, of which the coplanarity with the benzene ring is prevented by one or two adjacent bulky substituents and of which, consequently, the O atoms are forced out of the plane of the benzene ring, may function as a detail of the molecular profile in a way analogous to a tertiary butyl group, of which two methyl groups are necessarily projecting out of the plane of the ring. According to these postulates, (3) is a pseudo-*ortho* musk in which the nitro group in the *para* position with respect to the *tert*-butyl group has the osmophoric function and one of the nitro groups *ortho* to the *tert*-butyl group has the sterical function. These postulates do not explain why (1) is a strong musk, since both nitro groups are not in sterically unhindered positions. Contrary to these postulates, (2), which can easily be classified as a pseudo-*meta* musk, is odourless (Pesaro, 1990).

In (4), the *tert*-butyl group of Musk Xylene (3) has been replaced by a Br atom, resulting in a non-musk (Döpp, 1991).



(1) (2)



(3) (4)

In the light of these postulates, it was deemed useful to determine the structures of (2) and (4), thus enabling a comparison with the structures of the strong musks (1) and (3).