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Methyl [2,4,5-trihydroxy-6-(hydroxymethyl)-perhydropyran-3-yl]carbamate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.030
wR factor = 0.078
Data-to-parameter ratio = 6.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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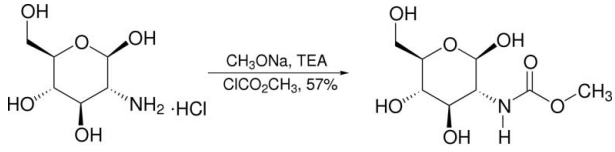
The title compound, $C_8H_{15}NO_7$, the methyl carbamate of β-D-glucosamine has been synthesized, in moderate yield, from the reaction of β-D-glucosamine hydrochloride and methyl chloroformate. There are two crystallographically independent molecules in the asymmetric unit. In both molecules, the pyranose ring adopts a slightly distorted chair conformation. In the crystal structure, molecules are packed along the a axis, with intra- and intermolecular O—H···O, N—H···O and C—H···O hydrogen bonds.

Comment

Amino-sugars have attracted growing interest due to their broad spectrum of application in chemistry, biochemistry, medicinal and pharmaceutical fields (Kirschning *et al.*, 1997; Johnson & Liu, 1998; Elchert *et al.*, 2004). For more than 30 years, non-steroidal anti-inflammatory drugs (NSAID) have been used in the treatment of osteoarthritis (OA). Serious and often life-threatening adverse effects due to these agents are common. Clinical findings have revealed that glucosamine sulfate and chondrotin sulfate are effective and safer alternatives for the alleviation of the symptoms of OA. Experimental evidence indicates that these compounds and their low molecular weight derivatives have a particular tropism for cartilage where they serve as substrates in the biosynthesis of component building blocks of glycosamineglycans (Ferguson 2005). Because joint pain is so debilitating, glucosamine alone is sometimes not enough, and it is important to further improve its biological activity.



(I) (II)

Our research group has recently taken an interest in the synthetic manipulations of amino-sugars to develop some efficient pharmacophores to combat OA. The title compound, (II), is the methyl carbamate derivative of β-D-glucosamine (Viscontini & Meier, 1952). However, their procedure did not produce (II) in sufficient yield. Instead, we employed the Boullanger strategy (Boullanger *et al.*, 1987]; this resulted in a moderate yield (57%) from the reaction of β-D-glucosamine hydrochloride, (I), with methyl chloroformate in the presence of triethylamine and sodium methoxide.

The conformation of the pyranose ring is $^4C_1$ in both independent molecules; the puckering parameters are Q = 0.565 (2)/0.564 (2) Å, θ = 5.1 (2)/6.2 (2)° and φ = 52 (3)/55 (2)°

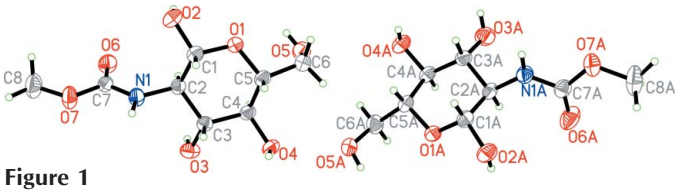


Figure 1
The asymmetric unit of (II), showing 50% probability displacement ellipsoids and the atom-numbering scheme.

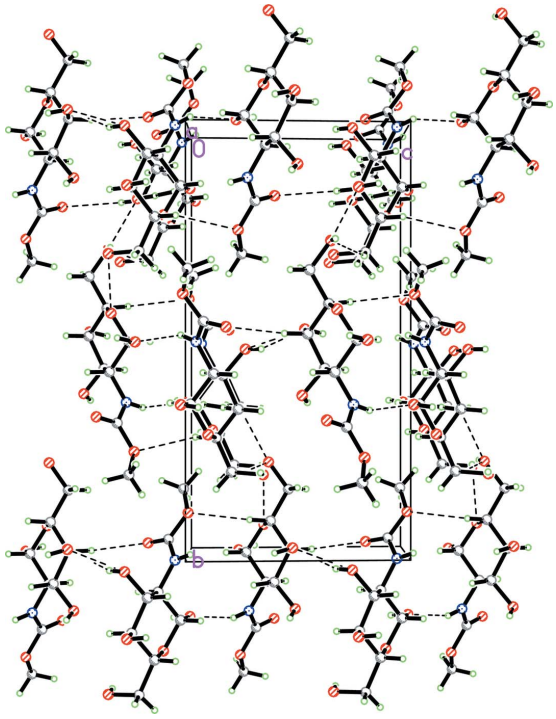


Figure 2
Molecular packing of (II), viewed along the *a* axis. Hydrogen bonds are indicated by dashed lines.

(Cremer & Pople, 1975). The pyranose rings are distorted from an ideal chair conformation, allowing the C1—O1—C5 and C1*A*—O1*A*—C5*A* bond angles to widen to 113.0 (2) and 114.3 (2)°, respectively, while the other internal ring angles remain close to the tetrahedral value. The C—C bond lengths lie in the range 1.516 (3)–1.530 (3) Å. The shortening of the O2—C1 and O2*A*—C1*A* bond lengths [1.391 (3) and 1.392 (3) Å, respectively] compared to the O1—C1 and O1*A*—C1*A* bond lengths [1.414 (3) & 1.416 (3) Å, respectively] indicates a significant anomeric effect, which is normally found in free sugar derivatives (Berman *et al.*, 1967). There is electron delocalization over O6═C7—O7 and O6*A*═C7*A*—O7*A*, resulting in the shortening of the O7—C7 and O7*A*—C7*A* bond lengths [1.344 (3) and 1.345 (3) Å, respectively]. The torsion angles C5—O1—C1—O2 = 174.2 (17)° and C5*A*—O1*A*—C1*A*—O2*A* = 172.6 (17) Å indicate the *β*-configuration of the substitutent at the C1 and C1*A* anomeric centers.

Extensive O—H···O type hydrogen bonding is present in (II), accounting for the molecular conformation and stability of the crystal structure. All available O and N atoms are involved in the hydrogen bonding (Fig. 2 and Table 1).

Experimental

β-D-Glucosamine hydrochloride, (I), (1.0 g, 4.6 mmol) was added to a sodium methoxide solution (4.6 ml methanol and 106 mg sodium metal were mixed and shaken at room temperature for 10 min and then at 273 K for 5 min). Triethylamine (0.3 ml, 4.6 mmol) was added dropwise to the reaction flask, with subsequent addition of methyl chloroformate (0.18 ml, 4.6 mmol) at 273 K. The reaction was completed after 20 min and the solvent was then evaporated. The title compound, (II), was purified by flash column chromatography, and crystallized from dichloromethane and methanol (20:80) in 57% yield (616 mg; m.p. 469 K).

Crystal data

$C_8H_{15}NO_7$
M_r = 237.21
Monoclinic, $P2_1$
a = 6.5236 (5) Å
b = 17.5861 (14) Å
c = 9.0279 (7) Å
β = 94.710 (1)°
V = 1032.23 (14) Å^3
Z = 4
D_x = 1.526 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5705 reflections
θ = 2.3–25.0°
μ = 0.14 mm^{-1}
T = 293 (2) K
Block, colorless
0.64 × 0.56 × 0.14 mm

Data collection

Siemens SMART CCD area detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.919, T_{max} = 0.981
5804 measured reflections
2082 independent reflections
2033 reflections with $I > 2\sigma(I)$
R_{int} = 0.023
θ_{max} = 26.0°
$h = -8 \rightarrow 7$
$k = -21 \rightarrow 15$
$l = -10 \rightarrow 11$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.078
S = 1.08
2082 reflections
324 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0456P)^2 + 0.1323P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.016 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*A*—H1*AA*···O2^{i}	0.86	2.19	3.007 (3)	159
N1—H1*A*···O2*A*^{ii}	0.86	2.22	3.016 (3)	155
O2—H2*A*···O4^{iii}	0.81 (4)	1.93 (4)	2.731 (2)	171 (3)
O3—H3*A*···O6^{iv}	0.84 (3)	1.98 (3)	2.800 (3)	168 (3)
O4—H4*A*···O5*A*^{v}	0.87 (4)	1.89 (3)	2.750 (3)	166 (3)
O5—H5*A*···O1*A*^{iii}	0.88 (7)	2.18 (6)	2.883 (3)	137 (5)
O2*A*—H2*AA*···O4*A*^{iv}	0.93 (3)	1.84 (4)	2.755 (3)	171 (3)
O3*A*—H3*AA*···O6*A*^{iii}	0.78 (4)	2.01 (4)	2.793 (3)	173 (4)
O4*A*—H4*AA*···O3^{vi}	0.78 (4)	1.99 (4)	2.766 (3)	171 (4)
O5*A*—H5*AA*···O5^{iv}	0.81 (5)	2.06 (5)	2.865 (3)	169 (4)
C2—H2*B*···O6^{v}	0.98	2.47	2.843 (3)	102
C2*A*—H2*AB*···O6*A*^{v}	0.98	2.46	2.821 (3)	101
C4—H4*B*···O5^{v}	0.98	2.58	2.931 (3)	101
C4—H4*B*···O6*A*^{vii}	0.98	2.51	3.388 (3)	149
C4*A*—H4*AB*···O6^{vi}	0.98	2.45	3.432 (3)	175
C5—H5*B*···O7*A*^{ii}	0.98	2.55	3.446 (3)	152
C5*A*—H5*AB*···O7^{i}	0.98	2.56	3.477 (3)	157
C6—H6*B*···O5*A*^{v}	0.97	2.56	3.395 (3)	144
C6*A*—H6*AA*···O4*A*^{v}	0.97	2.59	2.969 (3)	103
C8—H8*A*···O1^{viii}	0.96	2.57	3.229 (4)	126

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

All C– and N-bound H atoms were positioned geometrically and allowed to ride on their parent atoms, with C—H = 0.97–0.98 Å and N—H = 0.86 Å, and U_{iso}(H) = 1.5U_{eq}(C) for methyl H and 1.2U_{eq}(C) for others. A rotating group model was used for the methyl group. The hydroxyl H atoms were located in a difference map and their parameters were freely refined; the O—H distances lie in the range 0.78 (4)–0.93 (4) Å. In the absence of significant anomalous dispersion effects, Friedel pairs were averaged before the final refinement and the absolute configuration was assigned on the basis of the starting material.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*, *PARST* (Nardelli, 1995) and *PLATON* (Spek, 2003).

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