Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Methyl 2,3,6-tri-*O*-benzoyl-4-deoxy-4-methoxyamino-α-D-glucopyranoside

Olivier Renaudet, Pascal Dumy* and Christian Philouze

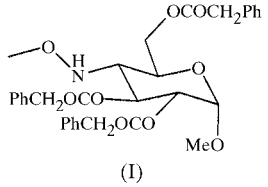
LEDSS, UMR CNRS 5616, Université Joseph Fourier, BP 53, 38041 Grenoble CEDEX 9, France
Correspondence e-mail: pascal.dumy@ujf-grenoble.fr

Received 6 November 2000
Accepted 1 December 2000

The crystalline-state conformation of the title compound, $C_{29}H_{29}NO_9$, has been established unequivocally. The *R* absolute configuration is observed at the 4-methoxyamino moiety and the pyranose ring adopts essentially a perfect $^4C_1$ chair. The torsion angle of the exocyclic hydroxymethyl group is shown to be *gauche–gauche* with respect to O1 and C4, respectively. The conformation along the methoxyamino bond is consistent with that observed for calicheamicin γ_1^I.

Comment

Hydroxylamine-substituted sugars are found in an important class of antitumor antibiotics, such as calicheamicin or esperamicin, that cleave DNA specifically (Nicolaou & Dai, 1991). Conformational studies have demonstrated a key role for this unusual N—O linkage in maintaining the oligosaccharide core in the minor groove of DNA (Walker *et al.*, 1994). In this context, the structures of sugars containing the hydroxylamine linkage, such as the title compound, (I), are of interest in order to assess and validate the latter theoretical studies. Reduction of methyl 2,3,6-tri-*O*-benzoyl-4-deoxy-4-methoxyimino-α-D-*xylo*-hexopyranoside with $NaBH_3CN$ at pH = 3 afforded a mixture of the corresponding *gluco*- and *galacto*-methoxyamino diastereoisomers. Recrystallization of the mixture from diethyl ether/petroleum ether allowed the



(I)

separation of each epimer. The structure of (I) (Fig. 1) displays interatomic bond distances and angles (Table 1) in good agreement with those given by Allen *et al.* (1987). The configuration at C4 is *R*, which implies the *gluco* configuration. The ring adopts a quasi-perfect $^4C_1$ chair conformation, as defined by the Cremer & Pople (1975) parameters Q = 0.593 (3) Å, Θ = 2.6 (2)° and Φ_2 = 195 (4)°. This conformation is also adopted in solution, as outlined by the large values of the NMR coupling constant (∼10 Hz). The exocyclic hydroxymethyl group adopts a staggered *gg* conformation [ω = O5—C5—C6—O6 = −70.1 (2)° and C4—C5—C6—O6 = −52.5 (2)°], which is the conformation usually observed in other structures containing *gluco* residues (Marchessault & Pérez, 1979).

The α (C3—C4—N4—O4) and β (C22—O4—N4—C4) torsion angles have values of −51.6 (2) and −160.6 (2)°, respectively, close to those of the global minimum calculated by Walker *et al.* (1994). However, the β value is decreased in comparison with the value of −120° calculated by Walker *et al.* (1994) in the monosaccharide, as well as in comparison with the value of −134° reported by Lee *et al.* (1987) for the crystal structure of calicheamicin γ_1^I. Moreover, NMR measurements in chloroform indicated a small value of $^3J'_{4,NH}$ (2.1 Hz) for the hydroxylamino H atom, which is consistent with an average conformation in which the hydroxylamine H atom is *gauche* to the C4 H atom.

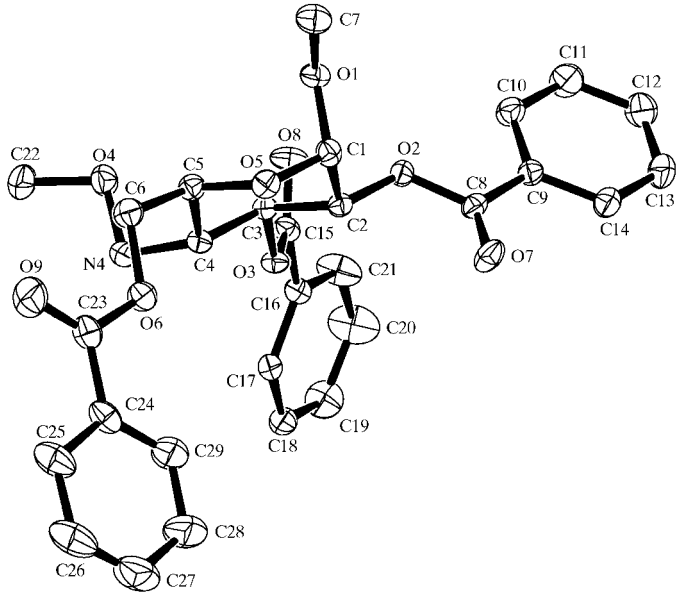


Figure 1
An *ORTEP*II (Johnson, 1976) molecular diagram of the title compound. Displacement ellipsoids are shown at the 40% probability level.

Two kinds of hydrogen bonds co-exist in the structure. The first is intermolecular and results from the crystal packing, forming an infinite chain of molecules running along the *b* axis. The second is intramolecular, linking the N4 atom to the benzoyl O3 atom. The hydrogen-bond details are given in Table 2.

Experimental

The title compound was prepared after reduction of methyl 2,3,6-tri-*O*-benzoyl-4-deoxy-4-methoxyimino-α-D-*xylo*-hexopyranoside (Tronchet *et al.*, 1989) using sodium cyanoborohydride (Borch *et al.*, 1971) with careful control of pH (optimum value = 3). The corresponding *gluco*- and *galacto*-methoxyamino diastereoisomers were separated by liquid chromatography and recrystallized from diethyl ether/petroleum ether (m.p. 396 K). ^{1}H NMR (300 MHz, $CDCl_3$,

p.p.m.): δ 8.12–7.34 (*m*, 15H, aromatic H), 6.17 (*t*, 1H, $^3J_{2,3}$ = $^3J_{3,4}$ = 10.0 Hz, H3), 5.91 (*d*, 1H, $^3J_{4,NH}$ = 2.1 Hz, H21), 5.20 (*dd*, 1H, $^3J_{1,2}$ = 3.6 Hz, H2), 5.16 (*d*, 1H, H1), 4.76–4.72 (*m*, 2H, H6, H7), 4.42 (*td*, 1H, $^3J_{5,6}$ = 3.6 Hz, $^3J_{4,5}$ = 10.3 Hz, H5), 3.51 (*s*, 3H, H8, H9, H10), 3.44 (*s*, 3H, H22, H23, H24) 3.19 (*bt*, 1H, H4); ^{13}C NMR (p.p.m): δ 166.7 (C═O), 166.2 (C═O), 166.0 (C═O), 133.4 [aromatic C (C_{ar})], 133.3 (C_{ar}), 130.1 (C_{ar}), 129.9 (C_{ar}), 129.7 (C_{ar}), 129.3 (C_{ar}), 128.6 (C_{ar}), 128.5 (C_{ar}), 97.2 (C1), 73.3 (C2), 67.8 (C3), 67.3 (C5), 64.3 (C6), 62.9 (C22), 61.4 (C4), 55.6 (C7).

Crystal data

$C_{29}H_{29}NO_9$
M_r = 535.55
Monoclinic, $P2_1$
a = 8.026 (2) Å
b = 12.359 (3) Å
c = 14.056 (3) Å
β = 96.63 (2)°
V = 1384.9 (5) Å^3
Z = 2
D_x = 1.284 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 24 reflections
θ = 10.2–13.3°
μ = 0.096 mm^{-1}
T = 293 K
Monoclinic prism, colorless
0.35 × 0.30 × 0.29 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω scans
4363 measured reflections
4225 independent reflections
3518 reflections with $I > 0.05\sigma(I)$
R_{int} = 0.015
θ_{max} = 29.96°
$h = -11 \rightarrow 11$
$k = 0 \rightarrow 17$
$l = 0 \rightarrow 19$
2 standard reflections
every 120 reflections
intensity decay: 4.23%

Refinement

Refinement on F
R = 0.068
wR = 0.040
S = 1.896
3518 reflections
351 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o) + 0.00008|F_o|^2]$
$(\Delta/\sigma)_{max}$ = 0.022
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.393 (2)	C1—C2	1.521 (3)
O2—C2	1.438 (2)	N4—C4	1.449 (3)
O3—C3	1.447 (2)	C2—C3	1.503 (3)
O4—N4	1.443 (2)	C3—C4	1.517 (2)
O5—C1	1.411 (2)	C4—C5	1.528 (3)
O5—C5	1.433 (2)	C5—C6	1.493 (3)
O6—C6	1.459 (3)		
N4—O4—C22	107.6 (2)	O3—C3—C2	109.3 (1)
C1—O5—C5	114.1 (1)	O3—C3—C4	107.9 (1)
C6—O6—C23	116.6 (2)	C2—C3—C4	108.6 (2)
O4—N4—C4	106.5 (1)	N4—C4—C3	116.0 (2)
O1—C1—O5	112.6 (2)	N4—C4—C5	111.5 (2)
O1—C1—C2	108.1 (1)	C3—C4—C5	108.5 (1)
O5—C1—C2	109.1 (2)	O5—C5—C4	109.4 (2)
O2—C2—C1	110.7 (1)	O5—C5—C6	108.8 (2)
O2—C2—C3	108.6 (1)	C4—C5—C6	114.3 (2)
C1—C2—C3	109.9 (2)	O6—C6—C5	107.4 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
N4—H21···O7^{i}	0.91	2.26	3.085 (2)	151
N4—H21···O3	0.91	2.53	2.895 (2)	105

Symmetry code: (i) $-x, \frac{1}{2}+y, 1-z$.

H atoms were located from a difference map but were not refined (N—H = 0.91 Å and C—H = 0.94–1.06 Å).

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1992–1997); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1993); program(s) used to refine structure: *TEXSAN*; software used to prepare material for publication: *TEXSAN*.

The authors acknowledge support of this work from the CNRS (ACI). This work was also supported by grant No. 98-4-23548 from MENRT (to OR).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1434). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans.* pp. S1–19.
Altomare, A., Cascarano, G., Giacovazzo, C. & Guagliardi, A. (1993). *J. Appl. Cryst.* **26**, 343–350.
Borch, R. F., Bernstein, M. D. & Dupont Durst, H. (1971). *J. Am. Chem. Soc.* **93**, 2897–2904.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Enraf–Nonius (1989). *CAD*-4 *Software.* Version 5.0. Enraf–Nonius, Delft, The Netherlands.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratotry, Tennessee, USA.
Lee, M. D., Dunne, T. S., Chang, C. C., Ellestad, G. A., Siegel, M. M., Morton, G. O., McGahren, W. J. & Borders, D. B. (1987). *J. Am. Chem. Soc.* **109**, 3466–3468.
Marchessault, R. H. & Pérez, S. (1979). *Biopolymers*, **18**, 2369–2374.
Molecular Structure Corporation (1992–1997). *TEXSAN.* Version 1.7. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Nicolaou, K. C. & Dai, W.-M. (1991). *Angew. Chem. Int. Ed. Engl.* **30**, 1387–1416.
Tronchet, J. M. J., Bizzozero, N. & Geoffroy, M. (1989). *Carbohydr. Res.* **191**, 138–143.
Walker, S., Gange, D., Gupta, V. & Kahne, D. (1994). *J. Am. Chem. Soc.* **116**, 3197–3206.