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N-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyloxy)-succinimide

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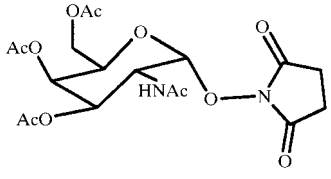
The crystal structure of the title compound, $C_{18}H_{24}N_2O_{11}$, a GalNAc mimic containing an α-glycosyloxysuccinimide linkage, has been determined. The pyranose ring geometry is an almost perfect $^4C_1$ chair. The torsion angle of the exocyclic hydroxymethyl group is shown to be *gauche–trans* with respect to O1 and C4, respectively.

Comment

2-Deoxy-*N*-acetyl-D-galactose (GalNAc) is found within the carbohydrate moiety of tumour-associated antigens such as Tn or TF, as well as in the corresponding silylated derivatives. These carbohydrates are abundantly expressed at the surface of tumour cells and therefore represent interesting biological targets for immunological studies and for immunotherapy. Recently, several groups have devised new synthetic routes which facilitate the chemical synthesis of the glycopeptide conjugate on the basis of chemoselective oxime bond formation (Cao *et al.*, 1995; Rodriguez *et al.*, 1998). In this context, the title compound, (I), a mimic of GalNAc bearing an α-glycosyloxysuccinimide linkage, has been synthesized and its structure determined.



(I)

The observed interatomic bond distances and angles are essentially in good agreement with those given by Allen *et al.* (1987), except for the distances O1—N1, O1—C1 and O5—C1, which are discussed below, and also, somewhat surprisingly, O3—C3 and O3—C13 (Table 1). If one considers the Cremer & Pople (1975) parameters [Q = 0.532 (3) Å, θ = 4.8 (3)° and φ_2 = 210.5 (3)°], the pyranose ring has a perfect $^4C_1$ chair conformation. This conformation is also adopted in solution, as evidenced by the large NMR coupling constant between H2 and H3 (11.8 Hz), indicating a *trans*-diaxial arrangement.

The exocyclic hydroxymethyl group adopts a staggered *gauche–trans* conformation [ω = O5—C5—C6—O6 = 64.9 (3)° and C4—C5—C6—O6 = −173.2 (2)°], which has been shown by Eriksson *et al.* (1996) to be the preferred conformation in crystal structures having the *galacto* configuration, as in (I). The torsion angle φ (H1—C1—O1—N1) has a value of −49°, corresponding to the staggered conformer where the exo-anomeric effect contributes to energy stabilization. The anomeric C1—O1 bond length of 1.449 (2) Å is greater than the average length of such bonds [1.401 (10) Å] reported by Sheldrick (1976). The O1—N1 and O5—C1 bonds also have unusually short values, of 1.373 (2) and 1.394 (3) Å, respectively, in contrast with the literature values of 1.462 (Walker *et al.*, 1994) and 1.430 (10) Å (Sheldrick, 1976). Together, these data may indicate a strong endoanomeric effect, which would result in a shortening of O5—C1 and a lengthening of C1—O1.

As shown in Table 2, an intermolecular hydrogen bond contributes to the crystal packing, forming infinite chains of molecules running along the 2_1 axis.

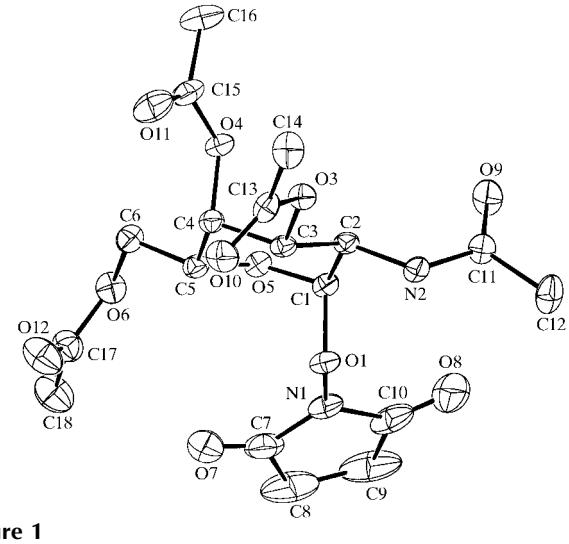


Figure 1
The molecular structure of (I) showing the atom-numbering scheme and with displacement ellipsoids drawn at the 35% probability level. H atoms have been omitted for clarity.

Experimental

Reductive acetylation of the azide *O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl)-*N*-hydroxysuccinimide [prepared following the procedure of Cao *et al.* (1995)], under Pd/C hydrogenation in MeOH/Ac_2O (9:1), provided the title compound after recrystallization from methylene chloride/diethyl ether (Rodriguez *et al.*, 1998). Spectroscopic data, ^{1}H NMR (300 MHz, $CDCl_3$, δ, p.p.m.): 6.07 (*bs*, 1H, $^3J_{2,NH}$ = 9.6 Hz, H15), 5.48 (*dd*, 1H, $^3J_{4,5}$ = 1.3 Hz, $^3J_{3,4}$ = 3.0 Hz, H4), 5.28 (*d*, 1H, $^3J_{1,2}$ = 3.5 Hz, H1), 5.26 (*m*, 1H, H3), 4.95 (*td*, 1H, $^3J_{5,6,7}$ = 6.1 Hz, $^3J_{5,7,6}$ = 6.6 Hz, H5), 4.71 (*ddd*, 1H, $^3J_{2,3}$ = 11.8 Hz, H2), 4.23 (*dd*, 1H, $^2J_{6,7}$ = 11.5 Hz, H6 or H7), 3.91 (*dd*, 1H, H7 or H6), 2.71 (*s*, 4H, H8–11), 2.13, 2.03, 2.02, 1.99 (4*s*, 12H, H12–14, H16–24); ^{13}C NMR (δ, p.p.m.): 170.9 (C═O), 170.7 (C═O), 170.6 (C═O), 170.4 (C═O), 170.1 (C═O), 104.2 (C1), 69.2, 67.3, 67.1 (C3, C4, C5), 61.6 (C6), 47.2 (C2), 25.4 (C8, C9), 23.2 (C12), 20.7 (C14, C16, C18).

Crystal data

$C_{18}H_{24}N_2O_{11}$
M_r = 444.39
Monoclinic, $P2_1$
a = 10.556 (4) Å
b = 9.191 (1) Å
c = 12.536 (6) Å
β = 114.28 (5)°
V = 1108.6 (7) Å^3
Z = 2
D_x = 1.331 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 20.2–26.8°
μ = 0.11 mm^{-1}
T = 293 K
Monoclinic prism, colourless
0.38 × 0.35 × 0.34 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω scans
3547 measured reflections
3470 independent reflections
2900 reflections with $I > 0.07\sigma(I)$
R_{int} = 0.009
θ_{max} = 30°
$h = -14 \rightarrow 14$
$k = 0 \rightarrow 12$
$l = 0 \rightarrow 17$
2 standard reflections
every 120 reflections
intensity decay: 5.5%

Refinement

Refinement on F
R = 0.069
wR = 0.055
S = 1.94
2900 reflections
279 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o) + 0.0002|F_o|^2]$
$(\Delta/\sigma)_{max}$ = 0.030
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—N1	1.373 (2)	N1—C7	1.375 (5)
O1—C1	1.449 (2)	N1—C10	1.390 (4)
O3—C3	1.436 (3)	N2—C2	1.444 (3)
O3—C13	1.362 (3)	N2—C11	1.322 (3)
O4—C4	1.446 (3)	C1—C2	1.503 (3)
O4—C15	1.347 (3)	C2—C3	1.518 (3)
O5—C1	1.394 (3)	C3—C4	1.525 (3)
O5—C5	1.440 (3)	C4—C5	1.511 (3)
O6—C6	1.443 (3)	C5—C6	1.497 (4)
O6—C17	1.339 (4)		
N1—O1—C1	109.9 (1)	N2—C2—C3	113.1 (2)
C3—O3—C13	116.8 (2)	C1—C2—C3	110.5 (2)
C4—O4—C15	117.6 (2)	O3—C3—C2	107.4 (2)
C1—O5—C5	114.7 (2)	O3—C3—C4	110.4 (2)
C6—O6—C17	116.8 (2)	C2—C3—C4	109.1 (2)
O1—N1—C7	121.4 (2)	O4—C4—C3	108.8 (2)
O1—N1—C10	120.2 (3)	O4—C4—C5	106.9 (2)
C7—N1—C10	118.0 (3)	C3—C4—C5	111.3 (2)
C2—N2—C11	122.2 (2)	O5—C5—C4	110.9 (2)
O1—C1—O5	111.0 (2)	O5—C5—C6	106.2 (2)
O1—C1—C2	105.8 (2)	C4—C5—C6	113.1 (2)
O5—C1—C2	114.5 (2)	O6—C6—C5	111.5 (2)
N2—C2—C1	110.6 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H15···O9^{i}	0.83	1.95	2.764 (2)	167

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

No s.u. on y is given for O1, since this parameter must be fixed in space group $P2_1$. H atoms were located geometrically (C—H = 0.94–0.96 Å). We were not able to determine the absolute configuration of the title compound from the analysis; the configuration chosen and shown in the Scheme and Fig. 1 is based on the known configuration of the starting reagent in the synthesis.

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*; molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *TEXSAN*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1176). Services for accessing these data are described at the back of the journal.

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