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A unique axially triacetylated xylopyranose structure, methyl 6-methoxy-2-methyl-1,3-dioxo-4-[(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)amino]-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine-7-carboxylate

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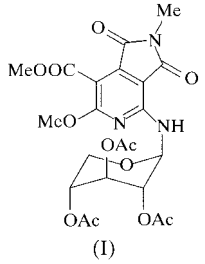
The title compound, $C_{22}H_{25}N_3O_{12}$, is unique amongst β-D-(tri-*O*-acetyl)xylopyranosyl compounds in having all three acetyl groups in axial positions.

Comment

Our investigations of the use of hetero-Diels–Alder reactions have resulted in the preparation of novel substituted nucleobase compounds containing acetylated xylopyranose substituents (Low *et al.*, 1996; Cobo *et al.*, 1996). In these compounds, all the substituent acetyl groups on the sugar rings were found to be equatorial. In the title compound, (I), all acetyl groups are axial to the sugar ring (Fig. 1). Relevant torsion angles are given in Table 1.



(I)

It is well known that β-xylopyranosides tend to adopt a chair conformation with all four substituents occupying equatorial positions ($^4C_1$ conformation). This is assumed to be the most stable of all possible conformations due to the relative low energy of the 1-equatorial–3-equatorial steric interactions between the hydroxyls (or functionalized hydroxyls) in comparison with the strong 1-axial–3-axial interaction found in the alternative chair conformation, the $^1C_4$ conformation (Schwarz, 1973, 1981). The conformational features found in our previous work with β-D-(per-*O*-acetyl)xylopyranosylamino derivatives, cited above, are in agreement with the above statement, the $^4C_1$ conformation being found in the crystal structures. In solution (DMSO-d_6) at 293 K, the $^4C_1$ conformation was also found for these compounds, as shown by the large values of the vicinal (^3J) coupling constants between the H atoms of the pyranose rings measured in their ^{1}H NMR spectra; values around 10 Hz for the $^3J_{H,H}$ coupling constants between 1′-2′, 2′-3′, 3′-4′ and 4′-5′$_{ax}$ are indicative of the all-equatorial $^4C_1$ conformation (Widmalm, 1998).

It was thus surprising to find an all-axial conformation in the crystal structure of (I) because its structural formula closely resembles that of our previously studied xylopyranosides, and its ^{1}H NMR data in $CDCl_3$ solution indicated absolutely, the preferred all-equatorial $^4C_1$ conformation (see *Experimental*). After inspection of the Cambridge Structural Database (CSD; Allen & Kennard, 1993), no similar all-axial conformation was found for any of the 15 β-D-(per-*O*-acetyl)xylopyranosides listed therein, thus confirming the unique features of the crystal structure described here. In fact, in all 15 β-D-xylo-

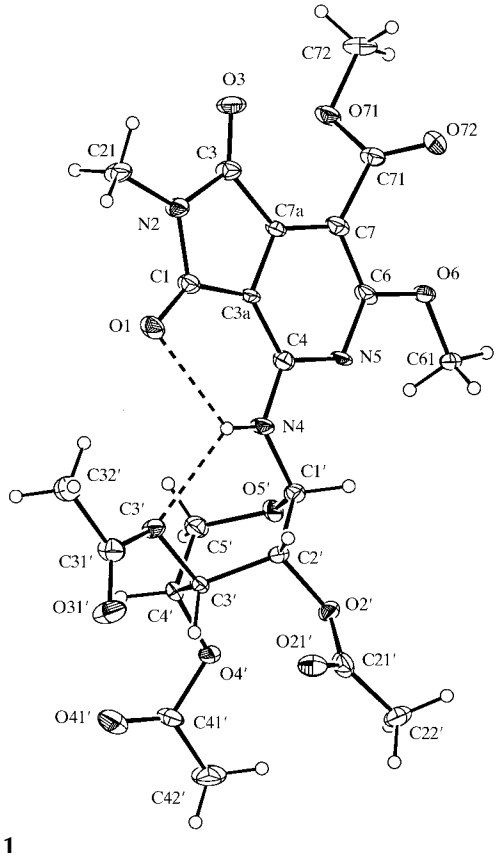


Figure 1
The asymmetric unit of (I) showing the atom-labelling scheme and the intramolecular hydrogen bonds. Displacement ellipsoids are drawn at the 30% probability level.

pyranose structures listed in the CSD, there is only one occurrence of an axial acetyl group, *i.e.* in 2,3,4-tri-*O*-acetyl-D-xylopyranosyl azide (ACXPAZ10; Luger & Gyorgydeak, 1993).

The principal structural factors that contribute to explain the preference for a $^1C_4$ conformation in compound (I) are: (i) the existence of a hydrogen bond between the 4-amino N atom and the O atom of the acetate group at C3′; this leads to the formation of a six-membered ring which fixes the pyranoside ring in the $^1C_4$ conformation. The same H atom participates in another intramolecular hydrogen bond involving a carbonyl O atom of the pyrrolo[3,4-*c*]pyridine moiety (Fig. 1), which helps to block the free rotation around the N—C4 single bond and confers additional rigidity to the structure. The degree of planarity of the atoms involved in the N9—H9···O1,O3′ hydrogen-bonding system can be seen when the O1···H4···O3′ angle of 102° is considered in conjunction with the others at H4 (Table 1). The angle sum at H9 is 356°, showing that the system is very close to being planar. (ii) The anomeric effect (Eliel & Wilen, 1994), which favours the axial position of anomeric electronegative substituents. It is worth noting the absence of a type called the *exo*-anomeric effect which usually operates in glycosylamine derivatives (Tvaroska & Carver, 1996). This is thought to be supported by the better electron-donor ability of the exocyclic nitrogen than that of the pyranose ring oxygen, thus cancelling the possibility of the anomeric effect and favouring the equatorial conformation for the anomeric substituents for steric reasons. However, no such effect can be found in (I) because the lone pair of the 4-amino N atom (directly linked to the anomeric position) is not available to help any *exo*-anomeric effect due to its large delocalization along the heterocyclic electron-deficient π system. This delocalization is confirmed by the planar geometry found for the N atom and the short distance of its bond to the heterocyclic C4 atom (shorter than a common single bond, see Table 1).

Examination of the structure with *PLATON* (Spek, 2000) showed that there were no solvent-accessible voids in the crystal lattice.

Experimental

Dimethyl acetylenedicarboxylate (1.28 g, 9.0 mmol) was added to a solution of 6-(tri-*O*-acetyl-β-D-xylopyranosylamino)-2-methoxy-3-methylpyrimidin-4(3*H*)-one (1.85 g, 4.5 mmol) in acetonitrile (20 ml) containing a catalytic amount of trifluoroacetic acid (0.11 g, 1.2 mmol). The mixture was stirred in refluxing acetonitrile for 15.5 h. The solvent was evaporated under reduced pressure and the title compound was isolated by flash column chromatography on silica gel (toluene/acetone). Recrystallization from acetone afforded yellow crystals. It proved very difficult to obtain crystals of suitable quality for X-ray diffraction (m.p. 543 K). Analysis calculated for $C_{22}H_{25}N_3O_{12}$: C 50.5, H 4.8, N 8.0%; found: C 50.2, H 4.9, N 8.0%. ^{1}H NMR ($CDCl_3$): 7.27 (*d*, 7.1 Hz, 1H, H-N), 5.58 (*dd*, 9.2 Hz, 8.4 Hz, 1H, H-1′), 5.38 (*d*, 8.6 Hz, 1H, H-3′), 5.08 (*d*, 8.5 Hz, 1H, H-2′), 5.01 (*m*, 1H, H-4′), 4.15 (*dd*, 5.3 Hz, 11.8 Hz, 1H, H-5′$_{eq}$), 4.03 (*s*, 3H, 6-OCH_3), 3.94 (*s*, 3H, 7-$COOCH_3$), 3.49 (*dd*, 9.3 Hz, 11.8 Hz, 1H, H-5′$_{ax}$), 3.09 (*s*, 3H, N-CH_3), 2.07 (*s*, 3H, OAc), 2.08 (*s*, 3H, OAc), 2.14 (*s*, 3H, OAc).

Crystal data

$C_{22}H_{25}N_3O_{12}$	D_x = 1.479 Mg m^{-3}
M_r = 523.45	Mo $K\alpha$ radiation
Monoclinic, *C*2	Cell parameters from 2704 reflections
a = 30.594 (6) Å	θ = 2.73–27.57°
b = 10.285 (2) Å	μ = 0.122 mm^{-1}
c = 7.4740 (10) Å	T = 150 (2) K
β = 91.07 (3)°	Plate, yellow
V = 2351.4 (7) Å^3	0.20 × 0.20 × 0.08 mm
Z = 4	

Data collection

KappaCCD diffractometer	1621 reflections with $I > 2\sigma(I)$
φ and ω scans with κ offsets	R_{int} = 0.080
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995, 1997)	θ_{max} = 27.57°
T_{min} = 0.976, T_{max} = 0.991	$h = -32 \rightarrow 39$
7395 measured reflections	$k = -12 \rightarrow 13$
2704 independent reflections	$l = -8 \rightarrow 8$
	Intensity decay: negligible

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.1363P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.082	$(\Delta/\sigma)_{max}$ = 0.042
$wR(F^2)$ = 0.226	$\Delta\rho_{max}$ = 0.42 e Å^{-3}
S = 0.999	$\Delta\rho_{min}$ = −0.35 e Å^{-3}
2704 reflections	Extinction correction: *SHELXL*97
328 parameters	Extinction coefficient: 0.017 (4)
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

C4—N4	1.349 (9)		
N4—C4—N5	117.4 (7)	N4—C4—C3a	123.1 (7)
N4—C1′—C2′—O2′	−165.4 (5)	C2′—C3′—C4′—O4′	75.1 (8)
O5′—C1′—C2′—C3′	−47.2 (8)	O3′—C3′—C4′—C5′	72.6 (8)
N4—C1′—C2′—C3′	78.6 (7)	C2′—C3′—C4′—C5′	−41.9 (9)
O2′—C2′—C3′—O3′	171.0 (5)	O4′—C4′—C5′—O5′	−66.5 (8)
C1′—C2′—C3′—O3′	−76.2 (7)	C3′—C4′—C5′—O5′	51.8 (9)
O2′—C2′—C3′—C4′	−73.1 (8)	N4—C1′—O5′—C5′	−66.1 (7)
C1′—C2′—C3′—C4′	39.6 (8)	C2′—C1′—O5′—C5′	58.6 (8)
O3′—C3′—C4′—O4′	−170.4 (5)	C4′—C5′—O5′—C1′	−61.4 (8)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4—H4···O1	0.88	2.46	3.081 (7)	128
N4—H4···O3′	0.88	2.32	2.924 (8)	126

Compound (I) crystallized in the monoclinic system; space group *C*2 was assumed and confirmed by the analysis. H atoms were treated as riding atoms, with C—H distances in the range 0.98–1.00 Å and an N—H distance of 0.88 Å. Methyl H atoms were placed in calculated positions and these positions were checked against contoured difference maps calculated in the plane of the calculated H atoms following a structure-factor calculation with the H atoms present with a site-occupation factor of 0.0001. This technique was also used to confirm the position of the amino hydrogen H9.

The high R factor for the title compound is probably due to non-merohedral twinning involving a small secondary component. This possibility is indicated by the strange location of the residual peaks and the large proportion of the 50 most disagreeable reflections being of the type $l = 1$ with F^2_{obs} higher than F^2_{calc}. To check this, the diffraction images were examined and found to contain additional weak reflections and split faults in this direction. A symptom of these additional spots is the loss of 00l reflections from the data file due to bad background during integration. Many of the twin reflections are close enough to the main reflections to contaminate the background and these will have been flagged as such and omitted from the final data set as unreliable. Due to the weak nature of the additional reflections, it is likely that the twin component is small and therefore a twin refinement was not attempted.

Data collection: *KappaCCD Server Software* (Nonius, 1997); cell refinement: *DENZO* (Otwinowski & Minor, 1997); data reduction: *DENZO*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2000); software used to prepare material for publication: *SHELXL*97 and *WordPerfect* macro *PRPKAPPA* (Ferguson, 1999).

X-ray data were collected at the EPSRC, X-ray Crystallographic Service, University of Southampton, using an Enraf–Nonius KappaCCD diffractometer. The authors thank the staff for all their help and advice. The authors also wish to thank a referee for comments about the possible twinning in this structure.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1119). Services for accessing these data are described at the back of the journal.

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