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2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl azide

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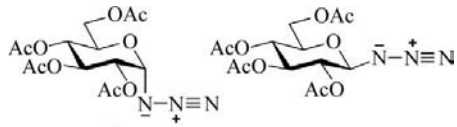
The Cu^{I}-catalysed 1,3-dipolar cycloaddition of an azide and a terminal alkyne is becoming an increasingly popular tool for synthetic chemists. This is the most representative of the so-called 'click reactions' and it is used to generate 1,4-disubstituted triazoles in high yield. During studies on such cycloaddition reactions, a reduced reactivity of an α-glucosyl azide with respect to the corresponding β-anomer was observed. With the aim of understanding this phenomenon, the structure of the title compound, $C_{14}H_{19}N_3O_9$, has been determined at 140 K. The glucopyranosyl ring appears in a regular $^4C_1$ chair conformation with all the substituents in equatorial positions, except for the anomeric azide group, which adopts an axial orientation. The observed bond lengths are consistent with a strong anomeric effect, which is reflected in a change in dipolar character and hence reduced reactivity of the α-glucosyl azide.

Comment

Glycosyl azides represent important and versatile building blocks in carbohydrate chemistry (Györgydeák & Thiem, 2006). They have been widely used as synthetic intermediates for the preparation of glycosyl amines, asparagine-linked glycopeptides (Herzner *et al.*, 2000) and, more recently, triazole-linked neoglycoconjugates (Dedola *et al.*, 2007; Dondoni, 2007). These last became available as a result of the discovery of the highly efficient Cu^{I}-catalysed cycloaddition reaction between azides and terminal alkynes (Rostovtsev *et al.*, 2002; Tornøe *et al.*, 2002), which is commonly referred to as 'click chemistry'. This cycloaddition process has been extensively used for the synthesis of a variety of neoglycoconjugates (Dedola *et al.*, 2007; Dondoni, 2007). In the course of our work on the synthesis of starch-like molecules, we experienced major problems with stereocontrol in the synthesis of inter-sugar chain glycosidic linkages (Marmuse *et al.*, 2005*a*). We therefore resorted to the preparation of pseudo-starch fragments based on glucosyl triazole linkages (Marmuse *et al.*, 2005*b*; Nepogodiev *et al.*, 2007). Initial studies were based on the immediately accessible β-linked sugar azides, which do not mirror the anomeric stereochemistry of starch. We report here the structural analysis of the title compound, (I), prepared according to Bianchi & Bernardi (2006). The X-ray structure of the corresponding β-linked anomer, *viz.* 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide, (II), has already been reported (Temelkoff *et al.*, 2004).



The six-membered pyranose ring in (I) adopts a chair conformation, with all exocyclic substituents adopting an equatorial arrangement, except for the anomeric azide which has the expected axial orientation (Fig. 1). The geometry of the pyranose ring and the orientation of the acetate groups of (I) are very similar to those features in the corresponding β-anomer, (II) (Temelkoff *et al.*, 2004). However, whereas the length of the C1—O5 bond in (I) [1.423 (3) Å] is the same as in (II) [1.420 (2) Å], the C1—N11 [1.510 (3) *versus* 1.460 (2) Å] and C5—O5 [1.459 (3) *versus* 1.432 (2) Å] distances are significantly longer in (I) than in (II). As in (II), the azide group in (I) appears as a nearly linear fragment [N11—N12—N13 = 173.0 (3)°, compared with 171.4 (2)° for (II)] and shows a very similar C1—N11—N12 bond angle [113.7 (2) *versus* 113.74 (14)° for (II)].

However, the N—N bond lengths for the azide group and the C1—N11 distances in (I) and (II) are different. The structural differences between the anomeric glucosyl azides

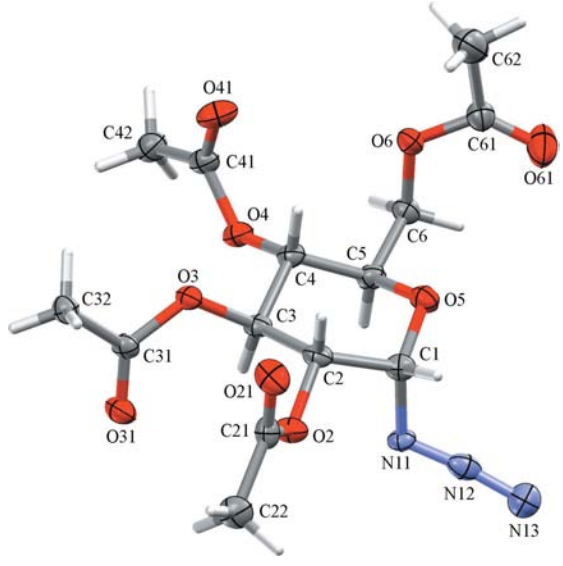


Figure 1
A view of the molecular structure of (I), showing the atom-numbering scheme. For clarity, only the major component of the disordered $-CH_2OCOMe$ group at C6 is shown. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as capped sticks.

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are all in keeping with the expected influence of the anomeric effect (Briggs *et al.*, 1984; Wolfe *et al.*, 1979). For (II), the terminal N12—N13 bond [1.119 (3) Å] is shorter than the N11—N12 bond [1.243 (2) Å], whereas in (I), these are more similar in value [1.195 (4) and 1.165 (3) Å, respectively]. One might therefore anticipate a significant reactivity difference between compounds (I) and (II) in dipolar cycloaddition chemistry, which we have indeed observed: a much lower reactivity of α-azide (I) compared with β-azide (II) is evident in the Cu^{I}-catalysed synthesis of triazoles. This is consistent with other experimental observations (Wilkinson *et al.*, 2006) and in accord with computational studies, which show the crucial role that a partial negative charge on atom N11 plays in the mechanism of the Cu^{I}-catalysed cycloaddition of azides and alkynes (Himo *et al.*, 2005).

Experimental

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl azide, (I), was prepared along with the β-anomer, (II), in a 9:1 ratio (determined by ^{1}H NMR spectroscopy) as described previously (Bianchi & Bernardi, 2006), using tetra-*O*-acetyl-β-D-glucopyranosyl chloride (Korytnyk & Mills, 1959) and Me_3SiN_3 (Soli *et al.*, 1999). Single isomers were obtained using purification by silica-gel column chromatography. Crystals of (I) suitable for X-ray diffraction analysis were obtained as colourless blocks by recrystallization from ethanol.

Crystal data

$C_{14}H_{19}N_3O_9$
M_r = 373.32
Monoclinic, $P2_1$
a = 10.806 (4) Å
b = 7.9840 (13) Å
c = 11.0107 (8) Å
β = 109.742 (2)°
V = 894.1 (3) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.12 mm^{-1}
T = 140 (1) K
0.45 × 0.43 × 0.30 mm

Data collection

Oxford Diffraction Xcalibur3/CCD diffractometer
Absorption correction: multi-scan (*CrysAlis RED*; Oxford Diffraction, 2006)
T_{min} = 0.940, T_{max} = 1.060 (expected range = 0.856–0.966)
8905 measured reflections
3125 independent reflections
2216 reflections with $I > 2\sigma(I)$
R_{int} = 0.039

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.087
S = 0.90
3125 reflections
257 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.16 e Å^{-3}
Absolute structure: Flack (1983), with 1440 Friedel pairs
Flack parameter: 0.6 (12)

Non-H atoms were refined with anisotropic displacement parameters, except those in the –CH_2OCOMe group on C6 where there was suspected disorder; the major C6/O6/C61/O61/C62 component [79.9 (5)%] was refined anisotropically, but the minor C7/O7/C71/O71/C72 component [20.1 (5)%] was not fully resolved and its C and O atoms were refined isotropically; the methyl C atom represented by C62/C72 was found to be common to both orientations and was refined with full occupancy for that site using the EXYZ and EADP restraints in *SHELXL97* (Sheldrick, 2008). H atoms were included in idealized positions, with C—H distances for the methyl, methylene and methine groups set at 0.96, 0.97 and 0.98 Å, respectively, and with U_{iso}(H) = 1.5U_{eq}(C) for the methyl group and 1.2U_{eq}(C) for the remaining groups. The absolute configuration of the C atoms could not be determined from the X-ray data; the assignment was based on the known configuration of the starting material.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2007); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXL97* and *publCIF* (Westrip, 2008).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM3053). Services for accessing these data are described at the back of the journal.

References

Bianchi, A. & Bernardi, A. (2006). *J. Org. Chem.* **71**, 4565–4577.
Briggs, A. J., Glenn, R., Jones, P. G., Kirby, A. J. & Ramaswamy, P. (1984). *J. Am. Chem. Soc.* **106**, 6200–6206.
Dedola, S., Nepogodiev, S. A. & Field, R. A. (2007). *Org. Biomol. Chem.* **5**, 1006–1017.
Dondoni, A. (2007). *Chem. Asian J.* **2**, 700–708.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Györgydeák, Z. & Thiem, J. (2006). *Adv. Carbohydr. Chem. Biochem.* **60**, 103–182.
Herzner, H., Reipen, T., Schultz, M. & Kunz, H. (2000). *Chem. Rev.* **100**, 4495–4537.
Himo, F., Lovell, T., Hilgraf, R., Rostovtsev, V. V., Noodleman, L., Sharpless, K. B. & Fokin, V. V. (2005). *J. Am. Chem. Soc.* **127**, 210–216.
Korytnyk, W. & Mills, J. A. (1959). *J. Chem. Soc.* pp. 636–649.
Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
Marmuse, L., Nepogodiev, S. A. & Field, R. A. (2005*a*). *Tetrahedron Asymmetry*, **16**, 477–485.
Marmuse, L., Nepogodiev, S. A. & Field, R. A. (2005*b*). *Org. Biomol. Chem.* **3**, 2225–2227.
Nepogodiev, S. A., Dedola, S., Marmuse, L., de Oliveira, M. T. & Field, R. A. (2007). *Carbohydr. Res.* **342**, 529–540.
Oxford Diffraction (2006). *CrysAlis RED*. Version 1.171.29.9. Oxford Diffraction Ltd, Abingdon, England.
Oxford Diffraction (2007). *CrysAlis CCD*. Version 1.171.32.5. Oxford Diffraction Ltd, Abingdon, England.
Rostovtsev, V. V., Green, L. G., Fokin, V. V. & Sharpless, K. B. (2002). *Angew. Chem. Int. Ed.* **41**, 2596–2599.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Soli, E. D., Manoso, A. S., Patterson, M. C. & DeShong, P. (1999). *J. Org. Chem.* **64**, 3171–3177.
Temelkoff, D. P., Norris, P. & Zeller, M. (2004). *Acta Cryst.* E**60**, o1975–o1976.
Tornøe, C. W., Christensen, C. & Meldal, M. (2002). *J. Org. Chem.* **67**, 3057–3064.
Westrip, S. P. (2008). *publCIF*. In preparation.
Wilkinson, B. L., Bornaghi, L. F., Poulsen, S. A. & Houston, T. A. (2006). *Tetrahedron*, **62**, 8115–8125.
Wolfe, S., Whangbo, M. H. & Mitchell, D. J. (1979). *Carbohydr. Res.* **69**, 1–26.