ELSEVIER

Carbohydrate Research 285 (1996) 151–157

CARBOHYDRATE RESEARCH

Note

# Crystal and molecular structure of 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranosyl fluoride

R. Willem Tjerkstra, Marcel L. Verdonk, Jan Kroon *

*Department of Crystal and Structural Chemistry, Bijvoet Center for Biomolecular Research, Padualaan 8, NL-3584 CH, Utrecht, The Netherlands*

Received 25 June 1995; accepted in revised form 21 December 1995

*Keywords:* X-ray structure; Idopyranosyl-ring conformation; 2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranosyl fluoride

2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranosyl fluoride (**1** $C_{34}H_{29}O_8F$), $M_r$ = 584.60, orthorhombic, space group $P2_12_12_1$, $a = 5.7211(2)$, $b = 17.298(4)$, $c$ = 30.140(5) Å, $V = 2982.7(9)$ Å$^3$, $Z = 4$, $D = 1.3018(4)$ g cm$^{-3}$, $F(000) = 1224$, $T = 298$ K, $R1 = 0.0445$ for the 2595 reflections for which $F_o > 4\sigma F_o$, $wR2 = 0.1232$ for all reflection data adopts the $^4C_1$ conformation.

Compound **1** is a suitably protected L-idose building block that has been used for the preparation of a pentasaccharide that resembles the antithrombin(III) binding region of heparin [1]. We now present its crystal and molecular structure.

## 1. Experimental

A crystal of size 0.3 × 0.3 × 1.0 mm was mounted on an Enraf–Nonius Fast diffractometer. Reflection data were obtained with Mo$K\alpha$ monochromatic radiation ($\lambda = 0.71073$ Å) using the MADNES [2] program. Unit-cell dimensions and standard deviations were obtained using the ENDEX and REFINE routines of MADNES with 93 reflections collected in four 4.65° $\phi$ scans separated by 90°. Frames were integrated for 10 s over an angle of 0.15°. Data were collected with a 190° $\phi$ rotation at $\kappa = 0°$

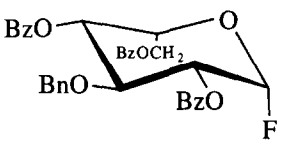
* Corresponding author.


*PII* S0008-6215(96)00001-8

followed by two 80° $\omega$ rotations at $\kappa = 134°$, the second after rotating $\phi$ 180° ($-5 \leq h \leq 3$, $-16 \leq k \leq 16$, $-27 \leq l \leq 29$). The reflections were interpreted using the EVAL14 procedure [3]. Due to the poor quality of the crystal, $\theta_{max} = 20.08°$. The number of reflections obtained was 8941. They were processed to give 2801 unique reflections ($R_{int} = 0.0514$). The space group was determined using systematic absences. The structure was solved in $P2_12_12_1$ using SHELXS-86 [4]. For the refinement, the program SHELXL-93 [5] was used. The hydrogen atoms were placed on calculated positions. The non-hydrogen atoms were refined anisotropically; the hydrogen atoms were constrained to ride on their carrier atoms and refined with an overall thermal parameter. In the final refinement 389 parameters were varied. Refinement of $F^2$ converged at $wR2 = 0.1232$ for all reflection data, where $w = 1/[\sigma^2(F_o^2) + (0.0862P)^2 + 0.20P]$, in which $P = [\max(F_o^2, 0) + 2F_c^2]/3$, $R1 = 0.0445$ for the 2595 reflections for which $F_o > 4\sigma F_o$, Goo$F = 1.107$. Lorentz-polarization (LP), but no absorption correction was applied. The final residual electron density was within $\pm 0.35$ Å$^{-3}$. The atomic coordinates and equivalent isotropic parameters of the non-hydrogen atoms can be found in Table 1, the bond distances only involving non-hydrogen atoms in Table 2. Relevant torsion angles are given in Table 3 [1]. Geometrical calculations were performed with the EUCLID package [6].

## 2. Results and discussion

The molecular structure of **1** is shown in an ORTEP plot (Fig. 1). As a consequence of the hydroxymethyl group being in an axial position, the idose ring is in the unusual $^4C_1$ conformation. Cremer–Pople puckering parameters [$Q = 0.514(4)$ Å, $\theta = 3.7(4)°$, $\phi_2 = 252.2(73)°$] point to a perfect chair.




**1**

A Cambridge Structural Database (CSD) search [7] revealed that 5-*C*-methyl-α-L-idopyranose hemihydrate [8] exhibits the same conformational features as **1**.

The conformation of α-L-idose derivatives in solution have been studied by van Boeckel and coworkers [9,10], using NMR techniques. The conformation depends strongly on the substituent groups. The most common conformations are $^1C_4$ and $^2S_0$.

[1] Atomic coordinates, bond lengths and bond angles, and (an)isotropic thermal parameters for these structures have been deposited with the Cambridge Crystallographic Data Centre. The coordinates may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EC, UK.

Table 1
Final coordinates and equivalent isotropic thermal parameters of the non-hydrogen atoms for 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranoyl fluoride (**1**)

| Atom | *x* | *y* | *z* | *U*(eq) [a] [Å$^2$] |
|---|---|---|---|---|
| F-11 | −0.0171(4) | 0.4799(1) | 0.26945(7) | 0.088(1) |
| O-5 | 0.3737(5) | 0.5032(2) | 0.27635(8) | 0.077(1) |
| O-21 | 0.0402(5) | 0.3308(1) | 0.24589(8) | 0.074(1) |
| O-22 | 0.1272(6) | 0.3561(2) | 0.17501(9) | 0.088(1) |
| O-31 | 0.3431(5) | 0.2752(1) | 0.31360(8) | 0.072(1) |
| O-41 | 0.4387(4) | 0.3884(1) | 0.37802(7) | 0.065(1) |
| O-42 | 0.8245(6) | 0.3919(3) | 0.3828(1) | 0.121(2) |
| O-61 | 0.2685(5) | 0.5429(2) | 0.39283(9) | 0.074(1) |
| O-62 | −0.0783(8) | 0.5973(3) | 0.4029(1) | 0.131(2) |
| C-1 | 0.2049(9) | 0.4598(2) | 0.2545(1) | 0.078(2) |
| C-2 | 0.2373(7) | 0.3744(2) | 0.2614(1) | 0.067(1) |
| C-3 | 0.2647(6) | 0.3531(2) | 0.3100(1) | 0.061(1) |
| C-4 | 0.4455(6) | 0.4043(2) | 0.3310(1) | 0.061(1) |
| C-5 | 0.4014(7) | 0.4902(2) | 0.3236(1) | 0.068(1) |
| C-6 | 0.1910(7) | 0.5251(2) | 0.3480(1) | 0.071(2) |
| C-21 | 0.0049(8) | 0.3240(2) | 0.2016(1) | 0.071(2) |
| C-22 | −0.1967(8) | 0.2737(2) | 0.1916(1) | 0.071(2) |
| C-23 | −0.3223(8) | 0.2348(2) | 0.2238(1) | 0.078(2) |
| C-24 | −0.5110(9) | 0.1902(3) | 0.2127(2) | 0.088(2) |
| C-25 | −0.5817(9) | 0.1842(3) | 0.1699(2) | 0.096(2) |
| C-26 | −0.463(1) | 0.2209(3) | 0.1375(2) | 0.106(3) |
| C-27 | −0.268(1) | 0.2666(3) | 0.1475(2) | 0.097(2) |
| C-31 | 0.1834(8) | 0.2241(2) | 0.3342(2) | 0.095(2) |
| C-32 | 0.2998(8) | 0.1474(2) | 0.3415(1) | 0.070(2) |
| C-33 | 0.498(1) | 0.1416(3) | 0.3654(2) | 0.099(2) |
| C-34 | 0.599(1) | 0.0720(4) | 0.3734(2) | 0.113(3) |
| C-35 | 0.505(1) | 0.0067(3) | 0.3583(2) | 0.107(3) |
| C-36 | 0.307(2) | 0.0116(3) | 0.3347(3) | 0.151(4) |
| C-37 | 0.202(1) | 0.0820(3) | 0.3262(2) | 0.120(3) |
| C-41 | 0.6366(7) | 0.3854(2) | 0.4002(1) | 0.069(2) |
| C-42 | 0.6052(7) | 0.3735(2) | 0.4480(1) | 0.072(2) |
| C-43 | 0.4022(8) | 0.3403(3) | 0.4649(1) | 0.087(2) |
| C-44 | 0.382(1) | 0.3279(4) | 0.5099(2) | 0.117(2) |
| C-45 | 0.551(1) | 0.3503(4) | 0.5380(2) | 0.127(3) |
| C-46 | 0.751(1) | 0.3866(4) | 0.5218(2) | 0.137(3) |
| C-47 | 0.7804(9) | 0.3956(3) | 0.4769(2) | 0.099(2) |
| C-61 | 0.109(1) | 0.5805(3) | 0.4170(1) | 0.083(2) |
| C-62 | 0.186(1) | 0.5966(3) | 0.4621(2) | 0.091(2) |
| C-63 | 0.385(1) | 0.5718(3) | 0.4801(2) | 0.123(3) |
| C-64 | 0.441(2) | 0.5864(4) | 0.5243(2) | 0.157(4) |
| C-65 | 0.298(2) | 0.6284(6) | 0.5496(2) | 0.173(5) |
| C-66 | 0.101(2) | 0.6565(8) | 0.5312(3) | 0.260(8) |
| C-67 | 0.043(1) | 0.6395(6) | 0.4886(2) | 0.197(4) |

[a] $U(\text{eq}) = 1/3$ of the trace of the orthogonalized $U$.

Table 2
Relevant bond distances only involving non-hydrogen atoms (Å) [a] in **1**

| | | | |
|---|---|---|---|
| F-11–C-1 | 1.392(5) | C-25–C-26 | 1.348(8) |
| O-5–C-1 | 1.389(5) | C-26–C-27 | 1.400(8) |
| O-5–C-5 | 1.450(4) | C-31–C-32 | 1.501(5) |
| O-21–C-2 | 1.435(5) | C-32–C-33 | 1.347(7) |
| O-31–C-3 | 1.424(4) | C-34–C-35 | 1.331(9) |
| O-41–C-4 | 1.444(4) | C-36–C-37 | 1.382(9) |
| O-61–C-6 | 1.455(4) | C-42–C-47 | 1.382(7) |
| C-1–C-2 | 1.503(5) | C-45–C-46 | 1.394(9) |
| C-2–C-3 | 1.519(4) | C-46–C-47 | 1.373(9) |
| C-3–C-4 | 1.502(5) | C-61–C-62 | 1.456(7) |
| C-4–C-5 | 1.524(5) | C-62–C-63 | 1.332(8) |
| C-5–C-6 | 1.534(5) | C-62–C-67 | 1.363(9) |

[a] Mean bond distances of the phenyl rings (Å): ring, connected to C-2: 1.378(3); ring, connected to C-3: 1.351(3); ring, connected to C-4: 1.380(3); ring, connected to C-5: 1.357(4).

For some compounds a $^{1}C_{4} \rightleftharpoons {}^{2}S_{0}$ equilibrium is found. Compound **1** will, however, probably have a $^{4}C_{1}$ conformation in solution. The strong anomeric effect of the β-fluoride will cause this conformation to be energetically more favoured.

The difference of 0.061(7) Å between the C-5–O-5 and C-1–O-5 distances is larger than usual. From observations on crystal structures of carbohydrates [11,12], it is well established that the difference between the endocyclic C–O bond lengths is larger in α-D- than in β-D-glycosides. This difference appears to be increased by the presence of a halogen atom at C-1, as we found by a search in the CSD on pyranoses having such an

Table 3
Relevant torsion angles (°) in **1**

| | |
|---|---|
| C-1–O-5–C-5–C-4 | 54.9(4) |
| O-5–C-5–C-4–C-3 | −53.1(4) |
| C-5–C-4–C-3–C-2 | 52.3(4) |
| C-4–C-3–C-2–C-1 | −49.5(4) |
| C-3–C-2–C-1–O-5 | 50.4(4) |
| C-2–C-1–O-5–C-5 | −54.7(4) |
| C-21–O-21–C-2–C-1 | 72.0(4) |
| C-2–O-21–C-21–C-22 | 176.7(3) |
| O-21–C-21–C-22–C-23 | −3.9(5) |
| C-2–C-3–O-31–C-31 | −115.4(4) |
| C-3–O-31–C-31–C-32 | −172.2(3) |
| O-31–C-31–C-32–C-33 | 57.5(6) |
| C-3–C-4–O-41–C-42 | 140.4(3) |
| C-4–O-41–C-41–O-42 | −3.4(5) |
| O-41–C-41–C-42–C-43 | 22.6(5) |
| O-5–C-5–C-6–O-61 | −154.7(3) |
| C-5–C-6–O-61–C-61 | 174.1(3) |
| C-6–O-61–C-61–C-62 | 178.7(4) |
| O-61–C-61–C-62–C-63 | −5.5(8) |

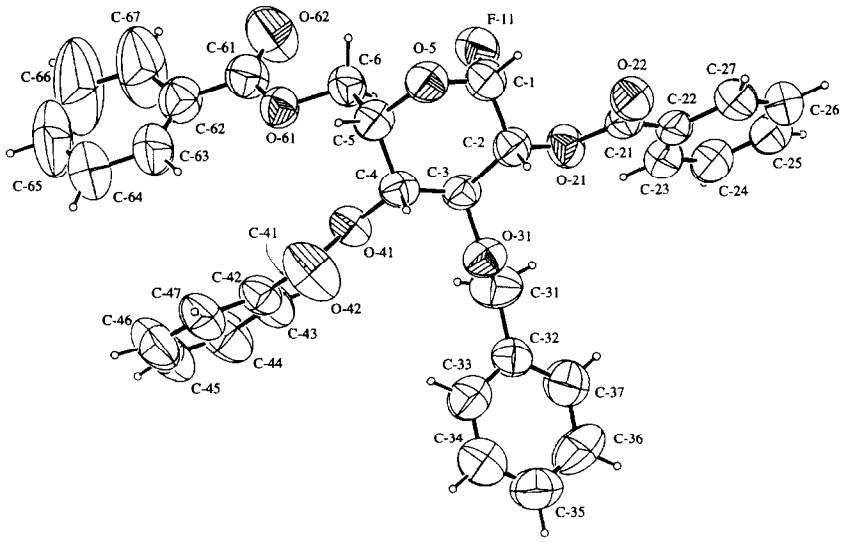



Fig. 1. ORTEP plot for 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranosyl fluoride (**1**).

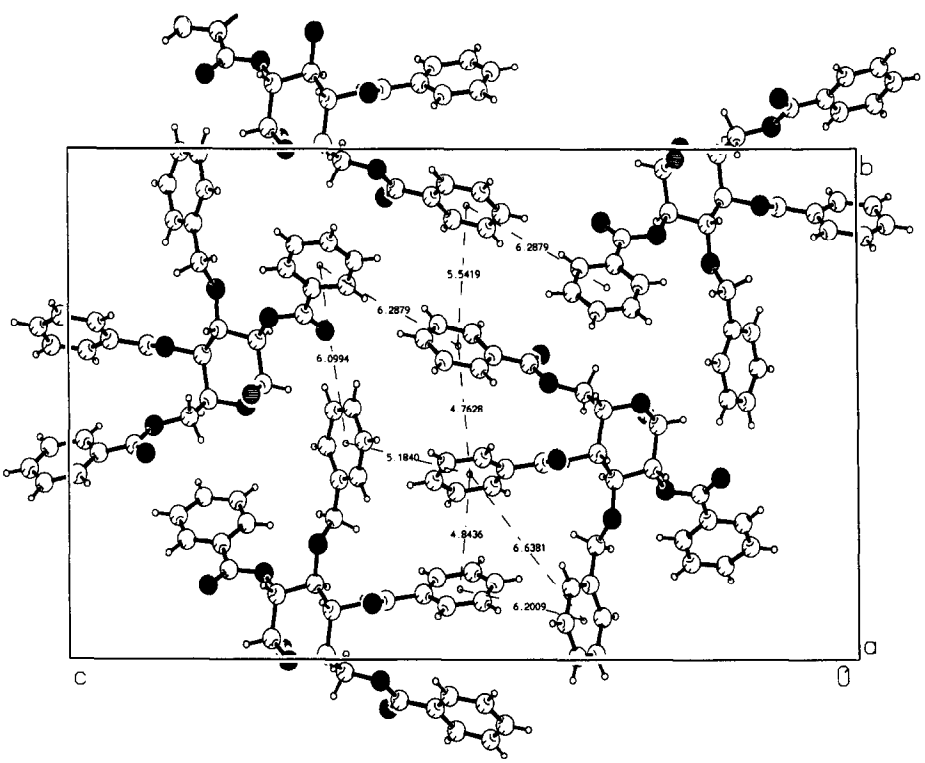



Fig. 2. Projection of the crystal structure of 2,4,6,-tri-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranosyl fluoride (**1**) along the *a* axis. The distances (in Å) between the centres of phenyl rings are displayed.

Table 4
C–H···O contacts

| | C···O (Å) | H···O (Å) | C–H···O (°) |
|---|---|---|---|
| C-25–H-25···O-62 [$-1-x, -\frac{1}{2}+y, \frac{1}{2}-z$] | 3.295(7) | 2.520(7) | 141.0(6) |
| C-3–H-31···O-42 [$-1+x, y, z$] | 3.407(5) | 2.465(5) | 161.1(3) |
| C-6–H-62···O-42 [$-1+x, y, z$] | 3.287(6) | 2.387(6) | 154.0(4) |

atom at C-1. The compounds concerned are methyl (2,3,4-tri-*O*-acetyl-α-D-glucopyranosyl bromide)uronate [13], 2,3,4,6-tetra-*O*-acetyl-1-bromo-D-galactopyranosyl cyanide [14], 2,3,4,6-tetra-*O*-acetyl-1-bromo-β-D-glucopyranosyl chloride [15], tetra-*O*-acetyl-α-D-glucopyranosyl bromide [16], tetra-*O*-acetyl-α-D-mannopyranosyl chloride [17], and 2,3,4,6-tetra-*O*-benzoyl-2-chloro-α-D-mannopyranosyl chloride [18]. The mean difference between C-5–O-5 and C-1–O-1 found was 0.063(5) Å.

The projection of the crystal structure along the *a* axis for **1** is shown in Fig. 2. From Fig. 2 it is apparent that parallel to (110) hydrophobic regions are present, containing the phenyl rings connected to atoms C-4 and C-6. The distances between the centres of the neighbouring rings are displayed; they lie between 4.8 and 5.5 Å. This type of packing also occurs in the crystal structures of methyl 6,7-di-*O*-acetyl-2,3,4-tri-*O*-benzoyl-6-deoxy-L-*threo*-β-D-*galacto*-octopyranoside [19], *N*-benzoyloxy-2,3,4,6-tetra-*O*-benzoyl-D-glucono-1,5-iminolactone [20], and 2,3,4,6-tetra-*O*-benzoyl-2-chloro-D-mannopyranosyl chloride [18].

Short intermolecular C–H···O contacts are displayed in Table 4. It is conceivable that, in the absence of strong hydrogen bond donors, the oxygen acceptors satisfy their affinity for hydrogen bonds with the much weaker C–H bonds [21].

## Acknowledgements

We thank Prof. Dr. C.A.A. van Boeckel of N.V. Organon Oss for supplying the 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranosyl fluoride.

## References

[1] C.A.A. van Boeckel and M. Petitou, *Angew. Chem., Int. Ed. Engl.*, 32 (1993) 1671–1690.
[2] J.W. Pflugrath and A. Messerschmidt, *MADNES*, distributed by Enraf–Nonius, Delft (1990).
[3] A.J.M. Duisenberg and A.M.M. Schreurs, *Technical Report STW 349-276* (1995).
[4] G.M. Sheldrick, *SHELXS-86, Program for Crystal-Structure Determination*, University of Göttingen, 1985.
[5] G.M. Sheldrick, *SHELXL-93, Program for Crystal-Structure Refinement*, University of Göttingen, 1992.
[6] A.L. Spek, *Acta Crystallogr., Sect. A, Suppl.*, 46 (1990) C34.
[7] F.H. Allen, O. Kennard, and R. Taylor, *Acc. Chem. Res.*, 16 (1983) 146–153.
[8] D.C. Craig and J.D. Stevens, *Aust. J. Chem.*, 43 (1990) 2087–2091.
[9] C.A.A. van Boeckel, S.F. van Aelst, G.N. Wagenaars, J.R. Mellema, H. Paulsen, T. Peters, A. Pollex, and V. Sinwell, *Recl. Trav. Chim. Pays-Bas*, 106 (1987) 19–29.

[10] H. Paulsen, A. Pollex, V. Sinnwell, and C.A.A. van Boeckel, *Liebigs Ann. Chem.*, (1988) 411–418.
[11] G.A. Jeffrey and S. Takagi, *Acta Crystallogr., Sect. B*, 33 (1977) 738–742.
[12] G.A. Jeffrey, J.A. Pople, J.S. Binkley, and S. Vishveshwara, *J. Am. Chem. Soc.*, 100 (1978) 373–379.
[13] R.M. Doherty, J.M. Steward, W.R. Benson, M.M. Maiental, and W.H. De Camp, *Carbohydr. Res.*, 116 (1983) 150–155.
[14] L. Párkányi, A. Kálmán, L. Somsák, and I. Farkas, *Carbohydr. Res.*, 168 (1987) 1–5.
[15] J.-P. Praly, L. Brard, G. Descotes, and L. Toupet, *Tetrahedron*, 45 (1989) 4141–4152.
[16] M. Takai, H. Watanabe, J. Hayashi, and S. Watanabe, *Bull. Fac. Eng. Hokkaido Univ.*, 79 (1976) 101–109.
[17] P. Herpin, R. Famery, J. Auge, S. David, and L. Guibe, *Acta Crystallogr., Sect. B*, 32 (1976) 209–215.
[18] F.W. Lichtenthaler, T. Sakakibara, and E. Oeser, *Carbohydr. Res.*, 59 (1977) 47–61.
[19] S.J. Danishefsky, E. Larson, and J.P. Springer, *J. Am. Chem. Soc.*, 107 (1985) 1274–1280.
[20] D. Beer and A. Vasella, *Helv. Chim. Acta*, 68 (1985) 2254–2274.
[21] O. Salas, J.A. Kanters, and E. Grech, *J. Mol. Struct.*, 27 (1992) 197–207.