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The crystal structure and conformational analysis of substituted 2,7-dioxabicyclo[4,1,0]heptanes: 1,2-anhydro-3,4,6-tri-*O*-benzyl-β-D-talopyranose

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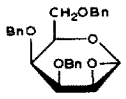
ABSTRACT

The title compound, $C_{28}H_{27}O_5$, is triclinic, space group $P1$ with unit cell dimensions $a = 12.763(2)$, $b = 11.130(2)$, $c = 4.764(3)$ Å, $\alpha = 73.78(3)$, $\beta = 82.89(3)$, $\gamma = 62.16(1)°$, $V = 574.8(4)$ Å^3, and $Z = 1$. The pyranose ring has an $^4H_5$ conformation with some flattening at C-4. Molecular mechanics calculations indicate that the $^4H_5$ conformation of the pyranose ring in the title compound is the most stable conformation.

INTRODUCTION

1,2-Anhydro-glycopyranose derivatives are important intermediates in the synthesis of oligosaccharides[1] and polysaccharides[2], and for the chemical modification of monosaccharides[3]. The synthesis of 1,2-anhydro-D-manno-[4],-D-gluco-[5], 6-deoxy-D-gluco-[6], -D-galacto-[7], -D- and -L-rhamno-[8], and -D-talopyranose[9] benzyl ether have been reported. Although their chemical properties and reactions have been investigated in great detail, there has been no report of a crystal structure. This work describes the crystal structure analysis of 1,2-anhydro-3,4,6-tri-*O*-benzyl-β-D-talopyranose.



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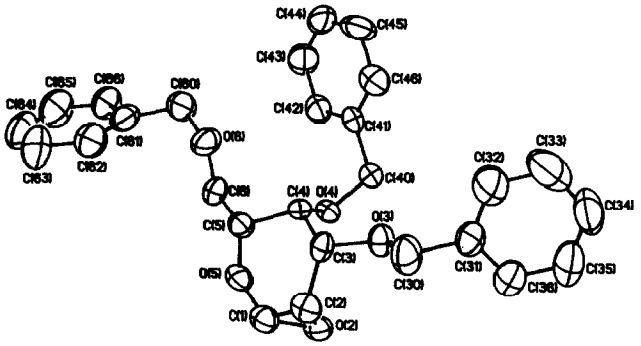

Fig. 1. ORTEP plot of 1,2-anhydro-β-D-talopyranose benzyl ether, showing the numbering of the nonhydrogen atoms. Thermal ellipsoids are drawn at the 50% probability level.

EXPERIMENTAL

1,2-Anhydro-3,4,6-tri-*O*-benzyl-β-D-talopyranose was prepared as described previously[9] and recrystallized from ether–acetone to give colorless prisms suitable for X-ray analysis. A Rigaku AFC-5R diffractometer was used for data collection. The unit cell parameters were determined at room temperature with Cu$K\alpha$ radiation by a least-squares fit of 20 reflections. Intensities for the independent reflections with 2θ less than 120° were measured with the $\omega/2\theta$ continuous scan mode at the rate of 16°/min. The scan width in 2θ was $(1.2 + 0.5 \tan \theta)°$ with background counts of 5 s on both sides of the peak. To check electronic and crystal stability, three reflections were measured after each 100 reflections. No variation was found. Lorentz and polarization factors were applied but no correction for adsorption was made.

The structure was solved by direct methods using the program SHELX86 to calculate phases for the lEl values greater than 1.2. The E-map revealed the positions of all nonhydrogen atoms. Refinement was carried out using the fullmatrix least squares technique. After several cycles of least-squares refinement, most hydrogen atoms were located on a Fourier difference map. The remaining hydrogen atoms were placed at the expected positions. In the final cycle of the least squares refinement, the nonhydrogen atoms were anisotropic and the hydrogen atoms were refined with individual isotropic temperature factors. The refinement yielded identical final R and R_w of 0.044 *.

* Tables of observed and calculated structure factors, bond lengths, bond angles, and related data have been deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA data deposition, P.O. Box 1527, Amsterdam, Netherlands. Reference should be made to No. BBA/DD/541/Carbohyde. Res., 247 (1993) 51–57.

RESULTS AND DISCUSSION

The molecular conformation and the atom-numbering scheme are illustrated in Fig. 1. The conformation of the talopyranose ring is $^4H_5$ with some flattening at C-4, having Cremer–Pople[10] puckering parameters of $Q = 0.523$ Å, and $\theta = 50°$, and $\phi = 275°$. Atoms O-5, C-1, C-2, and C-3 deviate from their mean plane by less than 0.002 Å. C-4 and C-5 deviate from the mean plane by 0.325 and −0.470 Å respectively, and the epoxide ring oxygen deviates by 1.18 Å.

The bond lengths of C-C(SP^3-SP^3, SP^3-SP^2 or SP^2-SP^2) and C–O of the title compound are in the usual range except for the C-1–C-2 bond (1.441 Å) that is substantially shorter than the nominal C–C bond length, but similar to the epoxide C–C bond length observed in some 2,3-anhydro[11–13] and 3,4-anhydro[14] sugar derivatives.

The bond angles O-5–C-1–C-2 (121.6°) and C-1–C-2–C-3 (119.3°) also show the planarity property of the O-5–C-1–C-2–C-3 fragment, and the bond angles O-2–C-1–C-2 (60.9°), C-1–O-2–C-2 (60.7°), and O-2–C-2–C-1 (58.4°) have normal magnitudes for a triangular geometry.

All intermolecular contacts are van der Waals interactions as found from the intermolecular atomic distances.

TABLE I

Crystal data, intensity-measurement data, and parameter-refinement data for 1,2-anhydro-3,4,6-tri-*O*-benzyl-β-D-talopyranose

Empirical formula	$C_{27}H_{28}O_5$		
Molecular weight	432.5		
Crystal dimensions	0.2×0.3×0.2 mm		
Melting point	77°		
Space group	*P*1		
Z	1		
Cell dimensions	$a = 12.763(2)$	$b = 11.130(2)$	$c = 4.764(3)$ Å
	$\alpha = 73.78(3)$	$\beta = 82.89(3)$	$\gamma = 62.16(1)°$
D_c (g/cm^3):	1.25		
Radiation Cu $K\alpha$ ($\lambda = 1.5418$ Å) with Ni filter; μ (mm^{-1}) 0.61			
Cell dimensions based on 20 reflections, with $12 < 2\theta < 32°$			
No. of reflection measured:	1694		
No. of reflection unique:	1123		
No. of reflection observed [$F_{obsd} > 3\,(F_{obsd})$]:	1123		
Function minimized, unit weight used			
R	0.0440		
R_w	0.0440		
Last difference Fourier map			
Max peak	0.180 e/Å^3		
Min peak	−0.157 e/Å^3		
$R\ \sigma(\text{del})/\sigma(F_{obsd})$			
EW $\sigma(\text{del}\cdot(\text{weight})^{1/2}/\text{sigma}(F_{obsd}\cdot(\text{weight})^{1/2})$			
del abs($F_{obsd} - F_{calcd}$)			

TABLE II

Fractional coordinates and temperature factors with their esd's in parentheses [a]

Atom	x/a	y/b	z/c	U_{eq} (A^2)
O-2	−0.9790(4)	0.9592(5)	0.0468(11)	0.052(3)
O-3	−0.8474(4)	0.6887(5)	−0.1777(11)	0.044(2)
O-4	−1.0339(3)	0.7104(4)	0.2150(10)	0.037(2)
O-5	−1.1754(4)	1.0011(5)	−0.0355(12)	0.054(3)
O-6	−1.2951(4)	0.7919(5)	−0.1723(13)	0.066(3)
C-1	−1.0819(6)	1.0353(7)	−0.1290(17)	0.051(4)
C-2	−0.9738(6)	0.9408(7)	−0.2418(17)	0.047(4)
C-3	−0.9614(5)	0.7988(7)	−0.2643(16)	0.041(4)
C-4	−1.0551(5)	0.7621(6)	−0.0943(15)	0.038(4)
C-5	−1.1754(6)	0.8934(7)	−0.1535(17)	0.046(4)
C-6	−1.2798(6)	0.8727(8)	−0.0125(19)	0.056(5)
C-30	−0.7599(6)	0.6834(9)	−0.3945(20)	0.065(6)
C-31	−0.6485(6)	0.5517(8)	−0.2813(19)	0.056(5)
C-32	−0.6286(10)	0.4277(12)	−0.3200(34)	0.142(10)
C-33	−0.5259(12)	0.3065(12)	−0.2119(34)	0.147(12)
C-34	−0.4423(8)	0.3126(12)	−0.0616(28)	0.090(8)
C-35	−0.4627(9)	0.4341(14)	−0.0228(36)	0.136(11)
C-36	−0.5669(8)	0.5575(10)	−0.1322(30)	0.116(8)
C-40	−0.9634(5)	0.5606(6)	0.3086(16)	0.044(4)
C-41	−1.0292(5)	0.4781(6)	0.2941(15)	0.039(4)
C-42	−1.1391(6)	0.5087(8)	0.4296(18)	0.056(4)
C-43	−1.1985(7)	0.4322(9)	0.4128(19)	0.071(6)
C-44	−1.1482(9)	0.3266(9)	0.2684(22)	0.081(6)
C-45	−1.0372(9)	0.2938(8)	0.1421(20)	0.083(6)
C-46	−0.9769(7)	0.3726(8)	0.1486(16)	0.056(5)
C-60	−1.3933(6)	0.7612(8)	−0.0676(24)	0.078(6)
C-61	−1.5128(6)	0.8862(8)	−0.1531(20)	0.066(5)
C-62	−1.5298(7)	0.9915(10)	−0.4051(20)	0.074(6)
C-63	−1.6441(9)	1.1013(12)	−0.4820(23)	0.086(7)
C-64	−1.7392(8)	1.0995(12)	−0.2972(27)	0.092(7)
C-65	−1.7206(8)	0.9953(11)	−0.0513(25)	0.093(7)
C-66	−1.6094(6)	0.8896(9)	0.0274(20)	0.072(6)

[a] $U_{eq} = 1/3\Sigma_i\Sigma_j U_{ij}\mathbf{a}_i^*\mathbf{a}_j^* a_i a_j$

For evaluation of the flexibility of the 1,2-anhydro sugar ether, calculation by molecular mechanics[15] was carried out using the MMX program[16] embedded in PCMODEL-386 on an AST-386. The dielectric constant used throughout the calculations was 1.5. Each calculated total energy consisted of stretching, bending, stretching–bending, torsional, van der Waals, and dipole–dipole contributions. The conformation of the pyranose ring of the molecule with the lowest energy, obtained by energy minimization of the crystal structure conformation, is a half chair with some flattening at C-4, very similar to the observed conformation. However, the conformation of the side chains of the model are quite different as shown in Table III. These differences are likely to have arisen because the predicted conformation is for an isolated gas phase molecule, but the observed one is in the solid state and subject to packing forces. Calculations for reproducing the

conformation of the crystal structure (Table III, Col. B) were carried out by energy minimization with fixed torsional angles for C-2–C-3–O-3–C-30 and O-6–C-60–C-61–C-62 at the observed values. Except for a little difference at the C-4 side chain, almost all of the torsional angles of the model were the same as those observed in the crystal structure. The reproduced conformation has a total energy 1.8 kcal/mol higher than the lowest energy. To evaluate the flexibility of the fused rings, calculations with a variety of side chain conformations were carried out. Starting from the torsional angle C-3–O-3–C-30–C-31 at −177.6°, a continuous change of ±30° about the O-3–C-30 bond (to 151.1 and −143.1° respectively) gave energies for each individual conformation of 59.43 to 58.12 kcal/mol, with little change (< 1° for the corresponding torsional angles) in the pyranose ring conformation. These results indicate that the 2,7-dioxabicyclo[4,1,0]heptane skeleton is rigid while

TABLE III

Selected torsional angles (°) obtained from X-ray study and from calculation by MMX

Angle	Magnitude (°) [a]				
	X-ray	MMX			
		A	B	C	D
O-5–C-1–C-2–C-3	0.9(8) [b]	−2.3	−1.3	−3.7	−0.4
C-1–C-2–C-3–C-4	−14.1(8)	−10.1	−12.4	16.2	−17.7
C-2–C-3–C-4–C-5	44.5(7)	42.9	45.1	−42.2	49.2
C-3–C-4–C-5–O-5	−65.4(7)	−67.8	−68.6	56.9	−68.0
C-4–C-5–O-5–C-1	53.5(7)	56.9	56.2	−45.7	51.3
C-5–O-5–C-1–C-2	−21.3(8)	−21.9	−21.5	20.0	−17.0
C-1–O-2–C-2–C-3	−109.2(10)	−108.8	−108.5	−108.4	
O-2–C-2–C-3–C-4	53.2(9)	55.3	53.3	80.5	
O-2–C-1–C-2–C-3	105.5(8)	102.2	102.8	102.4	
O-2–C-1–O-5–C-5	−91.5(7)	−89.3	−88.8	−47.7	
O-2–C-2–C-1–O-5	−104.6(9)	−104.5	−104.1	−107.3	
C-2–O-2–C-1–O-5	113.2(8)	111.4	111.7	111.1	
C-2–C-3–O-3–C-30	−79.1(8)	−91.3	−78.9	−150.0	
C-3–O-3–C-30–C-31	−173.4(9)	168.5	−177.6	57.8	
O-3–C-30–C-31–C-32	85.7(12)	57.7	−80.7	−118.8	
C-3–C-4–O-4–C-40	−88.9(8)	−96.5	−97.6	−164.6	
C-4–C-3–O-3–C-30	154.7(8)	140.1	154.1	85.4	
C-4–O-4–C-40–C-41	−72.1(8)	−70.4	-69.5	165.5	
C-4–C-5–C-6–O-6	−71.5(7)	−60.8	−63.2	−178.1	
O-4–C-40–C-41–C-42	−52.6(7)	−70.4	−70.2	61.7	
C-5–C-4–O-4–C-40	149.5(9)	143.5	142.9	64.1	
O-5–C-5–C-6–O-6	167.8(7)	177.5	175.4	54.8	
C-5–C-6–O-6–C-60	−179.8(8)	174.9	−173.3	−175.0	
C-6–O-6–C-60–C-61	74.2(9)	69.4	71.8	176.1	
O-6–C-60–C-61–C-62	29.3(11)	54.8	27.1	−58.8	

[a] A, The conformation with the lowest total energy of 57.37 kcal/mol, obtained by energy minimization from an input of the geometry of the crystal structure. B, The conformation with the total energy of 59.24 kcal/mol for reproducing the conformation of the crystal structure. C, The conformation with the total energy of 64.12 kcal/mol having an $^5H_4$ form for the pyranose ring. D, The conformation of the pyranose ring calculated by MMP2 (1977 version). [b] Standard deviations in parentheses.

TABLE IV

Selected bond lengths (Å) obtained from X-ray study and from calculation by MMX

Atoms	Distances (Å)	
	X-ray	MMX (59.24 kcal/mol)
C-1–O-2	1.407(9) [a]	1.439
O-2–C-2	1.435(11)	1.433
C-1–C-2	1.441(10)	1.507
C-2–C-3	1.546(13)	1.522
C-3–C-4	1.511(11)	1.547
C-4–C-5	1.535(8)	1.543
C-5–O-5	1.459(12)	1.425
O-5–C-1	1.402(12)	1.444
C-3–O-3	1.410(7)	1.424
O-3–C-30	1.417(10)	1.422
C-4–O-4	1.433(9)	1.429
O-4–C-40	1.439(7)	1.425
C-5–C-6	1.503(12)	1.541
C-6–O-6	1.417(14)	1.425
O-6–C-60	1.445(11)	1.424

[a] Standard deviations appear in parentheses.

TABLE V

Selected bond angles (°) obtained from X-ray study and from calculation by MMX

Angle	Magnitude (°)	
	X-ray	MMX (59.24 kcal/mol)
O-2–C-1–O-5	116.5(6) [a]	116.7
O-2–C-1–C-2	60.5(5)	58.2
C-1–O-2–C-2	60.9(5)	63.3
O-2–C-2–C-1	58.6(5)	58.5
O-2–C-2–C-3	116.9(6)	114.1
C-1–C-2–C-3	119.1(8)	117.4
C-2–C-3–C-4	112.8(6)	113.7
C-3–C-4–C-5	108.6(6)	108.2
C-4–C-5–O-5	109.9(7)	109.1
C-5–O-5–C-1	115.1(6)	114.7
O-5–C-1–C-2	121.8(8)	121.1
O-3–C-3–C-2	111.6(7)	112.6
O-3–C-3–C-4	110.2(5)	108.8
C-3–O-3–C-30	113.9(5)	114.1
O-4–C-4–C-3	114.2(7)	112.0
O-4–C-4–C-5	109.0(6)	108.8
C-4–O-4–C-40	113.7(6)	114.5
O-5–C-5–C-6	104.5(6)	108.4
O-6–C-6–C-5	104.3(7)	109.0
C-6–O-6–C-60	112.5(7)	112.5

[a] Standard deviations appear in parenthesis.

the side chains are quite flexible. Further evaluation of the fused ring rigidity was carried out by energy minimizations of several possible conformations, namely ^4E, E_4, ^5E, E_5, $^{3,0}B$, $B_{3,0}$, and $^5H_4$ involved in the pseudorotation[17] from $^4H_5$ form to $^5H_4$. Two torsional angles of the pyranose ring were fixed, and they were different for each energy minimization of the individual conformation. The calculations revealed that the fused ring is rigid as indicated by high energies of the $^{3,0}B$ (65.40 kcal/mol), $B_{3,0}$ (65.25 kcal/mol), ^5E (65.20 kcal/mol), E_4 (65.10 kcal/mol), and $^5H_4$ (64.12 kcal/mol) forms, and relatively high energies of the ^4E (60.08 kcal/mol) and E_5 (59.93 kcal/mol) forms.

The model gave basically the same bond lengths and bond angles as the crystal structure except for the C-1–C-2 bond length and its related bond angles (see Tables IV and V). We conclude that the MMX program is effective in describing the 2,7-dioxabicyclo[4,1,0]heptane skeleton conformation of 1,2-anhydro sugar ethers.

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REFERENCES

1 R.L. Halcomb and S.J. Danishefsky, *J. Am. Chem. Soc.*, 111 (1989) 6661–6665.
2 C. Schuerch, *Adv. Carbohydr. Chem. Biochem.*, 39 (1982) 157–212.
3 D.M. Gordon and S.J. Danishefsky, *Carbohydr. Res.*, 206 (1990) 361–366.
5 S.J. Sondheimer, H. Yamaguchi, and C. Schuerch, *Carbohydr. Res.*, 74 (1979) 327–332.
6 G. Yang and F. Kong, *J. Carbohydr. Chem.*, 11 (1992) 595–608.
7 F. Kong, J. Du, and H. Shang, *Carbohydr. Res.*, 162 (1987) 217–226.
8 Q. Chen, F. Kong, and L. Cao, *Carbohydr. Res.*, 240 (1993) 107–117.
9 J. Liu, F. Kong, and L. Cao, *Carbohydr. Res.*, 240 (1993) 295–300.
10 D. Cremer and J.A. Pople, J. Am. Chem. Soc., 97 (1975) 1354–1358.
11 A.M. Pilotti and B. Stansland, *Acta Crystallogr. Sect. B*, 28 (1972) 2821–2825.
12 J.W. Krajewski, P. Gluziński, Z. Urbańczyk-Lipkowska, A. Banaszek, L. Párkányi, and A. Kálmán, *Carbohydr. Res.*, 144 (1985) 13–22.
13 J.W. Krajewski, Z. Urbańczyk-Lipkowska, P. Gluziński, and A. Banaszek, *Carbohydr. Res.*, 194 (1989) 31–36.
14 J.W. Krajewski, P. Gluziński, and A. Banaszek, *Carbohydr. Res.*, 203 (1990) 195–203.
15 U. Burkert and N.L. Allinger, *Molecular Mechanics*, ACS Monograph 177, American Chemical Society, Washington, 1982.
16 PCMODEL Molecular Modeling Program, Serena Software, P.O. Box 3076, Bloomington IN 47402-3076, USA.
17 A.D. French and J.W. Brady, *ACS Symp.* Ser., 430 (1990) 1–19.