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Conformation of 2-*C*,1-*N*-carbonyl-2-deoxy-α-D-glycopyranosylamines*

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ABSTRACT

The conformations of 2-*C*:1-*N*-carbonyl-2-deoxyglycopyranosylamines (β-lactams) with the α-D-*gluco*, α-D-*galacto*, β-D-*arabino*, α-L-*xylo*, α-L-*gluco*, and β-D-*altro* configurations have been investigated by X-ray crystallography and n.m.r. spectroscopy. The n.m.r. data, interpreted in terms of an equilibrium of two rapidly interconverting half-chair forms, were supported strongly by the diffractometric data which showed almost regular half-chair conformations.

INTRODUCTION

We have reported[1–6] that cycloaddition of trichloroacetyl isocyanate to glycals leads to the stereospecific formation of a new class of β-lactams (2-*C*:1-*N*-carbonyl-2-deoxyglycopyranosylamines) having the unique bicyclic structure **1**. These β-lactams have potential biological activity and can be utilized for the synthesis of known and new antibiotics, particularly 1-oxapenams and 1-oxacephems.

The β-lactams **1** are crystalline compounds, stable under neutral conditions, and water-soluble, and can be stored in solution for several weeks at room temperature without decomposition.

The new sugar skeleton and its unexpected stability prompted an investigation of the spectral and conformational properties of β-lactams **1**. Thus, the compounds with the α-D-*gluco* (**2**), α-D-*galacto* (**8**), β-D-*arabino* (**13**), α-L-*xylo* (**17**), α-L-*gluco* (**21**), and β-D-*altro* (**25**) configurations were selected for n.m.r. studies, and **2**, **13**, and **26** for X-ray crystallography. N.m.r. data on other β-lactam derivatives, namely, **3–7**, **9–12**, **14–16**, **18–20**, **22–24**, and **26–29**, are also presented.

* Dedicated to Professor Aleksander Zamojski on the occasion of his 60th birthday.

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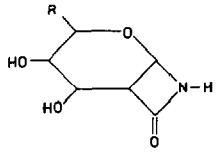
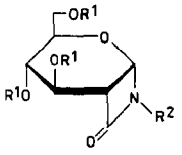
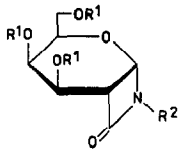


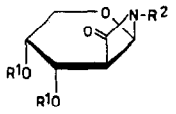
1 R = H, CH_3, CH_2OH



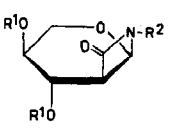
2 $R^1 = R^2 = H$
3 $R^1 = H, R^2 = Bn$
4 $R^1 = Bn, R^2 = H$
5 $R^1 = Ac, R^2 = Ts$
6 $R^1 = {}^tBuMe_2Si, R^2 = H$
7 $R^1 = {}^tBuMe_2Si, R^2 = Ts$



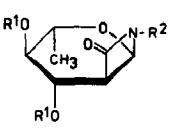
8 $R^1 = R^2 = H$
9 $R^1 = H, R^2 = Bn$
10 $R^1 = Bn, R^2 = H$
11 $R^1 = R^2 = Bn$
12 $R^1 = H, R^2 = {}^tBuMe_2Si$



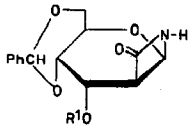
13 $R^1 = R^2 = H$
14 $R^1 = H, R^2 = Bn$
15 $R^1 = Me_3Si, R^2 = H$
16 $R^1 = Me_3Si, R^2 = Bn$



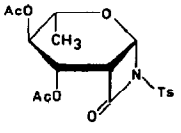
17 $R^1 = R^2 = H$
18 $R^1 = Ac, R^2 = H$
19 $R^1 = Ac, R^2 = Ts$
20 $R^1 = Ac, R^2 = COCCl_3$



21 $R^1 = R^2 = H$
22 $R^1 = Ac, R^2 = H$
23 $R^1 = Ac, R^2 = Ts$
24 $R^1 = Ac, R^2 = {}^tBuMe_2Si$



25 $R^1 = H$
26 $R^1 = Ac$



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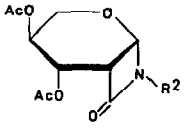
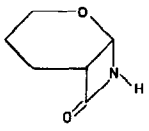


28 $R^2 = H$
29 $R^2 = COCCl_3$



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RESULTS AND DISCUSSION

X-Ray crystallography. — The fusion of a four-membered β-lactam ring to C-1 and C-2 of a pyranose unit causes major changes in the valence and torsion angles (Tables I and II). The pyranose ring in each compound adopts a half-chair conformation as illustrated in Figs. 1–3 for the α-D-*gluco* (**2**), β-D-*arabino* (**13**), and β-D-*altro* (**26**) compounds. Hence, the atoms O-1–C-1–C-2–C-3 that define plane A are coplanar within 0.05 Å for each compound, and C-4 and C-5, respectively, are out of the plane by +0.312(3) and −0.483(3) Å for **2**, −0.600(2) and +0.206(2) Å for **13**, and +0.362(4) and −0.403(5) Å for **26**. These data indicate that introduction of the 4,6-*O*-benzylidene group in **26** produces an almost regular half-chair conformation, whereas that of **13** is

TABLE I

Bond angles (degrees)

Angle	**2**	*Calc. for* $^4H_5$ *of* **30**	**13**	**26**	*Calc. for* $^5H_4$ *of* **30**
C-2–C-1–N-1	86.8(2)	88.5	87.0(1)	86.8(3)	87.8
C-2–C-1–O-1	118.7(2)	116.8	120.9(1)	118.9(3)	116.7
N-1–C-1–O-1	116.3(2)	118.6	115.8(1)	111.5(4)	110.9
C-1–C-2–C-3	117.5(2)	118.6	115.7(2)	118.4(4)	119.4
C-1–C-2–C-7	84.5(3)	82.3	83.9(1)	85.0(3)	83.1
C-3–C-2–C-7	113.2(2)	112.1	115.8(2)	117.2(4)	117.0
C-2–C-3–C-4	112.0(2)	111.3	108.3(2)	110.6(3)	112.3
C-3–C-4–C-5	109.5(2)	109.2	108.0(3)	111.6(4)	109.1
C-4–C-5–C-6	114.0(2)			109.5(4)	
C-4–C-5–O-1	108.6(2)	109.3	110.0(2)	109.8(3)	108.6
C-6–C-5–O-1	106.3(2)			106.3(4)	
C-2–C-7–N-1	92.9(2)	95.6	93.2(2)	92.1(4)	95.3
C-2–C-7–O-2	134.5(2)	132.4	134.9(2)	134.9(4)	132.5
N-1–C-7–O-2	132.5(2)	131.9	131.9(2)	132.9(4)	132.2
C-1–N-1–C-7	95.4(3)	93.0	94.4(2)	96.0(4)	93.3
C-1–O-1–C-5	115.6(2)	113.8	116.6(2)	116.3(3)	112.1

considerably distorted towards a sofa conformation with C-4 below plane A. Plane B includes C-1, C-2, C-7, and N-1, and forms dihedral angles with plane A of 115.5(1)°, 116.3(1)°, and 115.7(2)° for **2**, **13**, and **26**, respectively.

TABLE II

Torsion angles (degrees)

Angle	**2**	*Calc. for* $^4H_5$ *of* **30**	**13**	**26**	*Calc. for* $^5H_4$ *of* **30**
N-1–C-1–C-2–C-3	−109.39(0.24)	−105.69	107.56(0.17)	119.80(0.41)	−121.66
N-1–C-1–C-2–C-7	3.97(0.17)	5.28	−8.21(0.13)	1.43(0.34)	−4.52
O-1–C-1–C-2–C-3	8.91(0.35)	15.90	−10.89(0.24)	6.91(0.61)	−9.27
O-1–C-1–C-2–C-7	122.27(0.24)	126.87	−126.66(0.16)	−111.46(0.43)	107.87
O-2–C-1–N-1–C-7	−4.53(0.19)	−5.98	9.36(0.15)	−1.63(0.39)	5.11
O-1–C-1–N-1–C-7	−125.15(0.23)	−125.96	132.45(0.18)	118.16(0.40)	−112.74
C-2–C-1–O-1–C-5	−29.40(0.32)	−36.72	18.50(0.24)	−23.87(0.55)	36.71
N-1–C-2–O-1–C-5	72.12(0.29)	67.32	−84.32(0.21)	−122.43(0.38)	135.14
C-1–C-2–C-3–C-4	−19.24(0.31)	−21.96	32.04(0.23)	−19.92(0.53)	12.62
C-7–C-2–C-3–C-4	−115.34(0.26)	−115.17	127.91(0.20)	79.90(0.47)	−84.98
C-1–C-2–C-7–N-1	−4.35(0.19)	−5.84	9.03(0.14)	−1.55(0.36)	5.01
C-1–C-2–C-7–O-1	176.31(0.31)	176.36	−169.32(0.24)	−179.08(0.62)	−174.25
C-3–C-2–C-7–N-1	113.29(0.24)	111.94	−106.64(0.19)	−121.52(0.42)	124.58
C-3–C-2–C-7–O-2	−66.05(0.39)	−65.86	75.00(0.28)	60.96(0.78)	−54.69
C-2–C-3–C-4–C-5	47.89(0.26)	46.58	−60.94(0.20)	48.88(0.45)	−40.59
C-3–C-4–C-5–O-1	−69.01(0.28)	−69.50	70.94(0.21)	−67.42(0.47)	70.45
C-4–C-5–O-1–C-1	59.16(0.30)	63.95	−47.69(0.24)	52.91(0.51)	−67.92
C-2–C-7–N-1–C-1	4.63(0.20)	6.19	−9.55(0.15)	1.66(0.39)	−5.30
O-2–C-7–N-1–C-1	−176.01(0.29)	−175.99	168.89(0.23)	179.27(0.60)	−173.97

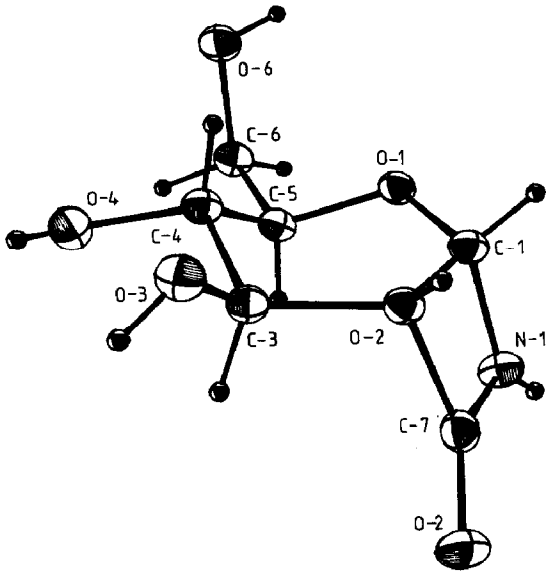


Fig. 1. ORTEP perspective drawing of 2-*C*:1-*N*-carbonyl-2-deoxy-α-D-glucopyranosylamine (**2**).

The β-lactam hydrogen is coplanar with plane B, and the lone pair of electrons on N-1 are perpendicular to plane B and delocalized towards the the C=O bond. Therefore, the exo-anomeric effect, resulting from the interaction of the unshared electron pair on N-1 and the polar C-1–O-5 bond, can be considered as negligible.

The endo-anomeric effect, which is negligible for *N*-acetylglycosylamines[7], does not influence the conformational equilibria in **2**–**29**. Compounds **2** and **13**, however, which adopt the conformation with the unshared electron pair on O-1 located suitably

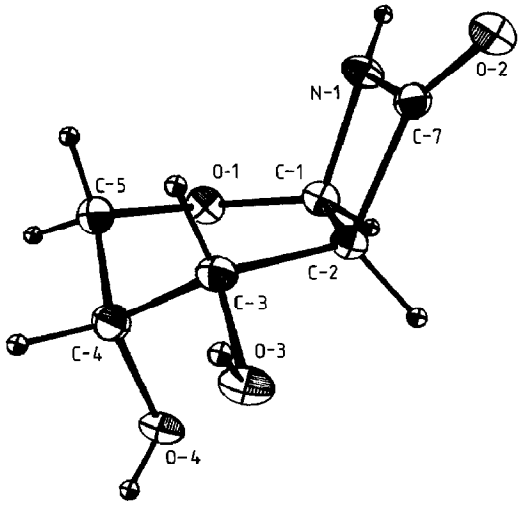


Fig. 2. ORTEP perspective drawing of 2-*C*:1-*N*-carbonyl-2-deoxy-β-D-arabinopyranosylamine (**13**).

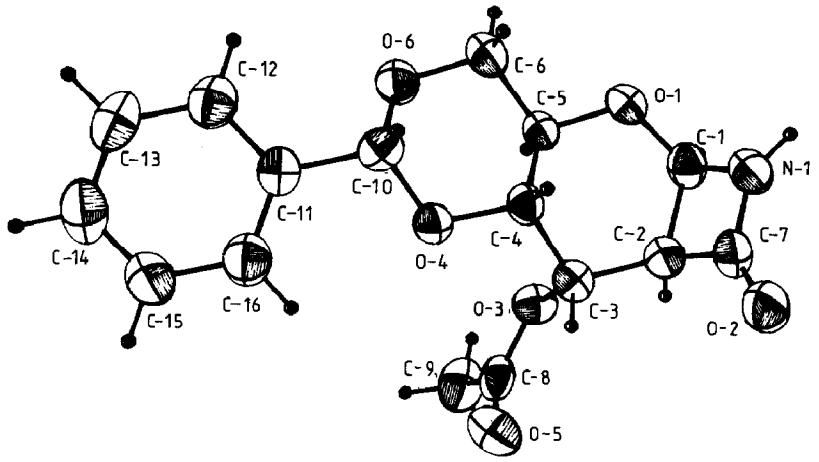


Fig. 3. ORTEP perspective drawing of 3-*O*-acetyl-4,6-*O*-benzylidene-2-*C*:1-*N*-carbonyl-2-deoxy-β-D-altropyranosylamine (**26**).

for interaction with the polar C-1–N-1 bond, exhibit noticeable changes in bond distances and valence angles as compared with **26** in which no such interaction can occur owing to the rigidity imposed by the 4,6-*O*-benzylidene group. The endo-anomeric delocalization in **2** and **13** is manifested by shortening of the O-1–C-1 bond and elongation of the C-1–N-1 bond as compared to the respective values found for **26**. The observed O-1–C-1 bond lengths are 1.402 Å for **2** and 1.403 Å for **13** (*cf.* 1.415 Å for **26**). On the other hand, the C-1–N-1 bonds in **2** (1.468 Å) and **13** (1.476 Å) are longer than that (1.453 Å) in **26** (Table III). The differences in bond lengths at the anomeric center of **2** and **26** are similar to those reported for methyl pyranosides[8]. There are also differences in the bond lengths in the remaining parts of **2** and **13**, as compared with those in **26**. It is clear that differences in the 3-, 4-, and 5-substituents and the configurations, as well as introduction of the 4,6-*O*-benzylidene ring in **26**, can cause geometrical changes other than in the vicinity of the ring fusion which is identical in each of the compounds.

In order to maximise overlap of the unshared electron pair on O-1 with the polar C-1–N-1 bond, the valence angles O-1–C-1–N-1 have to be 116.3(2)° and 115.8(2)° for **2** and **13**, respectively [*cf.* 111.7(4)° for **26**]. Owing to the larger values of the O-1–C-1–N-1 angle, the C-3–C-2–C-7 angle is markedly smaller [113.2° and 115.5°, respectively, for **2** and **13**; *cf.* 117.2(4)° for **26**].

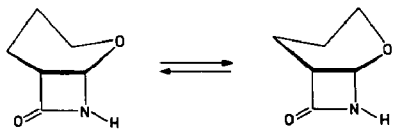
In each of the compounds (**2**, **13**, and **26**) subjected to X-ray structural analysis, hydrogen bonds to neighbouring molecules are formed. Four hydrogen bonds were found for **2** [N-1···O-2^{i} 2.924(3) Å, O-2···O-6^{ii} 2.709(3) Å, O-3···O-4^{iii} 2.741(3) Å, and O-4···O-6^{iii} 2.760(3) Å; symmetry related positions: (*i*) $1-x,-1/2+y,-z$, (*ii*) $x,1+y,z$, and (*iii*) $-x,1/2+y,1-z$]. The molecule **13** forms three hydrogen bonds [N-1···O-3^{i} 2.961(2) Å, O-2···O-4^{i} 2.683(2) Å, and O-3···O-4^{ii} 2.815(2) Å; symmetry-related positions: (*i*) $-1/2+x, 1/2-y, 1-z$ and (*ii*) $x, y, -1+z$]. The molecule **26** forms only one weak hydrogen bond [O-5···N-1 3.012(5) Å in which N-1 is derived from the molecule transformed by the symmetry operation $1-x,-1/2+y,1-z$].

TABLE III

Bonds lengths (Å)

Bond	**2**	*Calc. for* $^4H_5$ *of* **30**	**13**	**26**	*Calc. for* $^5H_4$ *of* **30**
C-1–C-2	1.559(4)	1.572	1.563(3)	1.553(6)	1.570
C-1–N-1	1.468(4)	1.472	1.476(2)	1.453(6)	1.478
C-1–O-1	1.402(4)	1.414	1.403(3)	1.415(6)	1.418
C-2–C-3	1.543(4)	1.530	1.539(3)	1.526(5)	1.525
C-2–C-7	1.528(4)	1.526	1.533(4)	1.523(6)	1.519
C-3–C-4	1.519(4)	1.530	1.524(4)	1.500(6)	1.529
C-4–C-5	1.529(4)	1.532	1.520(3)	1.520(6)	1.534
C-5–C-6	1.516(4)			1.507(7)	
C-5–O-1	1.438(3)	1.418	1.437(3)	1.433(5)	1.418
C-7–N-1	1.338(4)	1.336	1.342(4)	1.341(6)	1.337
C-7–O-2	1.221(3)	1.206	1.225(3)	1.199(6)	1.206

Conformational energy calculations. — Molecular mechanics MMP2 calculations[9], using MMP2 parametrization[10], were carried out to estimate the accessible conformations of the simplest structure having a tetrahydropyran ring fused to the azetidinone ring **30**. Energy minima were found for the two half-chair conformations **31** and **32**.



$^4H_5$ $^5H_4$

31 **32**

The calculated bond distances, as well as the valence and torsion angles of each conformation, are shown in Tables I–III. These data were compared with the experimental values obtained by the X-ray structure analysis of **2** and **26**. As the model representing the $^4H_5$ conformation, **2** was selected, the conformation of which was proved by diffractometric measurements. The geometric data fitting the alternative $^5H_4$ conformation were drawn from X-ray analysis of **26**, which occurs in a half-chair conformation that is enantiomeric with the calculated $^5H_4$ form. The calculated and experimental values were in acceptable agreement. The consistency of the calculated and experimental values is noteworthy because energy calculations were carried out for an isolated molecule bearing no 3-, 4-, and 5-substituents.

The $^4H_5$ form **31** was only slightly favoured (0.3 kcal/mol) over the $^5H_4$ form **32**. However, the accuracy of calculations does not allow conclusions to be drawn from so small an energy difference. On the other hand, the n.m.r. data (see below) obtained for solutions show a small preference for the conformation in which unshared electron pairs of O-1 are *gauche* to the polar C-1–N-1 bond. Such an arrangement is characteristic of substituents that show a reverse anomeric effect.

Molecular mechanics calculations revealed that the two half-chair conformations represent energy minima and that an equilibrium between them should provide a reasonable basis for a discussion of the conformational properties of the β-lactams **2**–**30**. However, the introduction of substituents at positions 3, 4, 5, and N-1 creates new polar and steric interactions which may change the geometry of the interconverting half-chair forms.

N.m.r. spectroscopy. — The ^{1}H-n.m.r. data for **2**–**29** are presented in Table IV. Consistent with the X-ray structural data for compounds **2**, **13**, and **26** as well as with energy minima calculations for **30**, the n.m.r. spectra of **2**–**29**, and hence the conformational behaviour in solution, were interpreted in terms of an equilibrium between two rapidly interconverting half-chair forms **31** and **32**.

The $J_{3,4}$ and $J_{4,5}$ values showed that, in aqueous solutions, the $^4H_5$ conformation of **2** and the $^5H_4$ conformation of **21** were favored in the conformational equilibrium, and even more so for the 6-deoxy compound **21**. This finding is consistent with the usually stronger tendency of the methyl group to occupy an equatorial position, as compared with the hydroxymethyl group.

The $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ values, *e.g.*, for the α-D- and α-L-*gluco* compounds **2**–**7** and **21**–**24**, were not entirely consistent with the model of interconverting half-chair forms **31** and **32**. The data suggest either distortion of the half-chair geometry or a conformational equilibrium involving more than two components.

The data for the tri-*O*-benzyl derivative **4** in solution in $CDCl_3$ indicate the conformational equilibrium to be similar to that of **2** in aqueous solution. Introduction of the bulky ^{t}BuMe$_2$Si substituents in **6** can cause a marked shift of the equilibrium towards the $^5H_4$ conformation, with the 4- and 5-substituents axial and the 3-substituent pseudo-axial. Such a shift of a conformational equilibrium has been observed for silylated glycals[11]. Acetyl substituents (**22**) exerted a similar but slighter effect.

The introduction of an electron-withdrawing (tosyl) group on nitrogen, as in **5**, **7**, and **23**, substantially changed the conformation. The simplest explanation of this phenomenon involves the reverse anomeric effect, *i.e.*, the dipole–dipole interaction of the polar C-1–N-1 bond and the dipole associated with the *gauche* electron pair on the ring oxygen atom[12] (**33** and **34**). With a partial positive charge at the nitrogen atom, this interaction results in a β-orientation of both dipoles. The orientation of dipoles can be achieved, owing to the interaction of the 3-, 4-, and 5-substituents, either by a shift of the conformational equilibrium towards the $^5H_4$ form or by deformation of the $^4H_5$ form into the boat conformation with C-4 and C-5 above plane A (O-1–C-1–C-2–C-3) or into the ^5S sofa conformation with C-5 above the plane O-1–C-1–C-2–C-3–C-4. By analogy, the reverse anomeric effect of the 1-carbamoyl group, which shifts the conformational equilibrium of the α-D-*gluco* derivative towards the regular $^1C_4$ chair form[13], can be compared with the effect of 1-pyridinium glucopyranose salts, where the conformation of the pyranoside ring is changed towards the boat form[14].

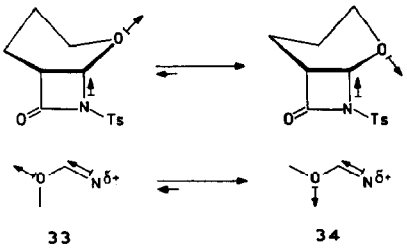
The $J_{3,4}$ and $J_{4,5}$ values indicate a similar situation for the α-L-*xylo* compounds **17**–**20**. The unsubstituted compound **17** prefers the $^5H_4$ conformation. Acetylation (**18**) and *N*-tosylation (**19**) shifted the conformational equilibrium towards the $^4H_5$ form.

TABLE IV

^{1}H-N.m.r. data (δ in p.p.m., J in Hz)

Compound	*Solvent*	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6* (*H-5'*)	H-6'	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$ ($J_{4,5'}$)	$J_{5,6}$ ($J_{5,5'}$)	$J_{6,6}$		
2	D_2O	5.67	3.52	4.16	3.64	3.97	3.87	3.95	4.3	3.3	6.9	8.5	6.2	2.7	12.2		
3	D_2O	5.49	3.44	4.06	3.55	3.45	3.57	3.68	4.2	3.1	7.0	7.7	2.7	5.1	12.3		
4	$CDCl_3$	5.52	3.44	4.11	3.65	4.01	3.69		4.3	2.7	6.7	8.7	$J_{5,6}+J_{5,6}=7.6$				
5	$CDCl_3$	5.88	3.55	5.27	4.91	3.67	4.20	4.01	5.2	2.6	4.7	6.4	3.7	5.5	12.1	$J_{2,4}$	1.1
6	$CDCl_3$	5.42	3.18	4.17	3.69	3.99	3.70	3.75	4.6	2.8	3.4	2.9	6.6	6.6	10.2	$J_{2,4}$	1.3
7	$CDCl_3$	5.76	3.24	4.11	3.77	3.52	3.56	3.67	5.6	3.3	2.9	2.0	7.9	6.0	9.5	$J_{2,4}$	1.5
8	D_2O	5.60	3.22	4.19	3.90	3.95	3.78	3.8	4.4	4.9	4.1	[a]	5.1	7.4	11.5		
9	$(CD_3)_2SO$	4.99	2.76	3.52	3.38		3.12–3.25		4.5	5.3	3.8	[a]	[b]	[b]	([b])		
10	$CDCl_3$	5.53	3.38	3.89	3.83	3.87	3.44	3.53	4.6	5.9	3.0	0.9	6.6	6.1	9.4		
11	$CDCl_3$	5.29	3.35	3.82	3.87	3.64	3.40	3.47	4.5	5.7	[b]	[a]	5.6	7.4	9.2		
12	CD_3COCD_3	5.47	3.25	3.99	3.93		3.64–3.82		4.7	4.7	3.9	[a]	[b]	[b]	[b]		
13	D_2O	5.57	3.37	4.27	4.06	3.90	(4.04)		4.3	4.6	3.9	4.8	(2.2)	(12.6)			
14	$CDCl_3$	5.14	3.23	4.09	3.81	3.48	(3.66)		4.3	4.3	2.9	3.8	(6.4)	(11.0)			
15	$CDCl_3$	5.37	3.26	4.11	3.91	3.74	(3.91)		4.7	4.6	2.9	5.9	(3.7)	(11.2)			
16	$CDCl_3$	5.14	3.23	4.09	3.81	3.48	(3.66)		4.3	4.3	2.9	3.8	(6.4)	(11.0)			
17	D_2O	5.51	3.38	4.04	3.7		(3.82)		4.2	3.2	7.0	[b]	[b]				
18	$CDCl_3$	5.53	3.80	5.40	5.00	3.87	(3.94)		4.6	2.4	6.3	7.8	(5.5)	(12.0)			
19	$CDCl_3$	5.84	3.51	5.26	4.80	3.48	(3.97)		5.3	2.3	4.8	5.8	(5.6)	(12.7)		$J_{2,4}$	1.0
20	$CDCl_3$	6.04	3.75	5.40	5.05	3.89	(4.15)		5.8	2.0	4.6	5.9	(4.7)	(13.1)		$J_{2,4}$	0.8
21	D_2O	5.49	3.37	3.95	3.27	3.88	1.24		4.3	3.0	7.7	9.2	6.3				
22	$CDCl_3$	5.51	3.40	5.31	4.80	4.08	1.25		4.5	2.3	6.3	8.8	6.3				
23	$CDCl_3$	5.85	3.52	5.22	4.71	3.48	1.12		5.3	2.4	5.4	7.5	6.5				
24	$CDCl_3$	5.40	3.49	5.31	4.81	3.98	1.23		4.6	2.0	6.1	8.7	6.2				
25	$CDCl_3$	5.40	3.64	4.50	3.94	4.13	3.65	4.33	4.0	1.4	2.9	9.5	10.2	5.3	10.5		
26	$CDCl_3$	5.48	3.68	5.79	4.09	4.15	3.67	4.35	3.9	1.5	3.0	9.7	9.9	5.1	10.6		
27	$CDCl_3$	5.68	3.91	5.08	4.85	3.74	1.21		4.7	8.4	7.5	7.4	6.6				
28	$CDCl_3$	5.45	3.78	5.19	4.97	3.82	(4.38)		4.6	8.1	5.4	3.0	(3.9)	(13.2)		$J_{3,5}$	0.9
29	$CDCl_3$	6.01	4.11	5.23	5.01	3.96	(4.24)		5.8	8.8	5.2	3.2	(3.6)			$J_{3,5}$	0.8

[a] Below resolution. [b] Not resolved or too complex for analysis.



33 34

For the β-D-*arabino* compounds **13–16**, the $J_{4,5}$ and $J_{4,5'}$ values indicated the preference for the half-chair conformation with an axial 4-substituent and a pseudo-equatorial 3-substituent. A similar preference may be postulated for α-D-*galacto* compounds **8–12**, but the evidence based on the $J_{2,3}$, $J_{3,4'}$, and $J_{3,5}$ values is not fully certain.

Owing to the rigid bicyclic structure of the β-D-*altro* compounds **25** and **26**, the $^4H_5$ conformation can be assigned in the crystalline state and in solution.

Because of the high stereoselectivity of cycloaddition reaction, the adducts with the 3-substituent *cis* to the β-lactam ring have been obtained only incidentally. In solution in $CDCl_3$, the β-L-*manno* compound **27** was present as an equilibrium of the half-chair conformations **31** and **32** with the $^5H_4$ form (**32**) preponderating. On the other hand, for the β-L-*lyxo* compounds **28** and **29**, the lack of the terminal CH_3 group caused a shift of the equilibrium towards the $^4H_5$ conformation.

The ^{13}C-n.m.r. data of the ring carbon atoms (Table V) of the α-D-*gluco* compounds **2** and **21**, as well as of the α-L-*xylo* compound **17**, showed characteristic similarities (C-1,2,3 resonances), which indicated similar conformational behavior in solution. Similar conclusions could be drawn for the α-D-*galacto* (**8**) and β-D-*arabino* (**13**) compounds.

Thus, the X-ray structures of **2**, **13**, and **26**, as well as the energy calculations carried out for the unsubstituted skeleton **30**, confirm the half-chair geometry. The difference between torsion angles found in crystalline **2** and **26** and those calculated for the idealized half-chair conformation of **30** are negligible. Larger differences found for **13** could be attributed to crystal packing.

The n.m.r. investigations did not point to any considerable conformational preferences of the fused β-lactam-pyranoid ring system, although the differences between the lengths of the C-1–O-1 and C-1–N-1 bonds found for **2** and **26** indicate an electronic effect in this part of the molecule. The conformational equilibrium of **2–29** depends on substitution at the nitrogen atom and on the *gauche* interaction of the substituents.

The unexpected stability of the β-lactams investigated does not depend on the conformation but can be attributed to the resistance of the anomeric centre to complexation with an acid catalyst required for opening of the four-membered ring.

EXPERIMENTAL

The 2-*C*:1-*N*-carbonyl-2-deoxyglycopyranosylamines were obtained according

TABLE V

^{13}C-N.m.r. data (δ in p.p.m.)

Compound	*Solvent*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C=O*
2	D_2O	78.38	57.60	71.55	72.02	73.98	63.62	173.25
	$(CD_3)_2SO$	75.23	56.72	69.44	70.64	71.71	61.22	168.12
8	D_2O	77.72	54.72	68.33	67.10	73.45	63.67	174.14
	$(CD_3)_2SO$	74.40	53.60	66.65	64.44	72.00	60.54	160.07
13	D_2O	76.93	55.28	67.62	66.53	65.05		173.84
	$(CD_3)_2SO$	73.86	54.86	65.38	64.31	63.50		168.38
17	D_2O	78.66	57.77	71.30	71.75	64.42		173.88
21	D_2O	78.40	58.22	71.43	77.25	69.52	19.34	179.49
25	$CDCl_3$	76.48	56.87	62.09	75.29	63.05	69.18	166.48

to the following references: **5**, **7**, **19**, and **27** (ref. 1), **24**, **28**, and **29** (refs. 2 and 6), **6** and **15** (ref. 4), **2**, **8**, **15**, **17**, **18**, **21**, and **30** (ref. 5), **20** and **22** (ref. 6), **3**, **4**, **9**, **10**, **11**, **14**, and **16** (ref. 15), and **12**, **25**, and **26** (ref. 16).

*Crystallography** (*Tables I–III*). — A well-formed colourless crystal of **2**, obtained from methanol, was selected for data collection (Table VI). The diffractometer used was designed and constructed at the University of Indiana. A Picker four-circle goniostat equipped with a Furnas Monochromator (HOG crystal) and a Picker X-ray generator was interfaced to a TI 980 minicomputer, with Sbo-Syn stepping motors to drive the angles. The minicomputer was interfaced by low-speed data lines to a CYBER 170–855 in which all computations were performed. The unit cell constants were determined at $-155°$ by least-squares treatment of 20 reflections. The monoclinic space group was determined from systematic absences ($k = 2n+1$ for $0k0$) to be $P2_1$. The $\theta-2\theta$ data collection technique over the range of $6° \leq 2\theta \leq 55°$ (Mo-K_α, $\lambda = 0.71069$ Å) was used to collect the data of which 963 with $F \geq 2.33\sigma$ (F_o) were used in the calculations. The data were corrected for Lorentz-polarization effects but not for absorption. The structure was solved by a combination of direct methods (MULTAN 78) and Fourier techniques. The positions of all hydrogens were clearly visible in a difference Fourier map phased on non-hydrogen atoms, and the coordinates were varied in the final cycles of refinement. No attempt was made to determine the absolute configuration of **2**. The absolute configuration of the sugar moiety found in the crystal structure was opposite to that of the starting glucal. Consequently, the final coordinates of all atoms were changed by applying an operation $1-x$, $1-y$, $1-z$, to obtain the proper enantiomer.

Crystallisation of **13** from methanol gave a suitable colourless single crystal that was used for data collection (Table VI). The unit cell constants were determined at

* Tables of positional parameters, thermal parameters, and F_oF_c values are deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/436/*Carbohydr. Res.*, 203(1990) 183–194.

TABLE VI

Crystal collection data

Compound	**2**	**13**	**26**
Formula	$C_7H_{11}NO_5$	$C_6H_9NO_4$	$C_{16}H_{17}NO_6$
Mol. wt.	189.2	159.1	319.3
Crystal size (mm)	0.30 × 0.30 × 0.40	0.25 × 0.25 × 0.30	0.10 × 0.30 × 0.30
Space group	$P2_1$	$P2_12_12_1$	$P2_1$
a (Å)	6.578(1)	13.480(2)	5.776(2)
b (Å)	7.928(2)	8.835(1)	8.941(1)
c (Å)	7.994(1)	5.562(1)	14.978(2)
β (°)	103.35(1)	–	99.73(2)
V (Å^3)	405.6	662.4	762.4
Z	2	4	2
D_x (g·cm^{-1})	1.549	1.596	1.391
μ (Mo-K_α) (cm^{-1})	1.244	1.267	1.004
Number of reflections measured	1256	950	1647
Number of unique data	1006	914	1583
Number of data above threshold	963	859	1044
Number of parameters	162	136	211
Weighting scheme	$1/\sigma^2(F)$	$1/\sigma^2(F)$	$1/\sigma^2(F)$
Av. shift to e.s.d ratio	0.05	0.05	0.08
Max. and min. (e·Å^{-3})	0.37	0.22	0.23
R, R_w	0.032, 0.036	0.033, 0.038	0.049, 0.041
S	1.11	1.04	2.19

– 156° by least-squares treatment of 30 reflections. The orthorhombic space group was determined from the systematic absences ($h = 2n + 1$ for $h00$, $k = 2n + 1$ for $0k0$, $l = 2n + 1$ for $00l$) to be $P2_12_12_1$. The θ–2θ scan mode over the range $6° \leqslant 2\theta \leqslant 55°$ (Mo-K_α, $\lambda = 0.71069$ Å) was used for data collection; 859 reflections with $F \geqslant 3\sigma(F_o)$ were used in further structural refinement. The data were corrected for Lorentz-polarization effects but not for absorption. The structure was solved by a combination of the direct method (MULTAN78) and Fourier techniques. The positions of all hydrogen atoms were clearly visible in a difference Fourier map phased on non-hydrogen atoms, and the coordinates and isotropic thermal parameters for hydrogens were varied in the final cycles of refinement. The absolute configuration found for the sugar moiety of **3** was the same as that of the starting D-arabinal derivative.

Crystallisation of **26** from acetonitrile–water gave a suitable colourless single crystal that was used for data collection (Table VI). Intensity data were collected at 20° with an Enraf–Nonius CAD4 diffractometer, using graphite single-crystal monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å). The unit cell constants were determined by least-squares treatment of 23 reflections. The monoclinic space group was determined from the systematic absences ($k = 2n + 1$ for $0k0$) to be $P2_1$. The ω-2θ scan mode over the range $4° \leqslant 2\theta \leqslant 52°$ was used for data collection. 1044 reflections with $F \geqslant 1.5\sigma(F_o)$ were used in further structure refinement. The data were corrected for Lorentz-polar-

ization effects but not for absorption. The structure was solved by direct methods (MULTAN11/82). The position and anisotropic thermal parameters of all non-hydrogen atoms and the coordinates of the hydrogen atom bond to N-1 were varied in the final cycles of refinement. The remaining hydrogens were calculated in their geometrical positions and refined as "riding" atoms at the distance of 0.95 Å from their carbons. All thermal parameters of H-atoms were set at 5.0 $Å^2$. The absolute configuration found for the sugar moiety of **26** was the same as that of the starting allal.

N.m.r. spectroscopy. — The ^{1}H-n.m.r. spectra of **2**–**29** were recorded at 25° for ~20-mg samples dissolved in D_2O or $CDCl_3$ (0.5 mL), using Bruker AM-400 and AM-500 spectrometers. HDO (δ 4.63) was the standard for the solutions in D_2O, and Me_4Si for solutions in $CDCl_3$. The chemical shifts and J values ($\pm$0.1 Hz) were obtained directly from the spectra on the assumption of first-order analysis.

The ^{13}C-n.m.r. spectra of **2**, **8**, **13**, **17**, **21**, and **25** were recorded at 25° for 5% solutions in D_2O, $(CD_3)_2SO$, or $CDCl_3$, using a Bruker AM-400 spectrometer. The assignments were proved by the HETCOR spectra.

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REFERENCES

1 M. Chmielewski, Z. Kaluza, C. Belzecki, P. Salanski, J. Jurczak, and H. Adamowicz, *Tetrahedron*, 41 (1985) 2441–2449.
2 M. Chmielewski, Z. Kaluza, C. Belzecki, P. Salanski, and J. Jurczak, *Heterocycles*, 24 (1986) 285–288.
3 M. Chmielewski and Z. Kaluza, *J. Org. Chem.*, 51 (1986) 2395–2397.
4 M. Chmielewski and Z. Kaluza, *Carbohydr. Res.*, 167 (1987) 143–152.
5 M. Chmielewski, Z. Kaluza, W. Abramski, D. Mostowicz, B. Hintze, and C. Belzecki, *Bull. Acad. Pol. Sci.*, 35 (1987) 245–249.
6 M. Chmielewski, Z. Kaluza, D. Mostowicz, C. Belzecki, E. Baranowska, J. P. Jacobsen, P. Salanski, and J. Jurczak, *Tetrahedron*, 43 (1987) 4555–4563.
7 A. J. Kirby, *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*, Springer-Verlag, Berlin, 1983, pp. 14–15.
8 Ref. 7, pp. 52–61.
9 E. Osawa and H. Musso, *Angew. Chem.*, 95 (1983) 1–12; N. L. Allinger, *Adv. Phys. Org. Chem.*, 13 (1976) 1–82; A. J. Kitajgorodsky, *Chem. Soc. Rev.*, 7 (1978) 133–163.
10 N. L. Allinger and H. Yuh, Operating instructions for MM2 and MMP2 program, University of Georgia, 1980.
11 D. Horton, W. Priebe, and O. Varela, *Int. Carbohydr. Symp. XIIth, Utrecht*, July 1–7, 1984, Abstr. D8.35, p. 519.
12 Ref. 7, pp. 71–72.
13 M. Chmielewski, J. N. BeMiller, and D. P. Cerretti, *J. Org. Chem.*, 46 (1981) 3903–3908; M. Sundaralingam, R. G. Brennam, P. Swaminathan, T. P. Haromy, W. B. Drendel, J. N. BeMiller, M. Chmielewski, and D. P. Cerretti, *J. Carbohydr. Chem.*, 1 (1982) 85–103.
14 R. U. Lemieux and A. R. Morgan, *Can. J. Chem.*, 43 (1965) 2205–2213; R. U. Lemieux, *Pure Appl. Chem.*, 27 (1971) 527–547.
15 J. Grodner and M. Chmielewski, unpublished results.
16 Z. Kaluza and M. Chmielewski, unpublished results.