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Carbohydrate Research 257 (1994) 25–33

CARBOHYDRATE
RESEARCH

X-ray and conformational investigation of 6-deoxy-6-*C*-(1,5-di-*O*-acetyl-2,3-*O*-isopropylidene-*β*-D-*allo*-pentofuranos-5-yl)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose and 6-*C*-(benzyl 5-deoxy-2,3-*O*-isopropylidene-*β*-D-ribofuranosid-5-yl)-1,2:3,4-di-*O*-isopropylidene-D-*glycero*-*α*-D-*galacto*-hexopyranose

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(Received July 5th, 1993; accepted October 22nd, 1993)

Abstract

The structures of the title compounds (**2b** and **3**) have been investigated in the solid state by X-ray methods. The crystals of **2b** are monoclinic, space group $P2_1$, and of **3** orthorhombic, space group $P2_12_12_1$. The cell dimensions are: for **2b**, $a = 9.910(2)$, $b = 11.745(1)$, $c = 11.810(3)$ Å, $\beta = 97.32(1)°$; and for **3**, $a = 6.103(1)$, $b = 15.954(1)$, $c = 28.855(3)$ Å. Both structures were solved by direct methods, and refined by a full-matrix, least-squares procedure giving for **2b**, $R = 0.0541$ (unit weight), and for **3**, $R = 0.0451$ ($R_w = 0.0445$). The galactopyranose rings of **2b** and **3** adopted a twist and a mixed twist-screw conformation, respectively. The absolute configuration at C-7 in **2b**, as well as at C-6 in **3**, was determined to be (*R*). Relatively strong intermolecular hydrogen bonds were observed in the crystal structure of **3**.

1. Introduction

Synthesis of eleven-carbon atom sugars composed of two sugar units, i.e., the hexopyranose and pentofuranose skeleton of tunicamine [1] linked at C-6–C-7, is far from simple. Usually, it demands a multistep elongation of one sugar unit [2,3].

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SSDI 0008-6215(93)E0402-M

An approach involving direct attachment of two sugars, i.e., derivatives of D-galactopyranose and D-ribofuranose, has been successfully accomplished by Secrist et al. [4], applying the Wittig reaction. Compounds of type **1**, thus obtained, containing a C-6–C-7 double bond, can be considered as excellent precursors for the synthesis of differently substituted higher sugars. We first explored the diborane addition reaction, followed by oxidation, as a method of introduction of one hydroxyl group to the C-6–C-7 linkage, which should offer a simple route to the 2-deamino-2-hydroxy-tunicamine derivative **2a**. Indeed, the reaction performed with the readily accessible compound **1b** [5] by the modified Secrist procedure [4] afforded **2a** as the predominant product [5] (60%) accompanied by the isomer **3** (20%); their two epimers were also present (20% altogether).

Structures **2a** and **3** were assigned by NMR spectroscopy [5]. However, to verify the assignments made, a full investigation of structures by X-ray crystallography seemed likely to provide most information about the configuration of the new hydroxyl group (*R* or *S*), and the conformation of the molecule. The results presented here can be compared with the previously reported [6,7] X-ray data of some analogous derivatives **4** and **5**.

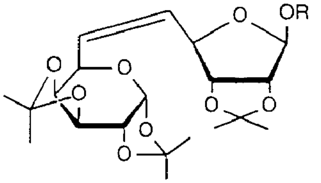
2. Experimental

X-ray diffractometry.—Colorless well-shaped crystals of compounds **2b** and **3** were chosen for X-ray diffractometric measurements. Characteristic data: **2b**, crystallized from diethyl ether, had; mp 157°C; $[\alpha]_D^{20}$ $-58.5°$ (c 1.0, $CHCl_3$); **3**, crystallized from ethanol, had; mp 194-195°C; $[\alpha]_D^{20}$ $-69.1°$ (c 1.0, $CHCl_3$). The cell constants for all cases were obtained from least-squares refinement based on 25 setting angles. The stability of the crystals was checked on 3 control reflections at 50 reflection intervals; no appreciable decay was observed. The Lorentz and polarization corrections were applied to all collected data. No absorption corrections were performed during the measurement stages. Table 1 gives the crystal data and measurement conditions for **2b** and **3**.

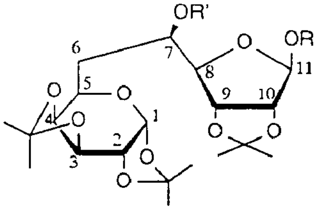
The solutions of both structures were obtained using program SHELX-76 [8] by a direct methods procedure. All atoms of **2b** and **3** were found in an E-map.

The same refinement procedure was applied in both cases; initially, the positional and isotropic temperature factors for non-hydrogen atoms were refined by the full-matrix, least-squares procedure (program SHELX-76 [9]). After convergence was reached, the empirical, spherical absorption correction was calculated (program DIFABS [10]) and applied to all observed reflections. The correction factors (minimum, maximum, average) for **2b** were: 0.794, 1.148, 0.986; and for **3**: 0.751, 1.159, 0.979.

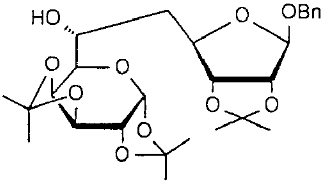
Further refinement steps were performed in the anisotropic mode for non-hydrogen atoms. The positional parameters for C-attached hydrogen atoms were calculated from assumed geometries, and those for the hydroxyl group of **3** from Fourier difference maps. They were added to parameter sets and refined in the isotropic mode. The final refinement steps converged at $R = 0.0541$ (unit weights)



1a R=Me
1b R=Bn



2a R=Bn; R'=H
2b R=R'=Ac



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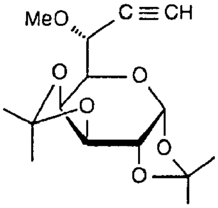

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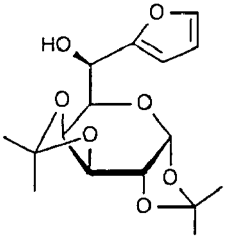

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and at $R = 0.0451$, $R_w = 0.0445$ ($w = 1.99/\sigma_F^2$), for **2b** and **3**, respectively. The highest residual electron density peaks observed for each case on final difference maps were below 1/4 eÅ^{-3}. The refined coordinates for non-hydrogen atoms, accompanied by their B_{eq} values, are listed in Table 2.

3. Results and discussion

Fig. 1 presents stereoviews of **2b** and **3** with crystallographic labelling of selected atoms.

The position of the OH group in **2b** was shown to be at C-7, and the configuration, based on the known absolute configuration of the sugar moiety, to

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* Fractional co-ordinates and isotropic temperature factors of the hydrogen atoms, anisotropic thermal parameters, bond distances, and valence angles for non-hydrogen atoms have been deposited with the Cambridge Crystallographic Data Centre. They may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Table 1
Crystal data and measurement conditions for **2b** and **3**

	2b	**3**
Formula	$C_{24}H_{36}O_{12}$	$C_{27}H_{38}O_{10}$
Molecular weight	516.54	522.59
Crystal system	monoclinic	orthorhombic
a (Å)	9.910(2)	6.103(1)
b (Å)	11.745(1)	15.954(1)
c (Å)	11.810(2)	28.855(3)
β (deg)	97.32(12)	–
V (Å^3)	1363.2(2.2)	2809.5(2.1)
Molecular multiplicity	$Z = 2$	$Z = 4$
Calculated density (g cm^{-3})	1.26	1.24
Space group	$P2_1$	$P2_12_12_1$
Radiation	Cu$K\alpha$ (graphite-monochromated)	
Wavelength (Å)	1.54178	
Linear absorption coeff. μ (cm^{-1})	7.7	7.4
Number of electrons $F(000)$	552	1120
Crystal size (mm)	0.15×0.28×0.45	0.10×0.25×0.50
Temperature	20±1°C	20±1°C
Diffractometer	CAD-4	
Scan mode	$\omega/2\theta$	
Scan range (2θ) (deg)	0–150	
Number of collected data:		
total measured	3253	3509
observed ($I > 2\sigma_I$)	2838	2785
unique	2798	2713
Max. h, k, l	12, 14, 14	7, 19, 36

be (R). In contrast, the location of the OH group in **3** was demonstrated to be at C-6, and the absolute configuration to be (R).

Contrary to earlier observations [6,11–15], no elongation of bonds was found for C-1/4 of the galactopyranose rings in **2b** and **3**. The only peculiarities were the values of endocyclic valence angles at C-2 and C-3, which were > 113°, indicating relatively high internal strain in the rings in both compounds.

Conformation of the galactopyranose rings in **2b** *and* **3**.—Previous investigations of 1,2:3,4-di-*O*-isopropylidene-ᴅ-galactopyranose derivatives [6,11–15] revealed various conformations of galactopyranose rings, including mixed screw-twist, almost "pure" twist, and twist-boat [7].

Comparison of the puckering parameters [16], endocyclic torsion angles, and asymmetry parameters [17] (see Table 3) suggests that the galactopyranose ring in **3** adopted the most energetically unfavoured hybrid twist-screw conformation, whereas in **2b** a deformed twist form was assigned.

Conformations parameters given in Table 3 for the galactopyranose ring indicate a deformed twist conformation in **4** and a hybrid twist-boat form in **5**.

Conformation of dioxolane rings in **2b** *and* **3**.—The results of conformational calculations for the dioxolane rings of **2b** and **3** are given in Table 4. The variety of

Table 2
Fractional co-ordinates ($\times 10^4$) [a] and B_{eq} values [b] for non-hydrogen atoms for **2b** and **3**

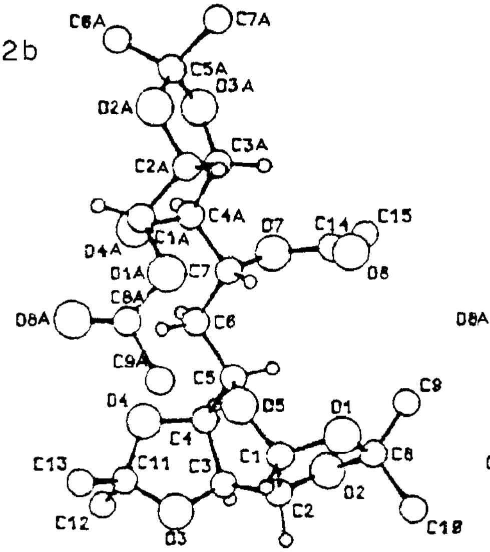
Atom	x/a	y/b	z/c	B_{eq}	x/a	y/b	z/c	B_{eq}
	2b				**3**			
O-1	906(3)	5221(0) [c]	7536(2)	4.2(1)	694(6)	8927(2)	6728(1)	5.9(1)
O-2	2901(3)	4486(3)	8373(3)	4.2(1)	−2417(6)	8448(2)	6421(1)	5.7(1)
O-3	1629(3)	4182(3)	11079(3)	4.2(1)	−2724(5)	6656(2)	7172(1)	5.2(1)
O-4	796(4)	2430(3)	10655(3)	4.8(1)	−3916(5)	7358(2)	7795(1)	4.8(1)
O-5	−187(3)	4068(3)	8738(3)	3.7(1)	−24(4)	8274(2)	7424(1)	3.6(1)
O-6					−4176(4)	9310(1)	8113(1)	3.8(1)
O-7	−671(3)	1629(3)	6627(2)	4.1(1)				
O-8	−1175(5)	3014(5)	5347(4)	7.2(2)				
C-1	718(4)	4993(4)	8687(4)	3.9(1)	328(7)	8156(2)	6949(1)	4.3(1)
C-2	2155(4)	4795(4)	9282(4)	4.0(1)	−1611(7)	7774(2)	6682(1)	4.1(1)
C-3	2274(5)	3823(4)	10134(4)	3.9(1)	−3422(7)	7443(2)	6995(1)	4.1(1)
C-4	1468(5)	2751(4)	9705(4)	3.8(1)	−3890(7)	7962(2)	7433(1)	4.0(1)
C-5	433(4)	2966(4)	8667(3)	3.3(1)	−2139(6)	8625(2)	7524(1)	3.1(1)
C-6	−722(5)	2105(4)	8569(4)	3.7(1)	−2096(6)	8911(2)	8028(1)	3.1(1)
C-7	−1551(4)	2086(4)	7414(3)	3.5(1)	−249(6)	9532(2)	8123(1)	3.5(1)
C-8	2315(5)	5108(5)	7387(4)	4.3(1)	−642(12)	9001(3)	6331(2)	6.6(2)
C-9	2435(6)	4412(6)	6341(5)	5.8(2)	−1451(17)	9861(3)	6290(2)	9.5(2)
C-10	2976(5)	6282(5)	7373(5)	5.5(2)	581(14)	8713(4)	5906(2)	8.3(2)
C-11	1135(5)	3193(4)	11588(4)	4.4(1)	−3766(8)	6554(3)	7604(2)	5.1(1)
C-12	2224(7)	2656(6)	12437(4)	5.9(2)	−6012(10)	6164(3)	7558(2)	6.7(2)
C-13	−122(7)	3502(7)	12078(6)	7.1(2)	−2291(11)	6036(4)	7913(2)	8.0(2)
C-14	−523(5)	2180(6)	5651(4)	5.0(2)				
C-15	519(6)	1609(8)	5058(5)	6.6(2)				
O-1A	−4159(3)	3315(3)	8061(3)	4.8(1)	3107(5)	8488(1)	8768(1)	4.4(1)
O-2A	−6076(3)	1177(4)	6454(4)	5.7(1)	2708(5)	10231(1)	9530(1)	4.3(1)
O-3A	−4260(3)	225(3)	5953(3)	5.5(1)	958(5)	11070(1)	9027(1)	4.5(1)
O-4A	−3535(3)	1400(3)	8272(3)	4.2(1)	−240(4)	9134(1)	8951(1)	3.8(1)
O-8A	−4327(5)	3155(5)	9922(4)	7.7(2)				
C-1A	−4616(4)	2156(4)	7898(4)	4.3(1)	1960(7)	8989(2)	9089(1)	4.1(1)
C-2A	−4970(4)	1964(4)	6650(4)	4.2(1)	3054(7)	9844(2)	9090(1)	3.9(1)
C-3A	−3749(4)	1332(4)	6278(4)	4.0(1)	1655(7)	10375(2)	8757(1)	3.8(1)
C-4A	−2743(4)	1247(4)	7349(3)	3.6(1)	−280(7)	9827(2)	8627(1)	3.6(1)
C-5A	−5677(5)	207(5)	5860(5)	5.3(1)	2162(8)	11083(2)	9444(1)	4.3(1)
C-6A	−6155(9)	−814(9)	6385(9)	9.6(4)	752(11)	11391(3)	9831(2)	6.5(2)
C-7A	−6271(6)	281(8)	4614(5)	7.3(2)	4243(10)	11595(3)	9390(2)	6.7(2)
C-8A	−4049(6)	3705(6)	9145(6)	5.9(2)	2240(8)	7655(2)	8710(1)	4.8(1)
C-9A	−3517(7)	4890(7)	9244(7)	7.8(3)	2572(7)	7109(2)	9121(1)	4.2(1)
C-10A					4583(8)	6704(3)	9194(2)	5.8(1)
C-11A					4886(12)	6188(3)	9568(2)	7.0(2)
C-12A					3286(15)	6069(4)	9879(2)	7.4(2)
C-13A					1261(13)	6478(4)	9819(2)	7.6(2)
C-14A					948(9)	6977(3)	9441(2)	6.1(2)

[a] In this and subsequent Tables, the values in parentheses are estimated standard deviations.

[b] Calculated from anisotropic thermal parameters as $B_{eq} = 8\pi^2 \cdot D_u^{1/3}$, where D_u is the determinant of the U_{ij} matrix in orthogonal space.

[c] Fixed co-ordinate.

2b



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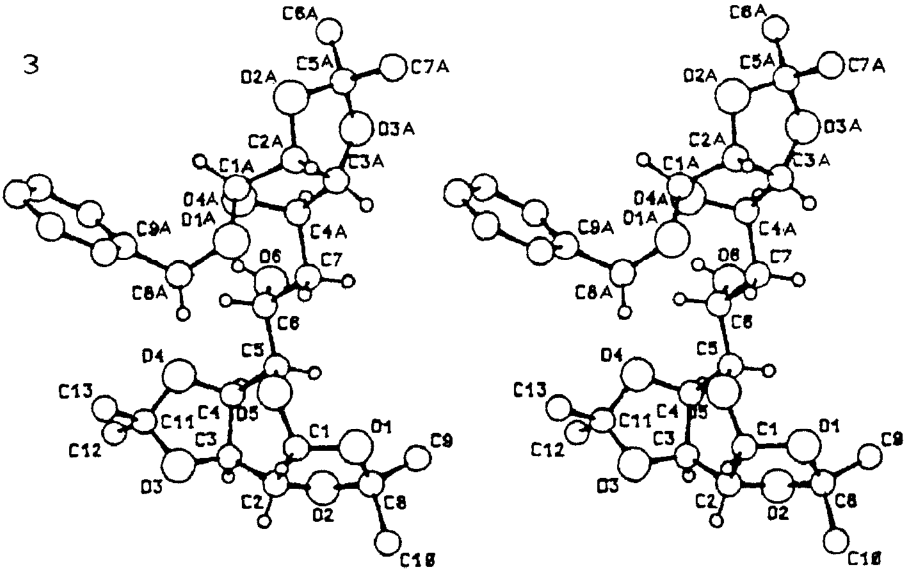

Fig. 1. A stereo-view of the arbitrarily oriented molecules of **2b** and **3**, with the crystallographic labelling of atoms.

Table 3
Conformational parameters of galactopyranose rings for **2b–5**

	2b	**3**	**4**[6]	**5**[7]
Puckering parameters				
Q (Å)	0.632	0.637	0.649	0.632
ϕ (°)	87.4	89.0	87.6	81.4
θ (°)	97.0	102.0	98.6	100.9
q_2 (Å)	0.627	0.623	0.641	0.635
Endocyclic torsion angles (degrees)				
O-5–C-1–C-2–C-3	−18.7(3)	−10.6(4)	−16.5(7)	−17.3(8)
C-1–C-2–C-3–C-4	43.7(4)	37.3(4)	42.6(7)	37.3(7)
C-2–C-3–C-4–C-5	−15.3(5)	−11.4(3)	−14.3(7)	−5.5(8)
C-3–C-4–C-5–O-5	−36.6(4)	−40.2(3)	−39.5(6)	−45.6(6)
C-4–C-5–O-5–C-1	65.9(4)	71.3(4)	70.5(5)	70.6(5)
C-5–O-5–C-1–C-2	−36.4(4)	−43.9(3)	−40.1(6)	−36.1(5)
Asymmetry parameters (degrees)				
ΔC_2	2.4(4)	2.7(4)	1.6(6)	11.2(6)
Conformation	$^{\mathrm{O}}T_2$def.	$^{\mathrm{O}}T_2 + ^{\mathrm{O}}S_5$	$^{\mathrm{O}}T_2$	$^{\mathrm{O}}T_2 + B_{2,5}$

Table 4
Conformational parameters of the dioxolane rings [a] for **2b** and **3**

1,2-Dioxolane ring	**2b**	**3**
Puckering parameters		
q_2 (Å)	0.305	0.287
ϕ (°)	115.2	98.2
Endocyclic torsion angles (degrees)		
O-1–C-1–C-2–O-2	−22.1(3)	−13.4(4)
C-1–C-2–O-2–C-8	33.0(4)	28.5(4)
C-2–O-2–C-8–O-1	−31.0(4)	−32.8(3)
O-2–C-8–O-1–C-1	16.5(4)	23.7(4)
C-8–O-1–C-1–C-2	3.4(5)	−6.5(3)
Asymmetry parameters (degrees)		
ΔC_s	4.2(4)	7.9(4)
ΔC_2		5.9(4)
Conformation	^{4}E	$^{4}T_3 + ^{4}E$

3,4-Dioxolane ring	**2b**	**3**
Puckering parameters		
q_2 (Å)	0.294	0.295
ϕ (°)	215.4	226.0
Endocyclic torsion angles (degrees)		
O-3–C-3–C-4–O-4	−18.4(3)	−13.5(3)
C-3–C-4–O-4–C-11	−0.6(4)	−6.7(4)
C-4–O-4–C-11–O-3	19.3(3)	24.8(4)
O-4–C-11–O-3–C-3	−31.8(4)	−33.9(3)
C-11–O-3–C-3–C-4	31.2(5)	28.8(4)
Asymmetry parameters (degrees)		
ΔC_s	0.8(4)	8.8(4)
ΔC_2		5.6(4)
Conformation	^{2}E	$^{3}T_2 + E_2$

[a] The indexing conforms to that for cyclopentane.

Table 5
Conformational parameters of the pentofuranose and dioxolane rings for **2b** and **3**

Pentofuranose ring	**2b**	**3**
Puckering parameters		
q_2 (Å)	0.296	0.292
ϕ (°)	318.9	335.7
Endocyclic torsion angles (degrees)		
O-4A–C-1A–C-2A–C-3A	−17.0(3)	−23.3(4)
C-1A–C-2A–C-3A–C-4A	−2.6(5)	6.0(3)
C-2A–C-3A–C-4A–O-4A	20.7(4)	13.0(3)
C-3A–C-4A–O-4A–C-1A	−32.7(4)	−29.0(4)
C-4A–O-4A–C-1A–C-2A	31.4(3)	33.1(4)
Asymmetry parameters (degrees)		
ΔC_s	2.8(3)	7.8(4)
ΔC_2		6.4(4)
Conformation	${}^4E$	${}^4T_{\mathrm{o}}+{}^4E$
2,3-Dioxolane ring	**2b**	**3**
Puckering parameters		
q_2 (Å)	0.151	0.151
ϕ (°)	80.5	80.5
Endocyclic torsion angles (degrees)		
O-2A–C-2A–C-3A–O-3A	−2.3(4)	8.7(3)
C-2A–C-3A–O-3A–C-5A	12.3(4)	12.0(3)
C-3A–O-3A–C-5A–O-2A	−17.5(3)	−28.4(4)
O-3A–C-5A–O-2A–C-2A	15.8(3)	34.3(4)
C-5A–O-2A–C-2A–C-3A	−8.1(5)	−26.2(4)
Asymmetry parameters (degrees)		
ΔC_s	3.2(3)	
ΔC_2	4.8(3)	2.8(3)
Conformation [a]	$E_3+{}^4T_3$	${}^2T_3$

[a] The indexing conforms to that for cyclopentane.

conformational assignments from envelope to the hybrid twist-envelope forms indicate a conformational lability of these rings.

Conformation of the pentofuranose and dioxolane rings in **2b** *and* **3**.—The β-D-*allo*-pentofuranose ring in **2b** has a "pure" envelope conformation (see Table 5), and the β-D-ribofuranoside ring in **3** adopts a twist-envelope hybrid conformation.

The 2,3-dioxolane rings in **2b** demonstrate an envelope-twist hybrid conformation, whereas they adopt a deformed twist form in **3**.

This difference of ring conformations in compounds **2b** and **3** can be explained by the intermolecular packing forces. The intermolecular packing forces in both compounds are completely different in nature. So, in **3**, the H-6o atom forms a strong intermolecular hydrogen bond to O-1A of the neighbouring molecule, whereas those in **2b** are predominantly van der Waals or dipole–dipole forces.

Hydrogen bonds in **3**.—An intermolecular hydrogen bond was observed in the crystal lattice of **3**. The distances and the angle at the H-atom are O-6–H-6o

0.90(4), O-6 ··· O-1A 2.836(5), H-6o ··· O-1A 1.97(4) Å; and O-6–H-6o ··· O-1A 160(1)°. The symmetry of the O-1A acceptor is $-1+x$, y, z. Considering the O–H ··· acceptor distances, the bond is relatively strong in nature. The bonded molecules form infinite chains in the crystal.

4. References

[1] A. Takasuki, K. Arima, and G.J. Tamura, *J. Antibiot.*, 24 (1971) 215–224.

[2] S.J. Danishefsky, S.L. De Ninno, S. Chen, L. Boisvert, and M.L. Barbachyn, *J. Am. Chem. Soc.*, 111 (1989) 5810–5818.

[3] J. Ramza and A. Zamojski, *Tetrahedron*, 48 (1992) 6123–6134.

[4] J.A. Secrist III and S.-R. Wu, *J. Org. Chem.*, 44 (1979) 1434–1439.

[5] W. Karpiesiuk and A. Banaszek, *Tetrahedron*, accepted.

[6] J.W. Krajewski, P. Gluziński, Z. Urbańczyk-Lipkowska, S. Jarosz, and A. Zamojski, *Carbohydr. Res.*, 173 (1988) 151–157.

[7] J.W. Krajewski, P. Gluziński, Z. Urbańczyk-Lipkowska, J. Ramza, and A. Zamojski, *Carbohydr. Res.*, 200 (1990) 1–7.

[8] G.M. Sheldrick, SHELX-76, Program for Crystal Structure Determination of Refinement, University of Cambridge, UK, 1976, 400-Atomic Version (Weizman Institute of Science, Rehovot, Israel, 1979); implemented on IBM PC/AT (1987).

[9] G.M. Sheldrick, in G.M. Sheldrick, C. Krüger, and R. Goddard (Eds.), *Crystallographic Computing 3*, Oxford University Press, UK, 1985, pp 175–189.

[10] N. Walker and D. Stuart, *Acta Crystallogr., Sect. A*, 39 (1983) 158–166.

[11] J.W. Krajewski, P. Gluziński, Z. Urbańczyk-Lipkowska, A. Zamojski, and P. Luger, *Carbohydr. Res.*, 139 (1985) 55–63.

[12] J.W. Krajewski, P. Gluziński, S. Jarosz, A. Zamojski, J. Bleidelis, A. Mishnyov, and A. Kemme, *Carbohydr. Res.*, 144 (1985) 183–195.

[13] J.W. Krajewski, P. Gluziński, Z. Urbańczyk-Lipkowska, A. Zamojski, G.D. Andretti, and G. Bocelli, *Carbohydr. Res.*, 148 (1986) 1–11.

[14] J.W. Krajewski, P. Gluziński, S. Jarosz, J. Bleidelis, A. Mishnyov, and A. Kemme, *Bull. Acad. Pol. Sci., Ser. Sci. Chim.*, 35 (1987) 91–102.

[15] B. Aebischer, J.H. Bieri, R. Prevo, and A. Vasella, *Helv. Chim. Acta*, 65 (1982) 2251–2258.

[16] D. Cremer and J.A. Pople, *J. Am. Chem. Soc.*, 97 (1975) 1354–1358.

[17] W.L. Duax, C.M. Weeks, and D.C. Rohrer, *Top Stereochem.*, 9 (1976) 271–383.