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THE SOLID STATE AND SOLUTION CONFORMATION OF 1,2-O-ALKYLIDENE-α-D-RIBOPYRANOSES. CHIRALITY ASSESSMENT OF PENTOSES FROM CRYSTALLOGRAPHIC TORSION ANGLES.

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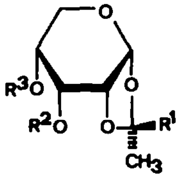
Abstract - The structure of 3,4-di-O-acetyl-1,2-O-(S)-(1-cyanoethylidene)-α-D-ribopyranose (1) has been determined from X-ray diffraction data and refined to a conventional R value of 0.050 for the 1259 observed reflexions (3 σ (I) criterion). The compound packs in the $P2_12_12_1$ space group with Z = 4 and lattice parameters of a = 20.0157 (7), b = 10.0552 (2), and c = 7.0870 (1) Å. The conformation of the pyranoid ring in the solid state can be described as chair $^1C_4$ (D) and that of the dioxolane ring, as envelope E_1. The use of configurational angles for characterization of pentoses is presented. NMR studies have been carried out to determine the major conformation in solution of 1 and its analogues 2 - 5. The results seem to indicate in all cases the presence of a conformational equilibrium between the chair-like, $^1C_4$, and the boat-like, $^OS_2$ conformation, in agreement with the results obtained from molecular mechanics calculations.

INTRODUCTION

The conformation of the pyranoid ring of 1,2-O-alkylidene hexopyranoses has been studied both in the solid state and in solution.[1] Although contradictory results on this subject have been published,[2-6] the conformational tendency of the pyranoid ring seems to depend on the nature of the sugar,[1,7] the configuration at C-2 of the dioxolane ring (C-6 in the discussion and data), and the nature of the substituents of the hydroxyl groups.[8] A skew-boat ($^OS_2$) conformation has been proposed for the pyranoid ring of tri-O-acetyl-1,2-O-alkylidene-α-D-glucopyranoses in which the alkyl group at C-2 of the dioxolane ring is in endo orientation, and a flattened chair ($^4C_1$) conformation for the isomers having this group exo.[1] However, the pyranoid ring of tri-O-acetyl-1,2-O-alkylidene-α-D-galactopyranoses presents a $^4C_1$ conformation that does not depend on the configuration at C-2 of the dioxolane ring.[1] A $^OS_2$ conformation has been found for the pyranoid ring of similar compounds in the α-D-allo- and α-D-gulo-pyranose series.[7]

In order to obtain reliable data to evaluate the different factors which govern the conformational tendency of these useful well known byciclic carbohydrate derivatives, we are now engaged in the conformational study of pentopyranoses 1,2-cis-fused to dioxolane rings. This paper constitutes the first report on this subject and deals with the solid state and solution conformation of 3,4-di-O-acetyl-1,2-O-(S)-(1-cyanoethylidene)-α-D-ribopyranose (1), and the solution conformation of 3,4-di-O-acetyl-1,2-O-(R)-ethylidene-α-D-ribopyranose (**2**), 1,2-O-(R)-ethylidene-α-D-ribopyranose (**3**), 3,4-di-O-benzoyl-1,2-O-(R)-ethylidene-α-D-ribopyranose (**4**), and 1,2-O-(R)-ethylidene-3,4-di-O-methyl-α-D-ribopyranose (**5**). X-Ray, ^{1}H- and ^{13}C-NMR studies and molecular mechanics calculations have been carried out. As far as we know only a few spectroscopic data have been published[9,10,11] on 1,2-O-alkylidene pentopyranoses.



1	$R^1 = CN$	$R^2 = Ac$	$R^3 = Ac$
2	$R^1 = H$	$R^2 = Ac$	$R^3 = Ac$
3	$R^1 = H$	$R^2 = H$	$R^3 = H$
4	$R^1 = H$	$R^2 = Bz$	$R^3 = Bz$
5	$R^1 = H$	$R^2 = Me$	$R^2 = Me$

RESULTS AND DISCUSSION

Details of the X-ray analysis of **1** are given in Tables 1 and 2, all according to the numbering scheme presented in Figure 1.[12] The conformation of the dioxolane ring can be described as distorted $\underline{E}_1$. The pyranoid ring adopts a chair $^1\underline{C}_4$ conformation, puckered around C5-O5 and less distorted around C2-C3, so that the distribution of torsion angles is quite uneven. Although C1-O5 bond is shorter and C1-O1 larger than the other C-O bonds, C1-O5 is larger and C1-O1 shorter than those found in the gluco, galacto and allo analogues, as expected for equatorial

TABLE 1. Torsion angles (°) for compound **1** from X-ray diffraction

O5-C1-C2-C3	-41.2(5)	O1-C1-C2-O2	-36.0(4)
C1-C2-C3-C4	37.7(5)	C1-C2-O2-C6	31.5(4)
C2-C3-C4-C5	-46.5(5)	C2-O2-C6-O1	-15.7(4)
C3-C4-C5-O5	60.2(5)	O2-C6-O1-C1	-8.5(4)
C4-C5-O5-C1	-66.8(5)	C6-O1-C1-C2	27.5(4)
C5-O5-C1-C2	56.2(5)	O5-C1-O1-C6	-91.7(4)
C5-O5-C1-O1	168.4(4)	C3-C2-C1-O1	-155.3(4)
O5-C1-C2-O2	78.1(4)	C4-C3-C2-O2	-76.1(5)
C1-C2-C3-O3	162.6(4)	C5-C4-C3-O3	-169.1(4)
C2-C3-C4-O4	70.9(5)	O5-C5-C4-O4	-60.0(5)
O2-C2-C3-O3	48.8(5)	O3-C3-C4-O4	-51.6(5)
C1-O1-C6-C8	-126.5(4)	C2-C3-O3-C9	145.3(4)
C1-O1-C6-C7	113.2(4)	C4-C3-O3-C9	-88.4(5)
C2-O2-C6-C7	-139.4(4)	C3-C4-O4-C11	116.3(5)
C2-O2-C6-C8	99.6(4)	C5-C4-O4-C11	-125.1(5)
C3-O3-C9-O6	-3.0(6)	C4-O4-C11-O7	-10.8(4)
C3-O3-C9-C10	176.9(5)	C4-O4-C11-C12	172.8(4)
H1-C1-C2-H2	-40(5)	C5-O5-C1-H1	-72(3)
H2-C2-C3-H3	42(5)	O5-C1-C2-H2	-166(4)
H3-C3-C4-H4	-52(4)	C1-C2-C3-H3	-82(3)
O5-C5-C4-H4	-174(3)	C2-C3-C4-H4	-172(3)
C5-C4-C3-H3	74(3)	O1-C1-C2-H2	80(4)
C4-C3-C2-H2	161(4)	O2-C2-C1-H1	-156(3)
C3-C2-C1-H1	85(3)	O2-C2-C3-H3	164(3)
O4-C4-C3-H3	-169(3)	O3-C3-C2-H2	-74(4)
O3-C3-C4-H4	65(3)	O4-C4-C5-H5	-179(4)
C1-O5-C5-H5	56(4)	O4-C4-C5-H5'	56(4)
C1-O5-C5-H5'	173(3)	C6-O1-C1-H1	149(3)
C3-C4-C5-H5	-58(4)	C6-O2-C1-H2	-84(3)
C3-C4-C5-H5'	177(4)		

TABLE 2. Bond distances (Å) and bond angles (°) for compound **1** from X-ray diffraction

C5-O5	1.424(6)	C1-O5	1.404(6)	C1-O1	1.413(6)
C2-O2	1.435(5)	C3-O3	1.436(5)	C4-O4	1.454(5)
C6-O1	1.425(5)	C6-O2	1.403(5)	C1-C2	1.520(6)
C2-C3	1.508(6)	C3-C4	1.510(7)	C4-C5	1.514(7)
C6-C8	1.489(7)	C6-C7	1.509(7)	C8-N	1.151(8)
C9-O3	1.342(5)	C11-O4	1.308(7)	C9-O6	1.194(5)
C11-O7	1.169(8)	C9-C10	1.485(9)	C11-C12	1.482(8)
C5-O5-C1	112.1(4)	O5-C1-O1	106.1(4)	O5-C1-C2	113.3(4)
O5-C5-C4	109.8(4)	C1-C2-C3	113.9(4)	C2-C3-C4	114.3(4)
C3-C4-C5	108.8(4)	C2-C3-O3	107.5(3)	C4-C3-O3	112.0(4)
C3-C4-O4	111.2(4)	C5-C4-O4	106.9(4)	C3-C2-O2	110.9(3)
C2-C1-O1	102.9(4)	C1-C2-O2	101.6(3)	C2-O2-C6	106.8(3)
C1-O1-C6	107.1(3)	O1-C6-O2	108.3(3)	O1-C6-C8	105.9(3)
O1-C6-C7	113.0(4)	O2-C6-C8	110.0(4)	O2-C6-C7	109.7(4)
C8-C6-C7	110.0(4)	C6-C8-N	179.1(6)	C3-O3-C9	117.4(3)
C4-O4-C11	119.4(4)	O3-C9-O6	123.3(4)	C4-C11-O7	121.7(6)
O3-C9-C10	111.7(4)	O4-C11-C12	112.5(5)	O6-C9-C10	125.0(4)
O7-C11-C12	125.7(7)				

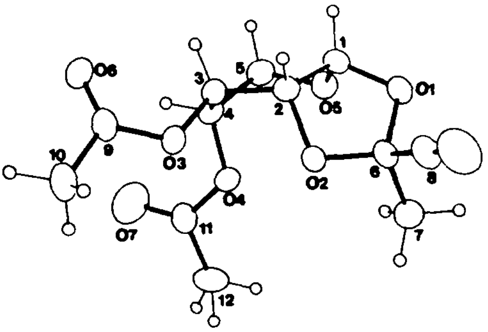


Fig. 1. An ORTEP view of compound **1** showing the atomic numbering

TABLE 3. Geometry of the short intramolecular contacts (Å and °) from X-ray diffraction

O2-C2...C4-O4	-4.3(3)	C9-O3-C3-H3	29(3)
O2...O4	2.994(5)	O7...C4	2.658(10)
O6...C3	2.233(4)	O7...H4	2.18(4)
O6...H3	2.29(4)	C4-H4...O7	108(3)
C3-H3...O6	103(3)	O7-C11-O4-C4	-10.8(9)
O6-C9-O3-C3	-3.0(6)	C11-O4-C4-H4	-5(3)

anomeric bonds.[13,14] It is remarkable the difference between C6-O1 and C6-O2 in the dioxolane moiety.[1,15] Table 3 shows some significant intramolecular contacts between the substituent chains. O6...H3 and O7...H4 could determine the conformation of these chains around C9-O3 and C11-O4. Moreover, there is a contact O2...O4 across the ring, which is in the order of those found in the absence of intramolecular hydrogen bond.[16] These interactions could account for the wide range of torsion angles, larger in the opposite side of the molecule, around C5-O5.

As previously reported in the hexopyranose series,[1] the crystallographic torsion angles have been used to assess the configuration in pentopyranose derivatives. The configurational angles of the first non-hydrogen substituents of the asymmetric carbon atoms were used.[1] That is, the exocyclic torsion angle minus the corresponding endocyclic one, both following a given sense around the ring, ... C1, C2, ... O5, ... For example, $\rho\,[\mathrm{C1\text{-}O1}] = \tau\,[\mathrm{C5\text{-}O5\text{-}C1\text{-}O1}] - \tau\,[\mathrm{C5\text{-}O5\text{-}C1\text{-}C2}]$. This operation allows to "flatten" and "open" the ring into the open-chain Fischer projection. Having the carbon chain vertical, and the aldehydic atom at the top, in D-series, the hydroxylic oxygen of the asymmetric carbon at the bottom has its ρ angle positive (on the right of the projection) and, for the α-anomer, the oxygen at the top has ρ with the same sign (both oxygen atoms on the same side). The signs for the other ρ angles, respect to that at the bottom, define the sugar type; that is, the relative position of the oxygen (see Table 4, which also presents the "exo/endo" characterization). Just looking at the Fischer projection, it is straightforward to notice that $\rho\,[\mathrm{C2\text{-}O2}]$ and $\rho\,[\mathrm{C2\text{-}O3}]$ are +, -; -, +; -, - for D-xylo, D-arabino and D-lyxo derivatives, respectively.

TABLE 4. Configuration angles (°, mod 2π) for the non-hydrogen first substituents at the chiral centers of the pyranoid ring, following the sequence: ... C1, C2, ...

Angle	Value	Type	Angle	Value	Type
[C1-O1]	+ 112.2(6)	α	[C2-O2]	+ 119.3(5)	Ribose
[C4-O4]	+ 117.4(6)	D	[C3-O3]	+ 124.9(5)	
[C6-C8]	- 118.0(6)	exo			

The 300 MHz ^{1}H-NMR spectra of **1** - **5** have been analyzed iteratively and the best computed values of chemical shifts and coupling constants are given in Table 5. There is a large and

TABLE 5. ^{1}H-NMR spectral parameters ν (δ) and J (Hz) of compounds **1** - **5** in $CDCl_3$

Parameters	Compound				
	1	**2**	**3**	**4**	**5**
ν_1	5.602	5.390	5.214	5.478	5.273
ν_2	4.499	4.168	4.130	4.376	4.191
ν_3	5.202	5.173	3.930	5.499	3.490
ν_4	5.283	5.246	3.871	5.630	3.722
ν_5	3.939	3.934	3.935	4.154	4.022
$\nu_{5'}$	3.831	3.866	3.650	4.032	3.635
J_{12}	4.1	3.9	2.7	3.7	3.7
J_{23}	3.3	3.3	3.0	3.3	3.0
J_{24}	1.0	1.0	1.0	0.8	0.8
J_{34}	5.1	5.2	4.2	5.0	4.7
J_{45}	5.2	5.1	3.3	4.7	4.8
$J_{45'}$	4.9	5.1	2.3	4.7	4.9
$J_{55'}$	-13.0	-12.7	-12.6	-12.9	-12.5

positive long-range coupling constant $^{4}J_{2,4}$, which has been previously taken[1,7] as indicative of planar arrangement of H-2 and H-4. This "W" disposition can be accounted for by both a $^{1}\underline{C}_{4}$ and a $^{O}\underline{S}_{2}$ conformation. Table 6 shows the expected values of $^{3}J_{H,H}$ for the chair $^{1}\underline{C}_{4}$ conformation, calculated by applying Altona's equation[17] to the vicinal proton torsion angles found for **1** by X-ray diffraction. The observed values are in all cases higher than those expected for this conformation. The temperature and solvent dependence of proton coupling constants is shown in Table 7 and 8, respectively. At low temperature, slight broadening of the signals and changes in the chemical shifts were observed, both in the proton and carbon spectra, although no coalescence temperature was reached. As temperature decreased, $^{3}J_{H,H}$ were closer to those expected for the $^{1}\underline{C}_{4}$ conformation. There is also a noticeable effect of the solvent on the $^{3}J_{H,H}$ values. The closest values of coupling constants to the chair were found in DMSO-$\underline{d}_{6}$. Vicinal and geminal carbon-proton coupling constants also provided evidence of the possible existence of a conformational equilibrium. Table 9 shows the chemical shifts and the best computed values of $^{n}J_{C,H}$ for **1** in $CDCl_3$ (see Experimental Part). Table 10 presents the observed proton-carbon and proton-oxygen torsion angles, related with the corresponding vicinal and geminal $J_{C,H}$[18,19].

TABLE 6. Calculated and observed $^{3}J_{H,H}$ for compound **1**

$^{3}J_{H,H}$	Observed[a]	$^{1}\underline{C}_{4}$[b]
1,2	4.1	2.9
2,3	3.3	4.1
3,4	5.1	3.4
4,5	5.2	1.0
4,5'	4.9	2.3

[a] In $CDCl_3$; [b] Values from X-ray data according to Altona's equation.[17]

TABLE 7. Temperature dependence of the conformational equilibrium for **1** in 1 : 1, acetone : methanol

$^{3}J_{H,H}$	Temperature (° C)			
	20	-40	-60	-100
1,2	3.6	3.3	3.1	2.9
2,3	3.6	3.7	3.8	3.9
3,4	4.8	4.5	3.9	3.5
4,5	4.1	3.8	3.5	-
4,5'	3.9	3.4	3.3	-

TABLE 8. Observed coupling constants for **1** in different solvents

$^{3}J_{H,H}$	Solvent			
	C_6H_6	$CDCl_3$	$(CD_3)_2CO : MeOD$ 1 : 1	$(CD_3)_2SO$
1,2	3.6	4.1	3.6	3.4
2,3	3.6	3.3	3.6	3.8
3,4	4.8	5.1	4.8	4.2
4,5	4.5	5.2	4.1	3.9
4,5'	4.4	4.9	3.9	3.4

TABLE 9. ^{13}C-NMR spectral parameters $\nu(\delta)$ and J(Hz) for compound **1**

ν		$^1J_{C,H}$		$^2J_{C,H}$ [a]		$^3J_{C,H}$	
ν_1	98.1	C1H1	180.4	C1H2	0	C1H3	0
ν_2	75.2	C2H2	155.7	C2H1	6.3	C1H5	6.1
ν_3	65.7	C3H3	142.9	C2H3	0	C1H5'	6.1
ν_4	64.4	C4H4	154.4	C3H2	-3.9	C2H4	5.4
ν_5	62.6	C5H5	146.7	C3H4	-3.8	C3H1	0.9
ν_6	100.6	C5H5'	150.6	C4H3	0	C3H5	3.9
				C4H5	-0.5	C3H5'	3.9
				C4H5'	-4.9	C4H2	4.7
				C5H4	0	C5H1	3.5
						C5H3	0
						C6H1	5.5
						C6H2	1.1

a) Signs of $^2J_{C,H}$ according to Perlin et al.[26]

For instance, $^3J_{C1,H5}$ and $^3J_{C1,H5'}$ have the same value of 6.1 Hz. In the chair conformation, these angles have values of 174° and 57°, which can not explain the observed value.

Conformational equilibria in pentoses have been described involving both chairs, $^4\underline{C}_1$ and $^1\underline{C}_4$, and twist-boat forms[20,21]. These equilibria seem to depend strongly on the anomeric effect and on the nature of the sugar. In order to have accurate geometries for all the possible conformations which could take part in the conformational equilibrium, molecular mechanics calculations using the MM2 program[22] were carried out for **1**. Although individual molecules can show a typical behaviour due to special crystal packing effects, the geometry of the calculated $^1\underline{C}_4$ conformation agrees quite well with that observed by X-ray analysis. Bond-lengths deviations are under 0.03 Å and torsion angles are reproduced also with reasonable accuracy, deviations being not larger than 4° for the pyranoid ring and than 10° for the dioxolane one. The other two global minima found for **1** correspond to the $^o\underline{S}_2$ and $^4\underline{C}_1$ conformations and have an "steric energy" 1.58 kcal/mol and 3.99 kcal/mol higher than that calculated for the $^1\underline{C}_4$ form, respectively. The destabilization of the $^4\underline{C}_1$ chair could be explained by the strong interactions between the <u>endo</u>-methyl group and the substituent at O-3 and between this substituent and O-2 (including lone pairs). This energetic differences would account for a conformational equilibrium containing about 93% $^1\underline{C}_4$, 7% $^o\underline{S}_2$ and less than 0.5% $^4\underline{C}_1$, if the entropic contributions were neglected. However, it is known that the entropy of skew conformations can be high relative to that of a chair[23] and the difference in free energy between the $^1\underline{C}_4$ and the $^o\underline{S}_2$ forms could be lower than calculated by the MM2 program. Proton-proton torsion angles for the calculated more stable $^1\underline{C}_4$ and $^o\underline{S}_2$ conformations are presented in Table 10, which also includes oxygen-proton and carbon-proton torsion angles for these two forms. Table 11 shows the expected values of $^3\underline{J}_{H,H}$ for the two conformers according to the empirical generalization of the Karplus equation[17] in comparison to the observed values for **1** in CDCl$_3$. These values are in between the skew and the chair conformation. On this basis, the equilibrium at room temperature could be described as 50% of $^o\underline{S}_2$ and 50% of $^1\underline{C}_4$ conformers. This percentage would indicate no free energy difference between both conformers, which accounts for an entropic difference about

TABLE 10. X-H torsion angles from MM2 calculations.[22]

Angle	$^{1}C_{4}$	$^{o}S_{2}$	Angle	$^{1}C_{4}$	$^{o}S_{2}$
H1H2	-42	-20	C5H3	69	83
H2H3	48	61	C6H1	144	114
H3H4	-51	-38	C6H2	-78	-83
H4H5	-58	-140	O1H2	76	97
H4H5'	60	-22	O5H2	-167	-139
C1H3	-76	-63	O2H1	-157	-135
C1H5	57	-172	O2H3	168	-178
C1H5'	174	-57	O3H2	-69	-59
C2H4	-167	-156	O3H4	70	80
C3H1	82	104	O4H3	-174	-155
C3H5	-60	-141	O4H5	179	98
C3H5'	180	100	O4H5'	59	-21
C4H2	166	179	O5H4	-179	97
C5H1	-72	-168			

TABLE 11. Expected $^{3}J_{H,H}$ values for the $^{1}C_{4}$ and $^{o}S_{2}$ conformations according to Altona[17] and MM2 calculations.[22]

$^{3}J_{H,H}$	$^{1}C_{4}$ (D)	$^{o}S_{2}$ (D)
1,2	2.8	5.0
2,3	3.9	2.3
3,4	3.4	5.2
4,5	1.0	9.2
4,5'	2.8	7.1

5 cal/°K. mol, in agreement with tnat found in some substituted cyclohexanes.[23]

The conformation of the pyranoid ring of the O-substituted ethylidene derivatives 2, 4 and 5 can be also described as an almost 1:1 $^{1}C_{4}$-$^{o}S_{2}$ equilibrium in $CDCl_3$ (Tables 5 and 11). The nature of the substituent, acetyl, benzoyl or methyl does not seem to influence the percentage of both forms. It is remarkable, however, that the unsubstituted ethylidene 3 presents $^{3}J_{H,H}$ closer to those expected for the $^{1}C_{4}$ form and, according to these values, the equilibrium can be described as 5:1 $^{1}C_{4}$ - $^{o}S_{2}$ in $CDCl_3$.

The lowering of the temperature seems to increase the amount of the $^{1}C_{4}$ conformation, which tends to become almost the exclusive form at -100° C (Tables 7 and 11). This could be explained by considering that the entropic contribution of the skew form decreases when the temperature does. On the other hand, the effects of the solvent on the equilibrium are not explainable merely on the basis of the polarity. Thus, both C_6D_6 and DMSO-d_6 exhibit the same, although in different magnitude, chair-directing effect in spite of their different dielectric constants (Tables 6 and 11).

According to all these results, it can be concluded that the conformation of the pyranoid ring of 1,2-O-alkylidene-α-D-ribopyranoses in solution can be described as an equilibrium between $^1C_4$(D) and $^OS_2$ (D) conformers.

It is not easy to rationalize the influence of the orientation and electronegativity of the substituents on the Karplus-like dependence of $^3J_{C,H}$.[18] The observed values for **1** can be explained under a broad, qualitative basis (Tables 9 and 10). The values outlined above of $^3J_{C1,H5} = {}^3J_{C1,C5'} = 6.1$ Hz can be now understood taking into account the axial-ecuatorial interconversion of the protons in the skew-chair equilibrium. From these and the other values, it could be deduced that $^3J_{C,H}$ across oxygen atoms are larger than those across carbon atoms. For instance, for the quasi-trans, in both conformations, angles $\phi_{C2,H4}$ and $\phi_{C4,H2'}$ the observed values of 5.4 and 4.7 Hz are smaller than $J_{C1,H5'}$, $J_{C1,H5''}$ and even $J_{C6,H1'}$ although $\phi_{C6,H1}$ is only about 130°. These effects agree quite well with those observed in substituted propanes in which the values of $^3J_{C,H}$ are uniformly smaller as the electronegativity of the substituent increases than those for the unsubstituted molecule[24]. On the other hand, angles close to 90° give $^3J_{C,H}$ values between 0 and 1.1 Hz, accounting for a typical Karplus-like relationship (for instance, $\phi_{C3,H1'}$, $\phi_{C5,H3'}$, $\phi_{C6,H2'}$). Geminal $^2J_{C,H}$ depend on the torsion angle between the proton and the electronegative substituents at the coupled carbon.[26] In 1,2-disubstituted ethanic fragments, $^2J_{C,H}$ are measurable only when gauche- or syn-arrangements are present ($\phi_{C3,H2}$ and $\phi_{C3,H4}$ for **1**). Almost zero values are observed when the angle is close to 180° ($\phi_{C2,H3'}$, $\phi_{C4,H3'}$).

Further studies on other pentopyranose analogues are presently being carried out and indicate that conformational equilibria involving $^1C_4$, $^OS_2$, and $^4C_1$ forms seem to occur depending on the nature of the sugar and the configuration and substitution at C-2 of the dioxolane ring.[27]

EXPERIMENTAL

General methods. Melting points were determined on a Kofler microscope and are uncorrected. Optical rotations were determined with a Perkin-Elmer 141 polarimeter. T.l.c. was performed on silica gel GF_{254} (Merck) with detection by charring with sulfuric acid.

Materials

3,4-di-O-acetyl-1,2-O-(S)-(1-cyanoethylidene)-α-D-ribopyranose **1** was prepared as described by Kochetkov[28] for the D-gluco analogue. Crystallization from ethanol gave **1** (90 %), m.p. 117-118°, $[\alpha]_D^{25}$ -10° (c2, chloroform).

Anal. Calcd. for $C_{12}H_{15}NO_7$: C, 50.53; H, 6.30; N, 4.91. Found: C, 50.72; H, 6.13; N, 5.02.

3,4-di-O-acetyl-1,2-O-(R)-ethylidene-α-D-ribopyranose (**2**) was prepared as described by Kochetkov[29] for the D-gluco analogue. Crystallization from 2-propanol gave **2** (80 %), m.p. 75°, $[\alpha]_D^{25}$ 2° (c 2, chloroform).

Anal. Calcd. for $C_{11}H_{16}O_7$: C, 50.76; H, 6.19. Found: C, 50.82; H, 6.08.

1,2-O-(R)-ethylidene-α-D-ribopyranose (**3**). Conventional treatment of **2** with methanolic sodium methoxide afforded **3** (95 %) as a syrup. $[\alpha]_D^{25}$ -39° (c2, chloroform).

Anal. Calcd. for $C_7H_{12}O_5$: C, 47.72; H, 6.86. Found: C, 47.55; H, 6.78.

3,4-di-O-benzoyl-1,2-O-(R)-ethylidene-α-D-ribopyranose (**4**). Conventional treatment of **3** with benzoyl chloride and pyridine and subsequent crystallization from ethanol afforded **4** (95 %), m.p. 100°, $[\alpha]_D^{25}$ -56° (c 2, chloroform).

Anal. Calcd. for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24. Found: C, 65.86; H, 5.17.

1,2-O-(R)-ethylidene-3,4-di-O-methyl-α-D-ribopyranose (**5**). Conventional treatment of **3** with sodium hydride and methyl iodide afforded **5** as a syrup (90 %). $[\alpha]_D^{25}$ -15° (c2, chloroform).

Anal. Calcd. for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 53.06; H, 7.85.

NMR data. The ^{1}H-NMR spectra (internal Me_4Si) were recorded on a Varian XL-300 spectrometer. Analyses were performed by using a PANIC program. The experimental and calculated spectra from the resulting best values matched satisfactorily. The ^{13}C-NMR spectra ($CDCl_3$, internal Me_4Si) were recorded on the same spectrometer. The proton-carbon coupling constants were measured by two methods:

Method A: Selective irradiation with low-intensity ($\frac{\gamma B_2}{2\pi}$ = 30 Hz) of the chosen proton and observation of the coupled carbon spectrum.

Method B: Selective 2D Heteronuclear J–resolved spectra by using the proton-flip technique[30] with decoupler pulse intensity $\frac{\gamma B_2}{2\pi}$ = 40 Hz, and length of 8.5 ms for the 90° pulse. The fully-coupled spectrum was finally computer-assisted simulated by using a PANIC program with X-approximation. When comparing both methods, Method A is faster than B and resulted very useful when there are not superimposed or very complicated carbon-multiplets. Method B allowed to determine easily long-range $J_{C,H}$ when the irradiated proton were far enough from the other protons ($\Delta\nu > 50$ Hz).

X-ray. Table 12 presents the crystal analysis parameters. Table 13 shows the final atomic co-ordinates for the non-hydrogen atoms.

TABLE 12. Crystal analysis parameters at room temperature

Crystal data	
Formula	$C_{12}H_{15}NO_7$
Crystal habit	Transparent, colourless, rhombic prism
Crystal size (mm)	0.46 x 0.17 x 0.17
Symmetry	Orthorrhombic, $P2_12_12_1$
Unit cell determination:	Least-squares fit from 90 reflexions ($\theta < 45°$)
Unit cell dimensions	20.0157(7), 10.0552(2), 7.08070(1) Å
Packing: ν (Å^3), Z	1426.34(6), 4
Dc (g.cm^{-3}), M, F(000)	1.328, 285.25, 600
Experimental data	
Technique	Four circle diffractometer: PW 1100 Phillips Bisecting geometry Graphite oriented monochromator: CuK w/2θ scans, scan width: 1.5° Detector apertures 1x1°, up θ max. 65° 1 min./reflex.
Number of reflexions:	
Independent	1459
Observed	1259 (3σ(I) criterion); 2 reflexions every 90 minutes Variation: no
Solution and refinement	
Solution	Direct Methods
Refinement	L.S. on Fobs with 1 block
Parameters:	
Number of variables	241
Degrees of freedom	1018
Ratio of freedom	5.2
H atoms	Difference synthesis
Final shift/error	0.05
w-scheme	Empirical as to give no trends in $\langle w\Delta^2 F\rangle$ vs. $\langle \lvert Fobs \rvert \rangle$ and $\sin\langle \theta/\lambda \rangle$
Max. thermal value	U33(07) = 0.30(1) Å^2
Final ΔF peaks	0.37 eÅ-3
Final R and Rw	0.052, 0.062
Computer and programs	VAX 11/750, MULTAN 80[32], X-RAY 76[33]
Scattering factors	Int. Tables for X-Ray Crystallography[34]

Supplementary material. Lists of structure factors, refined hydrogen parameters and components of the thermal model have been deposited at the Crystallographic data Center.

Molecular mechanics calculations. For all calculations, the MM2 program was used without modification. It was necessary to provide two parameters for torsion angles not included in the program data, namely, $C_{sp}-C_{sp^3}-O-C_{sp^3}$ and $C_{sp}-C_{sp^3}-O-LP$ ($V_1 = 0$, $V_2 = 0$, $V_3 = 0.2$) and one bending parameter for the angle $C_{sp}-C_{sp^3}-O$ (K(B) = 0.98, THETA (o) = 108.5). The default value for the bulk dielectric constant (1.5 D) corresponding to the gas phase was substituted by a value (10D), stated as a good efective dielectric constant for Cl_3CH.[31] Model coordinates of **1**

TABLE 13. Final atomic coordinates and thermal parameters as:

UEQ = (1/3).SUM (UIJ.AI*.AJ*.AI.AJ.COS(AI,AJ)).10**3

Atom	X/A	Y/B	Z/C	UEQ
O1	0.0330(1)	-0.2488(3)	0.4162(5)	57(1)
O2	0.1219(1)	-0.1058(3)	0.3985(5)	51(1)
O3	0.1305(1)	0.1615(3)	0.4135(5)	58(1)
O4	0.1213(1)	0.0365(3)	0.7696(5)	59(1)
O5	0.0120(1)	-0.1176(3)	0.6667(4)	54(1)
O6	0.0848(2)	0.3642(3)	0.4134(6)	64(1)
O7	0.1544(4)	0.2216(6)	0.8942(15)	205(5)
N	0.1276(3)	-0.3344(7)	0.0488(8)	98(2)
C1	0.0105(2)	-0.1208(5)	0.4688(7)	52(1)
C2	0.0618(2)	-0.0295(4)	0.3780(7)	49(1)
C3	0.0684(2)	0.1038(4)	0.4737(7)	50(1)
C4	0.0628(2)	0.0987(4)	0.6861(7)	52(1)
C5	0.0033(3)	0.0135(5)	0.7386(8)	58(2)
C6	0.1034(2)	-0.2402(4)	0.3897(6)	47(1)
C7	0.1423(3)	-0.3186(5)	0.5342(8)	61(2)
C8	0.1165(3)	-0.2937(5)	0.1973(7)	61(2)
C9	0.1324(2)	0.2941(4)	0.3922(7)	55(1)
C10	0.2002(3)	0.3409(6)	0.3398(16)	91(3)
C11	0.1600(3)	0.1062(5)	0.8806(9)	70(2)
C12	0.2121(3)	0.0240(7)	0.9725(9)	71(2)

for the three basic conformations: $^{1}\underline{C}_4$, $^{o}\underline{S}_2$, and $^{4}\underline{C}_1$ were used as input into the MM2 program. Driver option was used in order to cover all the possible skew conformations.

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