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Note

The conformation of pentakis-*O*-trimethylsilyl-β-D-galactofuranose in solution as determined by 220-MHz p.m.r. spectroscopy

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The occurrence of galactofuranosyl units in natural polymers[1–7] prompted us to study the conformation in solution of this structure In parallel with investigations of pertrimethylsilyl derivatives of mono- and oligo-saccharides[8,9], we have studied the TMS derivative of β-D-galactofuranose (TMS-β-D-Gal*f*) On the basis of the p m r data, obtained from 220-MHz spectra, it was concluded that TMS-β-D-Gal*f* occurs mainly in the ^4E(D) envelope conformation In the preferred conformation of the C-4–C-5–C-6 chain, H-4 and O-5, and also O-5 and O-6 are in trans-coplanar arrangement (Fig 1)

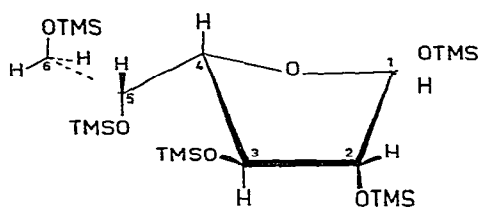

Fig 1 The preferred conformation of TMS-β-D-Gal*f*

The refined p m r data of TMS-β-D-Gal*f* in acetone-d_6, obtained after iterative computer simulation of the 220-MHz spectrum, are given in Table I

To determine the structure of the furanoid ring, the dihedral angles between the vicinal ring protons ($\phi_{1,2}$, $\phi_{2,3}$, and $\phi_{3,4}$, Table IIA) were calculated from the observed coupling constants by means of a modified Karplus relation[9] This relation takes into account the electronegativity of the substituents Only angles larger than 60° have physical significance, as all vicinal ring protons in TMS-β-D-Gal*f* have a trans relationship For the interpretation of these angles in terms of a preferred conformation, it must be realized that the energy barriers between the different forms of a furanoid ring are rather low[10] Consequently, the calculated dihedral angles probably reflect time-averaged contributions of different conformations and/or of

TABLE I

CHEMICAL SHIFTS δ (P P M) AND COUPLING CONSTANTS $J_{H\,H}$ (IN Hz) OF TMS-β-D-GALf IN ACETONE-d_6

Chemical shifts	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*
	5 11	3 92	4 08	3 91	3 80	3 67	3 57
Coupling constants	$J_{1\,2}$	$J_{2\,3}$	$J_{3\,4}$	$J_{4\,5}$	$J_{5\,6}$	$J_{5\,6}$	$J_{6\,6}$
	2 9	4 8	6 8	3 0	5 0	7 1	−10 0

different degrees of puckering of the ring[10–12] The forms contributing to the actual structure were traced as follows In each of the 10 ideal twist (T) and the 10 ideal envelope (E) conformations, which are usually[10–12] considered to describe the structure of furanoid rings, the magnitude of the dihedral angles was examined in relation to the degree of ring puckering by applying the model of Abraham and McLauchlan[13] It turned out that the dihedral angles of the ^4E(D) conformation*, in which C-4 is displaced 0 15Å out of the plane of the remaining ring atoms, fit, within 4°, with the calculated angles for TMS-β-D-Gal$f$ (Table II), The $^4T_3$(D) conformation, with out-of-plane displacements of ~0 18Å for C-4 and C-3, shows deviations of maximally 7° An agreement within 10° is found for the $^4T_0$(D) conformation, when O and C-4 are ~0 19Å out of the plane of C-1, C-2, and C-3 From a stereochemical point of view, the ^4E(D) conformation must be preferred as, in this structure, the largest ring substituent (C-5–C-6 side chain) is orientated equatorially, whereas the 3-OTMS and 1-OTMS groups have a pseudoaxial position (anomeric effect) In conclusion, the ^4E(D) conformation (Fig 1) makes the major contribution to the actual structure of the ring of TMS-β-D-Gal$f$.

TABLE II

CALCULATED DIHEDRAL ANGLES $\phi_{H\,H}$ IN TMS-β-D-GALf (A) AND ESTIMATED DIHEDRAL ANGLES IN DIFFERENT CONFORMATIONS OF THE RING (B) (Z IS THE OUT-OF-PLANE DISPLACEMENT OF THE INDICATED ATOMS)

	Z	$\phi_{1\,2}$	$\phi_{2\,3}$	$\phi_{3\,4}$
A TMS-Gal$f$		122	131	149
B $^4T_3$(D) conformation	0 18Å (C-4,C-3)	127	137	142
^4E(D) conformation	0 15Å (C-4)	120	135	145
$^4T_0$(D) conformation	0 19Å (C-4,O)	113	127	139

*For the nomenclature of conformations, see Ref 14

This conformational preference is another example of the diversity of structures which furanoid rings can adopt For several aldofuranosides[10], in solution as well as in the crystalline state, it has been found that C-2 and/or C-3 have the largest out-of-plane displacements Analogously, in ketofuranosides[10,15–20], C-3 and/or C-4 usually have the largest displacements However, several exceptions are known in the pentofuranose ester series For instance, methyl 2,3,5-tri-*O*-benzoyl-α-D-arabino-furanoside, which is configurationally related to β-D-galactofuranose, adopts mainly the ${}^{0}T_{1}$(D) conformation[11] Also, in the crystalline state, galactofuranose behaves differently from other furanoid derivatives, *e g*, methyl 1,2,3,5-tetra-*O*-acetyl-β-D-galactofuranuronate occurs in the ${}^{1}E$(D) conformation[21].

For the determination of the conformation of the C-5–C-6 side chain, it is assumed that the energy barriers for rotation around the carbon–carbon bonds are low. From the various conformations which arise by rotation, only the staggered rotamers are considered[22,23]. *a1*, *a2*, and *a3* of the fragment C-4–C-5, and *b1*, *b2*, and *b3* of the fragment C-5–C-6 (Fig 2) In the fragment C-4–C-5, rotamer *a2* is neglected because of the unfavourable 1,3-parallel interaction[9] between 3-OTMS and 5-OTMS On the basis of the theoretical values of $J_{4,5}$ in both remaining rotamers, calculated by using the modified Karplus relation, the mole fractions of *a1* and *a3* were derived from the observed values of $J_{4,5}$ (Table III). A strong

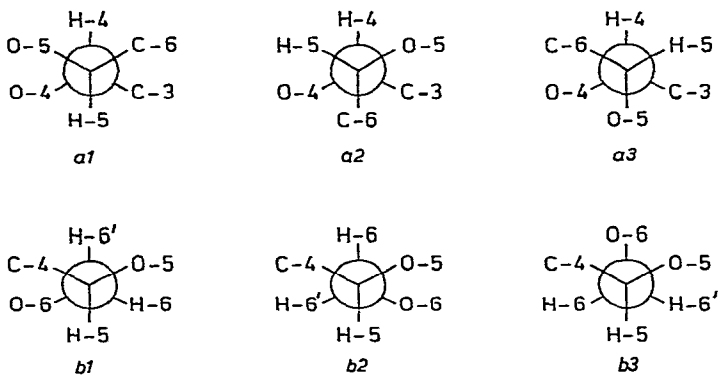

Fig 2 The staggered rotamers of the C-4–C-5 fragment *a1*, *a2*, and *a3*, and of the C-5–C-6 fragment *b1*, *b2*, and *b3*.

TABLE III

CALCULATED MOLE FRACTIONS (*n*) FOR THE ROTAMERS *1*, *2*, AND *3* OF THE C-4–C-5 FRAGMENT (*a*) AND THE C-5–C-6 FRAGMENT (*b*)

Fragment	n_1	n_2	n_3
C-4–C-5 (*a*)	0 16	0 00[a]	0 84
C-5–C-6 (*b*)	0 52	0 34	0 14

[a]Excluded, because of the unfavourable 1,3-parallel interaction between 3-OTMS and 5-OTMS

preponderance of the trans orientation of H-4 and 5-OTMS is found For the C-5–C-6 fragment, the mole fractions of the rotamers *b1*, *b2*, and *b3* were deduced from the observed coupling constants $J_{5,6}$ and $J_{5,6'}$, in combination with the theoretical values of $J_{5,6}$ and $J_{5,6'}$ in each of the three rotamers (Table III) In the preferred rotamer (*b1*), 5-OTMS and 6-OTMS are as far remote from each other as possible The geminal coupling constant $J_{6,6'}$ also reflects this conformational preference In TMS-aldohexopyranoses, $J_{6,6'}$ varies[9] between −9 5 and −12 Hz When the C-5–O bond is trans-coplanar with C-6–O, values between −9 5 and −10 Hz are found, whereas trans-coplanarity with H-6 or H-6′ gives rise to values between −11 and −12 Hz The observed value of $J_{6,6'}$ (−10 Hz) in TMS-β-D-Gal*f* indicates that the rotamer (*b1*) in which C-5–O and C-6–O are trans-coplanar prevails.

EXPERIMENTAL

Preparation of pentakis-O-trimethylsilyl-β-D-galactofuranose —D-Galactose was anomerized in dry pyridine at 80° for 2 h, and subsequently treated[8] with hexamethyldisilazane and chlorotrimethylsilane at 80°. The isolation of TMS-β-D-Gal*f* from the anomeric mixture was performed by preparative g l c on a Pye Model 105 Preparative Gas Chromatograph, equipped with a glass column (2 m × 9 6 mm) containing 10% of XF 1150 on Chromosorb W/NAW (30–60 mesh), at 135°, using nitrogen as carrier gas The identity and purity of TMS-β-D-Gal*f* was determined by analytical g l c and mass spectrometry

P m r spectroscopy. — The 220-MHz p m r spectrum of a 3% (w/v) solution of TMS-β-D-Gal*f* in acetone-d_6 was recorded on a Varian HR-220 spectrometer operating in the field-sweep mode at a probe temperature of ~25° Spectrum simulations were run on a 16 k Varian 620i computer coupled with a Varian XL-100 spectrometer, using a modified SIMEQ[24] spin-simulation program

The p m r parameters of the protons H-1 up to and including H-6′, obtained from a first-order sub-spectral analysis, were checked and refined by calculation of theoretical spectra until a good agreement was obtained between the observed and calculated spectra In these calculations, the spin system was treated as a seven-spin system XABCDEF (H-1 up to and including H-6′) The vicinal and geminal coupling constants were taken to be positive and negative, respectively The refined p m r parameters are given in Table I

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