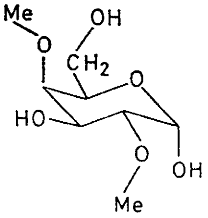
Crystal and Molecular Structure of 2,4-Di-*O*-Methyl α-D-Galactopyranose Monohydrate

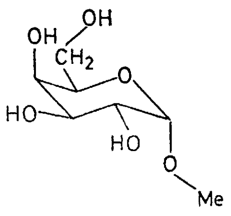
By **Iain C. M. Dea** and **Peter Murray-Rust,*** Chemistry Department, University of Stirling, Stirling, Scotland
William E. Scott, Chemistry Department, University of Edinburgh, West Mains Road, Edinburgh, Scotland

The crystal structure of the title compound (I) has been determined from photographic data, solved by direct methods and refined by full-matrix least-squares techniques to a final R of 0·095 for 1267 reflections. Crystals are orthorhombic, space group $P2_12_12_1$ with $Z = 4$ in a unit cell of dimensions $a = 1172(2)$, $b = 1895(3)$, $c = 478(1)$ pm. Bond lengths and angles are as expected but the two methyl ether substituents have unusual conformations, being eclipsed with the neighbouring C–H bonds. There are three systems of hydrogen bonds, but the axial ether oxygen at C(4) is not involved in any of them.

NATURALLY occurring polysaccharides occasionally contain methyl ether groups attached to the sugar ring. There is evidence that the presence of such groups can materially affect the conformational behaviour of the polysaccharide. Thus naturally occurring agarose samples, in which some of the D-galactose residues are 6-*O*-methylated, gel at much higher temperatures than normal agarose.[1] This indicates that the conformational change necessary for gelation occurs at higher temperature for the methylated agaroses. Similarly Ballou and co-workers[2] have examined a regular polysaccharide comprising eighteen sugar residues from *Mycobacterium phlei* which is essentially a 1-α-4-linked D-glucan containing a block of ten 6-*O*-methylated residues in the middle of the polymer. They believe that methylation influences the polysaccharide to adopt a helical conformation. While in such cases hydrophobic forces may play an important role, methyl ether groups are found on both axial and equatorial substituents and may cause some distortion of the sugar ring, thus altering the conformation of the polymer.



(I)



(II)

2,4-Di-*O*-methyl-D-galactose (I) was obtained as a methylation product from *Acacia drepanolobium* gum.[3]

---

[1] K. B. Guiseley, *Carbohydrate Res.*, 1970, **13**, 247.

[2] M. H. Saier and C. E. Ballou, *J. Biol Chem.*, 1968, **243**, 4332.

[3] D. M. W. Anderson and I. C. M. Dea. *Carbohydrate Res.*, 1968, **7**, 109.

It is a good model compound for examination of the methyl ether geometry and its effect on ring conformation as it contains both axial and equatorial groups. An accurate crystal structure[4] analysis has been made of methyl α-D-galactopyranoside monohydrate (II), so that comparison between the two compounds should indicate the effect of the methyl ether groups.

EXPERIMENTAL

The preparation and crystallisation from water of the monohydrate of (I) has already been described.[3] Density measurement confirmed that the crystal was the monohydrate. It was suspected that the crystal contained the α-isomer from the initial value of the optical rotation when the crystal was dissolved in water.

Crystal Data.—$C_8H_{18}O_7$, $M = 226{\cdot}23$. Space group $P2_12_12_1$ (D_2^4) No. 19; $a = 1172(2)$, $b = 1895(3)$, $c = 478(1)$ pm, $U = 1{\cdot}062$ nm^3, D_m (by flotation) $= 1{\cdot}41$ g cm^{-3}, $Z = 4$, $D_c = 1{\cdot}414$ g cm^{-3}. Cu-K_α Radiation, $\lambda = 1{\cdot}5418$ Å; μ(Cu-K_α) $= 11{\cdot}72$ cm^{-1}.

Crystallographic Measurements.—A crystal of dimensions $0{\cdot}4 \times 0{\cdot}3 \times 0{\cdot}2$ mm was used for X-ray analysis, and cell dimensions were obtained from calibrated zero-level Weissenberg photographs using Cu-K_α radiation. Absent spectra ($h00$, $h = 2n + 1$; $0k0$, $k = 2n + 1$; $00l$, $l = 2n + 1$) determined the space group uniquely.

Layers $hk0$—4 and $h0$—$5l$ were collected photographically by the Weissenberg multiple-film technique. Intensities were measured visually by comparison with a calibrated strip and were corrected for Lorentz and polarisation effects. No allowance was made for absorption. Layer scale-factors were calculated. and applied and the two sets of data merged to give a unique set of 1267 reflections. The data were put on an absolute scale by the Wilson-plot method and a sharpened Patterson function was calculated.

Structure Determination.—Inspection of this function in the region within 300 pm of the origin revealed vectors which were compatible with a galactose skeleton, but the intermolecular vectors could not be interpreted to find the position of this molecule in the unit cell. Accordingly a solution by direct methods was undertaken. The K-curve method of Karle and Karle[5] was used to calculate $|E|$ values for intensity data and statistics of these were compared with theoretical values and those from (II) (Table 1).

TABLE 1

Intensity statistics on $|E|$ values

	(I)	(II)	Non-centric	Centric
$\langle\lvert E\rvert\rangle$	0·837	0·855	0·798	0·886
$\langle\lvert E^2 - 1\rvert\rangle$	0·852	0·895	0·968	0·736
$\%E > 1{\cdot}00$	33·0		36·8	32·0
$\%E > 2{\cdot}00$	3·5		1·8	5·0
$\%E > 3{\cdot}00$	0·372		0·01	0·3

It will be seen that both compounds have intensity distributions midway between those predicted for centric and non-centric cases. This is to be expected in $P2_12_12_1$ where there is a significant percentage of reflections with centric phases. A set of 263 reflections with $|E| > 1{\cdot}25$ was used in the phase determination, performed by the MULTAN programs.[6]

Four origin- and enantiomorph-defining reflections were selected and two others were assigned arbitrary phases ($\pm\pi/2$ and $n\pi \pm \pi/4$). This gave rise to 8 sets of phases, each of which was taken as a starting set for the tangent formula process. The set of phases with the highest figure of merit was taken and used to calculate an E map which revealed clearly the sugar skeleton and the water molecule. All atoms, except one methyl group, were used to calculate structure factors and a Fourier synthesis confirmed the position of all the atoms. The R value at this point was 0·23.

Structure Refinement.—The structure was refined by seven cycles of full-matrix least-squares, on the last four of which anisotropic temperature factors were introduced. Unit weights were used throughout, as no other weighting scheme gave better weighted differences [unit weights were used throughout for (II) (ref. 4)]. The final R was 0·096. Many of the hydrogen atom positions were revealed on the final difference synthesis but were not included in the calculations. The CRYSTAL 69 set of programs[7] was used for the refinement and scattering-factor curves were taken from ref. 8. Final positional

TABLE 2

Positional parameters $\times 10^4$, with standard deviations in parentheses

	x/a	y/b	z/c
C(1)	3803(4)	4686(3)	10710(13)
C(2)	5035(4)	4533(3)	9793(13)
C(3)	5851(4)	4993(3)	11467(13)
C(4)	5579(4)	5776(3)	11054(13)
C(5)	4295(4)	5903(3)	11807(13)
C(6)	3951(5)	6647(3)	11180(19)
C(7)	5759(7)	3439(3)	8098(18)
C(8)	6528(5)	6569(3)	7933(14)
O(1)	3672(3)	4532(2)	13519(10)
O(2)	5219(3)	3804(2)	10399(10)
O(3)	6987(3)	4845(2)	10549(10)
O(4)	5774(3)	5974(2)	8193(8)
O(5)	3574(3)	5430(2)	10226(9)
O(6)	2786(3)	6780(2)	12067(11)
O(7)	3327(5)	2938(2)	12137(11)

TABLE 3

Anisotropic temperature factors * ($\times 10^4$), with with standard deviations in parentheses

	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	32(2)	22(1)	475(25)	4(1)	0(7)	10(4)
C(2)	37(3)	25(1)	484(27)	3(2)	0(8)	3(5)
C(3)	31(2)	31(1)	411(24)	4(2)	3(7)	8(5)
C(4)	42(3)	30(1)	410(26)	−2(2)	3(7)	−9(5)
C(5)	38(3)	27(1)	430(26)	−3(2)	−21(7)	17(5)
C(6)	59(4)	24(1)	790(44)	4(2)	14(11)	7(6)
C(7)	97(6)	32(2)	738(42)	14(3)	69(15)	−20(8)
C(8)	77(4)	25(1)	563(31)	−15(2)	24(10)	−2(6)
O(1)	47(2)	26(1)	533(21)	5(1)	20(6)	12(4)
O(2)	59(2)	25(1)	467(20)	8(1)	41(6)	4(4)
O(3)	36(2)	39(1)	421(18)	3(1)	3(5)	15(4)
O(4)	61(2)	26(1)	396(16)	−8(1)	13(5)	−9(3)
O(5)	40(2)	20(1)	531(19)	1(1)	−24(5)	5(3)
O(6)	68(3)	33(1)	641(24)	15(2)	21(8)	−6(5)
O(7)	98(4)	29(1)	585(23)	2(2)	7(9)	11(5)

* The temperature factor expression is: $T = \exp -(\beta_{11}h_2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)$.

---

[4] B. M. Gatehouse and B. J. Poppleton, *Acta Cryst.*, 1971, **B27**, 654.

[5] J. Karle and I. L. Karle, in ' Computing Methods in Crystallography,' ed. J. S. Rollett, Pergamon, 1965.

[6] P. Main, M. M. Woolfson, and G. Germain, program MULTAN, University of York, 1971.

[7] A. Griffiths and M. T. G. Powell, Program System CRYSTAL 69, Portsmouth Polytechnic, 1969.

[8] ' International Tables for X-Ray Crystallography,' vol. III Kynoch Press, Birmingham, 1962.

and vibrational parameters are given in Tables 2 and 3 and structure factors are listed in Supplementary Publication No. SUP 20882 (9 pp., 1 microfiche).†

DISCUSSION

The molecule of 2,4-di-*O*-methyl α-D-galactopyranose monohydrate has the generally expected chair conformation (C1) (Figure 1) with axial substituents at C(1) and C(4). The conformation of the CH_2·OH group is *gauche-trans*,[9] exactly as found for (II)[4] where the authors suggested that the conformation was due to the axial substituent at C(4). However the conformations of the methyl ether groups are quite different, taking up eclipsed arrangements.

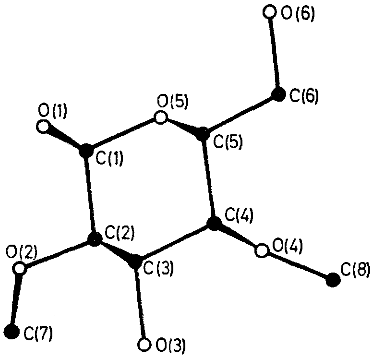


FIGURE 1 Numbering of the 2,4-di-*O*-methyl α-D-galactopyranoside molecule. Oxygen atom O(7) of the water molecule is not shown

TABLE 4

Intramolecular bond distances (pm) *

C(1)–C(2)	153·6	C(2)–O(2)	142·9
C(2)–C(3)	152·1	C(3)–O(3)	143·0
C(3)–C(4)	153·0	C(4)–O(4)	143·7
C(4)–C(5)	156·6	C(5)–O(5)	144·6
C(5)–C(6)	149·6	C(6)–O(6)	145·2
C(1)–O(1)	138·3	C(7)–O(2)	144·4
C(1)–O(5)	145·4	C(8)–O(4)	143·7

* Standard deviations in C–C bonds are *ca.* 0·8 pm and in C–O bonds *ca.* 0·7 pm.

TABLE 5

Intramolecular bond angles (°)

O(5)–C(1)–O(1)	109·8	C(3)–C(4)–O(4)	110·1
C(2)–C(1)–O(1)	110·0	C(5)–C(4)–O(4)	109·3
C(2)–C(1)–O(5)	108·1	C(4)–C(5)–C(6)	111·0
C(1)–C(2)–C(3)	109·4	C(4)–C(5)–O(5)	110·3
C(1)–C(2)–O(2)	105·5	C(6)–C(5)–O(5)	108·8
C(3)–C(2)–O(2)	110·6	C(5)–C(6)–O(6)	111·0
C(2)–C(3)–C(4)	110·9		
C(2)–C(3)–O(3)	108·2	C(5)–O(5)–C(1)	114·3
C(4)–C(3)–O(3)	110·1	C(2)–O(2)–C(7)	112·0
C(3)–C(4)–C(5)	108·6	C(4)–O(4)–C(8)	112·7

Estimated standard deviations *ca.* 0·4°.

Bond lengths and angles in the sugar molecule with their estimated standard deviations are given in Tables 4 and 5. The C–C bond lengths all fall within the range found in other similar molecules with the exception of C(4)–C(5), which is 4 pm longer than in other saccharides.[10,11] This is statistically just significant (*ca.* 3σ) but might be due to experimental error. The C–O bond lengths are all in the range 144 ± 1 pm except for C(1)–O(1) (138 pm) which is significantly shorter. The shortening of the anomeric bond has been observed in methyl pyranosides [10–12] and although not very pronounced in (II) it is clearly a significant effect in sugar molecules. The C–O bond lengths in the ether groups do not appear to be different from the normal C–O lengths in sugar hydroxy-groups.[11] The bond angles at carbon all lie in the range 109 ± 2, except for C(1)–C(2)–O(2), whose slightly low value (105·5°) is unlikely to be significant. The angles at oxygen (113 ± 1°) agree well with those for other sugars.[11,13] The torsion angles in the pyranose ring (Table 6) range from 53·9 to 61·7°. The mean value of these for a pyranose ring range from 53·0 to 62·2°,[14] suggesting that there is no unusual distortion of the sugar skeleton in the present compound.

TABLE 6

Intramolecular torsion angles (°)

(*a*) Pyranose ring			
O(5)–C(1)–C(2)–C(3)	59·2	C(3)–C(4)–C(5)–O(5)	−53·9
C(1)–C(2)–C(3)–C(4)	−58·5	C(4)–C(5)–O(5)–C(1)	59·6
C(2)–C(3)–C(4)–C(5)	54·9	C(5)–O(5)–C(1)–C(2)	−61·7
(*b*) Substituents			
C(1)–C(2)–O(2)–C(7)	133·8	C(5)–C(4)–O(4)–C(8)	114·6
C(3)–C(2)–O(2)–C(7)	−107·9	C(4)–C(5)–C(6)–O(6)	−175·8
C(3)–C(4)–O(4)–C(8)	−126·1	O(5)–C(5)–C(6)–O(6)	62·7

The torsion angles are positive if the rotation is clockwise looking down the bond; estimated standard deviations are *ca.* 0·6°.

The conformations of the flexible side groups are shown in Figure 2. The CH_2·OH group is in essentially the same conformation as in (II) and other sugars[9] but the MeO groups both have unexpected eclipsed conformations. If the C–H vectors are determined by standard methods,[15] the dihedral angles between these and the corresponding Me–O bonds are calculated to be 5° [C(2)] and 13° [C(4)]. Since the barrier to rotation[16] in dimethyl ether is *ca.* 11 kJ mol^{-1} these conformations must be energetically unfavourable. The axial methoxy-group at C(1) in (II) is capable of taking up a *trans-gauche* arrangement and there would seem to be no reason why the C(4)–O(4)–C(8) group in the present structure cannot do the same, especially as it is not involved in hydrogen bonding. However, the interactions between the methyl group and the neighbouring equatorial substituents in the *trans-gauche* arrangement might be quite large as the distances would be *ca.* 260 pm. Therefore the unfavourable

---

† See Notice to Authors No. 7 in *J.C.S. Dalton*, 1972, Index issue.

[9] M. Sundaralingam, *Biopolymers*, 1968, **6**, 189.

[10] H. M. Berman, S. S. C. Chu, and G. A. Jeffrey, *Science*, 1967, **157**, 1576.

[11] S. Arnott and W. E. Scott, *J.C.S. Perkin II*, 1972, 324.

[12] H. M. Berman and S. H. Kim, *Acta Cryst.*, 1967, **B24**, 897.

[13] G. A. Jeffrey and R. D. Rosenstein, *Adv. Carbohydrate Chem.*, 1964, **19**, 7.

[14] S. H. Kim and G. A. Jeffrey, *Acta Cryst.*, 1967, **22**, 537.

[15] J. S. Rollett in ref. 5.

[16] J. P. Lowe, *Progr. Phys. Org. Chem.*, 1968, **6**, 1.

energy of the eclipsed conformation may be compensated by the relief of the 1,4-interactions and the final dihedral angle represent the best compromise. That the methoxy-group at C(2) has the same conformation, although it is equatorial, is even more surprising. A satisfactory *trans-gauche* arrangement can be made with C(7)–O(1) *ca.* 340 pm with no other serious interactions, and this would seem to be energetically favourable to the actual conformation. The answer may lie in the hydrogen bond in which O(2) participates, but it is difficult to see the increase in torsional energy being offset by the formation of one hydrogen bond. An alternative possibility is that in these compounds the barrier to rotation may be very much less than in dimethyl ether.

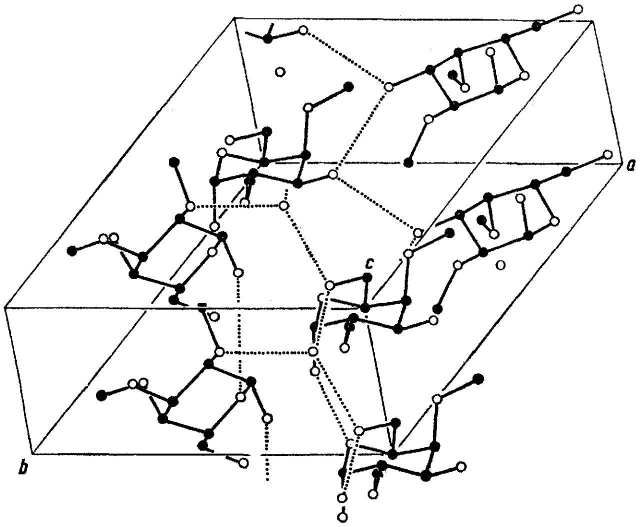


FIGURE 2 Packing of the molecules in the unit cell with the hydrogen-bonding scheme

The hydrogen bonding (Figure 2, and Table 7) involves three separate systems. In the first a two-fold screw axis parallel to *c* links O(3) of one molecule to O(3) of an adjacent molecule forming an infinite zig-zag chain. The second system consists of a single intermolecular bond between the ring oxygen O(5) of one molecule and O(1)–H of another which serves to link molecules related by the *c* translation. The third scheme involves one OH bond of the water molecule and the $CH_2{\cdot}OH$ group, which alternate to form an infinite chain up the *c* axis. The other hydrogen atom of the water molecule acts as donor to the ether oxygen at C(2) which joins molecules in the *ab* plane. The water molecule thus participates in three hydrogen bonds and the angles at this molecule based on the other oxygen atoms are **91**, **119**, and **118°** so that the hydrogen bonds are arranged pyramidally. O(4) Does not participate in hydrogen bonding. Since it is not particularly hindered sterically this is most likely to be due to a lack of hydroxy-groups. In the crystal there are seven oxygen atoms and only five hydroxy-protons, so that it is difficult to arrange for every acceptor oxygen atom to be linked to a hydroxy-group.

TABLE 7

Hydrogen-bonded contacts between molecules (pm)

$O(1)–H \cdots O(5^{I})$	275·6	$O(2) \cdots H–O(7)$	288·1
$O(3) \cdots O(3^{II})$	274·0	$O(7) \cdots O(6^{II})$	280·4
$O(3) \cdots O(3^{III})$	274·0	$O(7) \cdots O(6^{III})$	274·7

Estimated standard deviations are *ca.* 0·6 pm.

Roman numeral superscripts refer to the following equivalent positions relative to the reference molecule at x, y, z:

I $x, y, 1 + z$
II $\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$
III $\frac{1}{2} - x, 1 - y, z - \frac{1}{2}$

The thermal parameters of the molecule can be interpreted in terms of a rigid-body vibration of the sugar molecule. For (II) a plot of B_{iso} *vs.* the distance of the atom from the centre of the pyranose ring was linear, suggesting a rigid-body vibration.[4] If the volume (V) of the thermal ellipsoids of (I) is plotted against this distance (r) a straight line is obtained corresponding to the equation: $V = a + br$, with $a = $ **19,700** and $b = $ **8930** pm². The intercept a corresponds to a conventional B_{iso} of 2·20 Å², which is a rough estimate of the magnitude of the translational vibration of the molecule.

We thank the S.R.C. for research fellowships (to I. C. M. D. and W. E. S.).

[3/1562 *Received*, 25*th July*, 1973]