# Crystal Structure of Methyl 3,6-Anhydro-α-D-galactoside

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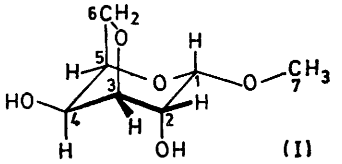
The crystal structure of the title compound has been determined using three dimensional *X*-ray diffraction data. The structure was solved by direct methods. The positional and anisotropic thermal parameters were refined using a full matrix least squares procedure to give an *R* factor of 0·097 for 1926 reflections. Standard deviations were ±0·004 Å in the bond lengths and ±0·2° in the bond angles. The geometry of the molecule is compared with that of other monosaccharide structures and the effect of the 3,6-anhydro-bridge is discussed. Crystal data: orthorhombic space group $P2_12_12_1$, $Z = 4$, $a = 9{\cdot}46 \pm 0{\cdot}01$, $b = 12{\cdot}05 \pm 0{\cdot}01$, $c = 6{\cdot}93 \pm 0{\cdot}015$ Å.

THE reactions of methyl 3,6-anhydro-α-D-galactoside, (I), have been studied by Haworth *et al.*[1] Two reactions clearly indicate the presence of strain within the molecule, caused by the formation of the 3,6-anhydro-bridge, both by the products of the reactions and by the readiness with which the reactions take place. First, hydrolysis with 0·1N-sulphuric acid at room temperature gives 3,6-anhydrogalactose, the properties of which indicate that it has an aldehydic structure rather than the usual hemiacetal, *i.e.* that the pyranose ring has been opened and second, treatment with excess of 0·5% methanolic hydrogen chloride at room temperature again causes opening of the pyranose ring with the formation of the dimethyl acetal. The presence of strain within the dicyclic system influences the method of preparation of angal as the pyranose ring must be stabilised as the methyl glycoside before the 3,6-anhydro-ring is formed.



(I)

The structure of (I) was determined in order to obtain a set of co-ordinates for calculations on the conformation of the polysaccharide ι-carrageenan.[2]

## EXPERIMENTAL

*Crystal Data.*—$C_7H_{12}O_5$, $M = 176{\cdot}3$. Orthorhombic, $a = 9{\cdot}46 \pm 0{\cdot}01$, $b = 12{\cdot}05 \pm 0{\cdot}01$, $c = 6{\cdot}93 \pm 0{\cdot}015$ Å, $U = 790{\cdot}1$ Å$^3$, $D_m = 1{\cdot}48$, $Z = 4$, $D_c = 1{\cdot}482$. Space group $P2_12_12_1$, $\mu(\text{Mo-}K_\alpha) = 1{\cdot}37$ cm$^{-1}$.

(I) was prepared as previously described[1] and recrystallised (×3) as needles of rectangular or six-sided cross section. The structure was solved and the initial refinement carried out with intensity data (746 reflections) measured from equi-inclination Weissenberg photographs taken by use of Cu-$K_\alpha$ radiation ($\lambda = 1{\cdot}5418$ Å). Further refinement was carried out with intensity data (1926 reflections) collected (in collaboration with Dr. H. C. Watson, in the Biochemistry Department, University of Bristol) on a Hilger and Watts four-circle diffractometer with Mo-$K_\alpha$ radiation ($\lambda = 0{\cdot}7107$ Å).

*Solution of the Structure.*—The structure was solved by the symbolic addition procedure and tangent formula refinement of phases for non-centrosymmetric space groups as described by Karle and Karle.[3-5] Sixty phases of reflections with $|E| \geqslant 1{\cdot}5$ were found in terms of a single unknown symbol $c$ of value $\pm\pi/2$. The set of phases with $c = +\pi/2$ was refined, expanded to 136 phases for reflections with $|E| \geqslant 1{\cdot}18$ and again refined by use of the tangent formula. A three-dimensional $E$ map was computed with the 136 phases and structure factors were calculated for a seven-atom partial trial structure based on this map. A set of 52 calculated phases, for reflections with $|E| \geqslant 1{\cdot}5$ and with $|F_c| \geqslant 0{\cdot}4|F_o|$, was refined and expanded to a set of 145 phases ($|E| \geqslant 1{\cdot}17$) by use of the tangent formula. A three-dimensional $E$ map calculated from these phases gave the positions of three more atoms. A Fourier synthesis was calculated including terms for which $|F_c| \geqslant 0{\cdot}4|F_o|$ and the positions of the remaining two non-hydrogen atoms were easily identified.

*Refinement of the Structure.*—Isotropic full-matrix least-squares refinement, based on the film data, gave $R$ 0·157 for 730 reflections. A difference-Fourier synthesis showed the positions of the hydrogen atoms on C(1)—(6). Chemically sensible positions were calculated for the hydrogen atoms on C(1)—(6) and on O(2) and O(4) and the contributions of these atoms to $F_c$ were included. They were assigned isotropic thermal parameters equal to those of the atoms to which they were attached. No attempt was made to refine the hydrogen atom parameters. Further refinement was done by use of the diffractometer data. Anisotropic thermal parameters and positional parameters of the carbon and oxygen atoms were refined in separate least-squares cycles until convergence had been achieved. The final $R$ was 0·097 (1926 reflections). The structural parameters together with their estimated standard deviations are listed in Tables 1—3. A diagram of the crystal structure is shown in the Figure.

Observed and calculated structure factors are listed in Supplementary Publication No. SUP 20459 (14 pp., 1 microfiche).*

## DISCUSSION

The geometry of the five-membered ring of (I) [C(3)—(6), O(2)] is similar to that found in furanose rings and that of the rest of the molecule is typical of a

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* For details see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20.

[1] W. N. Haworth, J. Jackson, and F. Smith, *J. Chem. Soc.*, 1940, 620.

[2] N. S. Anderson, J. W. Campbell, M. M. Harding, D. A. Rees, and J. W. B. Samuel, *J. Mol. Biol.*, 1969, **45**, 85.

[3] J. Karle and I. L. Karle, *Acta Cryst.*, 1966, **21**, 849.

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TABLE 1

Atomic co-ordinates (as fractions of the cell edge) and isotropic temperature factors assigned to the hydrogen atoms, with standard deviations in parentheses

| Atom | $x$ | $y$ | $z$ | $B$/Å$^2$ |
|---|---|---|---|---|
| C(1) | 0·4159(3) | 0·2103(2) | −0·0396(4) | |
| C(2) | 0·4347(3) | 0·3364(2) | −0·0249(4) | |
| C(3) | 0·4411(3) | 0·3853(2) | −0·2291(4) | |
| C(4) | 0·3042(3) | 0·3565(2) | −0·3371(3) | |
| C(5) | 0·3344(3) | 0·2335(2) | −0·3697(4) | |
| C(6) | 0·4880(3) | 0·2358(3) | −0·4331(4) | |
| C(7) | 0·3635(4) | 0·0529(2) | 0·1560(5) | |
| O(1) | 0·3650(3) | 0·1728(2) | 0·1342(3) | |
| O(2) | 0·3185(3) | 0·3879(2) | 0·0727(3) | |
| O(3) | 0·5502(2) | 0·3297(2) | 0·3339(3) | |
| O(4) | 0·2973(2) | 0·4101(2) | −0·5196(3) | |
| O(5) | 0·3145(2) | 0·1782(1) | −0·1860(3) | |
| H(1) | 0·5073 | 0·1676 | −0·0673 | 2·73 |
| H(2) | 0·5354 | 0·3553 | 0·0497 | 2·87 |
| H(3) | 0·4637 | 0·4733 | −0·2256 | 2·56 |
| H(4) | 0·2107 | 0·3710 | −0·2508 | 2·30 |
| H(5) | 0·2678 | 0·1960 | −0·4808 | 2·23 |
| H(6) | 0·4914 | 0·2520 | −0·5909 | 2·82 |
| H(7) | 0·5421 | 0·1612 | −0·3958 | 2·82 |
| H(8) | 0·3250 | 0·3880 | 0·2271 | 3·57 |
| H(9) | 0·2750 | 0·5000 | −0·5000 | 2·73 |

H(6) and H(7) are on C(6); H(8) is on O(2); H(9) is on O(4).

TABLE 2

Anisotropic thermal parameters ($\times 10^4$) * for the non-hydrogen atoms

| Atom | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ | $\beta_{23}$ | $\beta_{13}$ | $\beta_{12}$ |
|---|---|---|---|---|---|---|
| C(1) | 95 | 43 | 114 | 3 | −12 | −2 |
| C(2) | 108 | 40 | 107 | −10 | −19 | 1 |
| C(3) | 98 | 46 | 110 | −1 | −19 | −15 |
| C(4) | 90 | 38 | 87 | 2 | 2 | 7 |
| C(5) | 78 | 43 | 103 | −5 | −9 | −1 |
| C(6) | 100 | 69 | 121 | −14 | 4 | 19 |
| C(7) | 189 | 36 | 187 | 23 | 17 | 5 |
| O(1) | 156 | 49 | 107 | 6 | 28 | 12 |
| O(2) | 183 | 52 | 98 | 2 | 7 | 36 |
| O(3) | 70 | 80 | 161 | 3 | −7 | 7 |
| O(4) | 127 | 53 | 91 | 7 | −11 | 21 |
| O(5) | 110 | 39 | 129 | 7 | −19 | −11 |

* Defined by the expression exp $-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2kl\beta_{23} + 2hl\beta_{13} + 2hk\beta_{12})$.

TABLE 3

Bond lengths and angles for non-hydrogen atoms

(*a*) Bond lengths (Å)

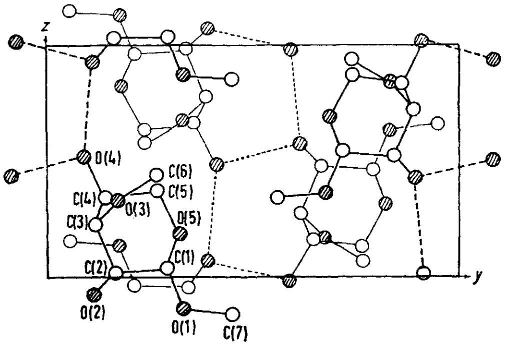
| | | | |
|---|---|---|---|
| C(1)–C(2) | 1·533(3) | C(2)–O(2) | 1·432(4) |
| C(2)–C(3) | 1·534(4) | C(3)–O(3) | 1·429(3) |
| C(3)–C(4) | 1·535(4) | C(4)–O(4) | 1·422(3) |
| C(4)–C(5) | 1·526(3) | C(5)–O(5) | 1·449(3) |
| C(5)–C(6) | 1·518(4) | C(6)–O(3) | 1·449(4) |
| C(1)–O(5) | 1·449(3) | C(7)–O(1) | 1·453(3) |
| C(1)–O(1) | 1·374(4) | | |

(*b*) Bond angles (deg.)

| | | | |
|---|---|---|---|
| C(2)–C(1)–O(5) | 112·8(2) | C(3)–C(4)–O(4) | 111·7(2) |
| C(2)–C(1)–O(1) | 108·0(2) | C(5)–C(4)–O(4) | 108·5(2) |
| O(5)–C(1)–O(1) | 107·1(2) | C(4)–C(5)–O(5) | 107·0(2) |
| C(1)–C(2)–C(3) | 108·9(2) | C(4)–C(5)–C(6) | 101·8(2) |
| C(1)–C(2)–O(2) | 111·9(2) | O(5)–C(5)–C(6) | 112·8(2) |
| C(3)–C(2)–O(2) | 107·4(2) | C(5)–C(6)–O(3) | 105·4(2) |
| C(2)–C(3)–C(4) | 109·3(2) | C(7)–O(1)–C(1) | 114·9(2) |
| C(2)–C(3)–O(3) | 108·5(2) | C(3)–O(3)–C(6) | 108·3(2) |
| C(4)–C(3)–O(3) | 104·8(2) | C(1)–O(5)–C(5) | 114·0(2) |
| C(3)–C(4)–C(5) | 97·7(2) | | |

pyranose sugar.[6-10] Apart from C(1)–O(1) the bond lengths do not differ significantly from the expected values. C(1)–O(1), 1·374 Å, is 0·067 Å ($>18\sigma$) shorter than the average C–O bond length. There is no significant asymmetry in the lengths of the C–O(5) bonds. These two observations are in accordance with the empirical rules concerning the glycosidic bond as suggested by Chu and Jeffrey.[7] The bond angles, also, have typical values though the angle C(3)–C(4)–C(5) (97·7°) is rather smaller than average.

The distance across the pyranose ring from C(3) to C(5) is 2·30 Å which is 0·2 Å less than that found for an unbridged pyranose ring. The distances of the four atoms C(2), C(3), C(5), and O(5) from their best plane are 0·015, 0·017, 0·018, and 0·012 Å. C(1) and C(4) are 0·543 and 0·921 Å out of the plane while the mean distance out of the plane for C(1) and C(4) of a glucopyranose residue is *ca.* 0·66 Å.[11] C(4) of (I) is forced further out of the plane by the formation of the 3,6-anhydro-bridge. On the other hand, the pyranose ring is slightly flattened at C(1). This flattening could relieve two sources of strain: first, a tendency for O(5) and C(2) to be pushed apart when the anhydro-ring is formed, and second, to relieve a rather short contact distance between H(1) and H(7) (distance between calculated hydrogen atom positions is 2·3 Å). C(3), O(3), C(6), and C(5) were 0·015, 0·018, 0·023, and 0·014 Å out of their best plane and C(4) was 0·706 Å from this plane.



The crystal structure of (I), (100) projection, showing the packing of the molecules within the unit cell and the hydrogen bonds; hydrogen atoms are omitted

The position of the methyl group is also of interest. It is close to the position of the potential-energy minimum for non-bonded interactions as calculated by use of the Kitaygorodsky potential-energy function.[12] The position can also be explained in terms of dipole interactions between the unshared electron pairs on O(1) and O(5) and is consistent with the position of the

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methyl group in other similar monosaccharides.[13] The dihedral angle in (I), O(5)–C(1)–O(1)–C(7), is 68·1 compared with 72·3, 69·2, and 64·8° for the methyl glycosides of β-xylose,[10] β-maltose,[7] and 1-thio-β-D-xylose.[14]

There are two hydrogen bonds, O(2) · · · O($4^{I}$) and O(2) · · · O($4^{II}$),† 2·845 and 2·744 Å, making double chains of molecules parallel to the $c$ axis. As in other methyl glycosides there are no hydrogen bonds involving O(5).[15]

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† Molecule I is at $x, y, z - 1$; molecule II is at $\frac{1}{2} - x, 1 - y, z - \frac{1}{2}$.

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