

## Crystal Structure of Methyl $\alpha$ -D-Altropyranoside

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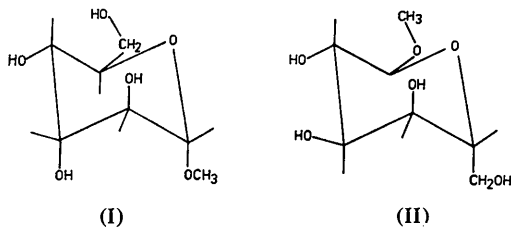
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(Received 22 June 1970)

Methyl  $\alpha$ -D-altropyranoside crystallizes in the orthorhombic space group  $P2_12_12_1$  with cell dimensions  $a = 7.486$ ,  $b = 9.098$ ,  $c = 13.330$  Å. The structure was solved using diffractometer data and the tangent formula, and refined using a full-matrix least-squares procedure with unit weights. The final value of the reliability index is 0.039. The primary hydroxyl group is *gauche-gauche* with respect to O(5) and C(4); the methyl group is *gauche-trans* to O(5) and C(2). The ring has a distorted chair (C1) conformation. All oxygen atoms participate in hydrogen bonds, and all, with the exception of O(2), are donors and/or acceptors in at least one of the two bifurcated bonds in the hydrogen-bonding network.

### Introduction

Methyl  $\alpha$ -altropyranoside is a compound of particular interest in the study of hydrogen-bonding patterns and conformational stability in pyranose sugars and their derivatives. The interest in this compound centres principally on the observation that, at least in aqueous solutions, its two alternative chair conformations I and II have approximately equal energies. If allowance is made for the slightly greater interaction energy of a methoxyl group over that of a hydroxyl group (0.5 kcal.mole<sup>-1</sup>) there is a preference, amounting to only 0.3 kcal.mole<sup>-1</sup>, for the 1C(II) conformation (Angyal, 1968). Other workers, from calculations based on a Kitaigorodsky-type function prefer the C1 (I) conformation (Sundararajan & Rao, 1968).



The actual conformation of the molecule in the crystal therefore will be controlled by hydrogen bonding and packing requirements. In an attempt to understand further the nature of these forces the crystal structure of methyl  $\alpha$ -altropyranoside has been determined.

### Crystal data

Methyl  $\alpha$ -D-altropyranoside, C<sub>7</sub>H<sub>14</sub>O<sub>6</sub>  
 M.W. 194.19  
 $a$  7.486,  
 $b$  9.098  
 $c$  13.330 Å;  
 $D_x$  1.417 g.cm<sup>-3</sup>,  $Z = 4$ ;  
 $\mu$  Cu  $K\alpha$  10.9 cm<sup>-1</sup>

Systematic absences:  $h00$  for  $h$  odd,  $0k0$  for  $k$  odd and  $00l$  for  $l$  odd.

Space group:  $P2_12_12_1$

Cell dimensions were measured on a Picker diffractometer from five high-angle reflexions for which the Cu  $K\alpha$  doublet was resolved.

The crystal had forms  $\{101\}$  and  $\{010\}$ , and a shape which approximated a plate. Dimensions in the directions  $[101]$ ,  $[\bar{1}01]$ ,  $[001]$  and  $[010]$  were 0.137, 0.135, 0.074 and 0.315 mm respectively.

### Experimental

Methyl  $\alpha$ -D-altropyranoside was prepared according to the procedure described by Richtmeyer (1962) and recrystallized from water. The sharp edged well formed crystals produced by this method grew slowly, and were removed from the syrupy mother liquor after a short period to prevent excessive growth.

One of these crystals was mounted for rotation, about the  $b$  axis, on the Picker four-circle diffractometer and data collected to a  $\sin \theta$  limit of 0.9 using Cu  $K\alpha$  radiation by scanning in the  $\theta$ - $2\theta$  mode over a range of 0.65° on each side of a reflexion ( $\alpha_1$ ,  $\alpha_2$ ). Background count times were 20 sec. The 135 reflexion was selected as standard and measured every fifty reflexions; there was no significant deterioration of the crystal over the period of data collection.

No corrections were made for absorption.

Calculations were executed using the C.S.I.R.O. CDC3200 and 3600 computers. The major programs were modified versions of the full-matrix least-squares program of Busing, Martin & Levy (1962), the Fourier summation of White (1965), and the direct-phasing series of Hall (1968) the *modus operandi* of which is described by Oh & Maslen (1968).

Scattering curves for all atoms were those quoted in *International Tables for X-ray Crystallography* (1962).

### Structure determination and refinement

A solution to the structure was first attempted using

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3.2 Å<sup>2</sup> in a cycle of refinement of all heavy-atom parameters, followed by a difference electron-density map allowed the remaining hydrogen atoms to be located.

An inspection of the structure-factor list revealed that those reflexions requiring more than one attenuator had anomalously large differences between observed and calculated  $F$  values; these discrepancies may be explained in part by absorption, multiple reflexion and extinction with the latter thought to be the dominant contributor. No attempt was made to

correct quantitatively for these factors so the affected reflexions were omitted from subsequent refinement cycles.

The last cycle of least-squares, with unit weights, varying heavy-atom positions and anisotropic thermal parameters as well as hydrogen positions gave an  $R$  of 0.039. A difference electron-density map showed one peak, other than bonding electron details of 0.3 e.Å<sup>-3</sup>; other fluctuations were less than 0.15 e.Å<sup>-3</sup>.

The estimated standard deviations of the heavier atom positional parameters are isotropic and approximately 0.004 Å which implies an estimated standard deviation of 0.006 Å in bond length and 0.3 Å in bond angle. As mentioned earlier there is good evidence that the crystal in this analysis suffered extinction and therefore a more realistic estimate of accuracy would be to double these figures (Hamilton & Abrahams, 1970). The hydrogen atom positions probably have a standard deviation of about 0.10 Å and suffer significantly as a result of the spherical atom approximation used in the refinement.

The final observed and calculated structure factors are given in Table 1; atom position and thermal parameters are listed in Table 2.

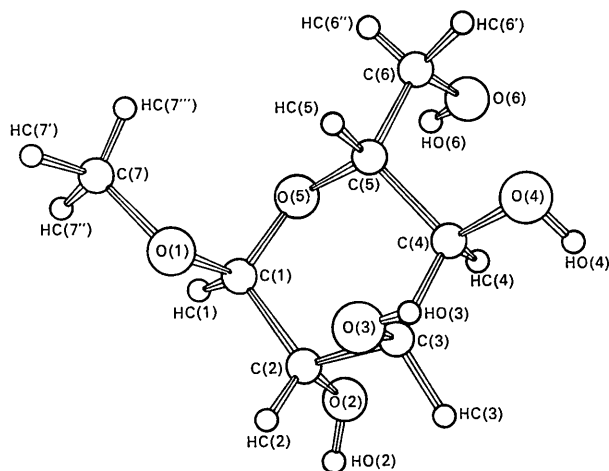


Fig. 1. Molecular configuration and atom designation of methyl  $\alpha$ -D-altropyranoside: Drawn by the program ORTEP (Johnson, 1965).

#### Description of the structure and discussion

Methyl  $\alpha$ -D-altropyranoside in the crystal has the C1 chair conformation with the ring substituents disposed 1(a) 2(a) 3(a) 4(e) 5(e) as shown in Fig. 1. The primary hydroxyl oxygen atom, O(6), is *gauche* to the pyranose

Table 2. Atomic position and thermal parameters

Terms are  $\times 10^4$ . Temperature-factor expression  
 $\exp [-2\pi^2(a^*2h^2U_{11} + b^*2k^2U_{22} + c^*2l^2U_{33} + 2a^*b^*hkU_{12} + 2a^*c^*hlU_{13} + 2b^*c^*klU_{23})]$ .

	$x/a$	$y/b$	$z/c$	$U_{11}$	$U_{22}$	$U_{33}$	$U_{12}$	$U_{13}$	$U_{23}$
C(1)	1493	2927	1669	278	327	323	49	83	25
C(2)	3145	2794	2330	264	278	425	-22	82	9
C(3)	2889	1751	3211	253	277	366	1	-41	-8
C(4)	1095	1978	3725	275	281	259	-26	13	12
C(5)	-423	2006	2693	209	293	271	-18	10	6
C(6)	-2196	2333	3430	271	357	437	13	46	10
C(7)	40	1717	327	767	790	482	143	-228	-147
O(1)	1403	1652	1076	419	393	290	110	-40	-8
O(2)	3486	4236	2727	361	300	732	-85	91	-23
O(3)	3040	271	2847	297	291	460	58	50	11
O(4)	730	772	4378	400	423	279	-90	-77	68
O(5)	-87	3144	2236	252	282	309	46	20	58
O(6)	-2186	3659	4012	497	323	407	66	203	23
HC(1)	1529	3827	1212	405	405	405			
HC(2)	4173	2401	1983	405	405	405			
HC(3)	4174	1889	3662	405	405	405			
HC(4)	1176	3011	4062	405	405	405			
HC(5)	-679	1073	2603	405	405	405			
HC(6')	-2700	1498	3857	405	405	405			
HC(6'')	-3017	2362	2958	405	405	405			
HC(7')	57	721	-173	405	405	405			
HC(7'')	370	2532	-102	405	405	405			
HC(7''')	-1097	1478	604	405	405	405			
HO(2)	4614	4484	2622	405	405	405			
HO(3)	2333	-250	3166	405	405	405			
HO(4)	1402	1002	4829	405	405	405			
HO(6)	-2050	4426	3660	405	405	405			

ring oxygen atom, O(5), and *gauche* to C(4) which is an arrangement similar to that found in a number of other sugars (Sundaralingam, 1968). The methyl group on C(7) is *gauche* to O(5) and *trans* to C(2). This is observed frequently in methyl glycosides and in fact appears to be the preferred conformation.

The geometric centre of the pyranose ring is positioned at  $x/a=0.1353$ ,  $y/b=0.2433$ ,  $z/c=0.2689$  and the mean plane through the six atoms of the pyranose ring is given by I.

$$0.0567X + 0.8957Y + 0.4411Z = 3.621. \quad \text{I}$$

The primary hydroxyl O(6) and atom O(4) of one molecule are hydrogen bonded across one screw axis in the [100] direction to the corresponding atoms of a second molecule. The methyl groups are similarly disposed and form a second column, but one in which only van der Waals forces operate, across a second screw axis parallel to [100] (Fig. 2).

Bond lengths calculated using the coordinates of Table 2 are listed in Table 3. The mean values of C–C and C–O bonds are 1.518 and 1.423 Å respectively which agree well with values observed in other carbohydrates (Berman, Chu & Jeffrey, 1967). The carbon–carbon bonds show very little variation from the mean except in the case of the C(5)–C(6) bond which was short at 1.495 Å. A similar shortening of the same bond has been observed in methyl  $\alpha$ -galactoside monohydrate (Gatehouse & Poppleton, 1970). The differences of the bonds C(1)–O(1), C(1)–O(5) from the mean C–O length are respectively  $-0.018$ ,  $-0.007$  and  $0.017$  Å. These are consistent both in sign and magnitude with the variation in other structures (Berman, Chu & Jeffrey, 1967). The mean lengths of the C–H and O–H bonds, 1.02 and 0.84 Å, agree with those observed in other carbohydrates although the O–H bonds are somewhat shorter than expected (Sutton, 1965). Although these minor variations in bond length appear to be genuine features of pyranose sugars in that they have been observed in a number of structures, we believe that, without suitable confirmation they are best viewed as manifestations of systematic errors relating to crystal shape and perfection and of the deficiencies in the choice of the crystal model to be refined.

Bond angles, Table 3, between the heavier atoms range from  $106.1$  to  $113.9^\circ$  with a mean of  $109.9^\circ$ ; angles involving hydrogen show a much wider variation of  $\pm 10^\circ$  from the mean of  $109^\circ$ . The two ether oxygen atoms, O(1) and O(5), have bond angles of  $113.2$  and  $113.9^\circ$ , which are greater than the mean although normal for carbohydrates.

Those atoms which comprise the ring and to which is attached an axial substituent have angles (mean  $112.5^\circ$ ) that are consistently greater than tetrahedral and indicate a flattening of the ring in this region. This distortion is manifest similarly in the dihedral angles which range between  $44.0$  and  $62.3^\circ$ ; these are to be compared with values for an idealized pyranose ring

(Kim & Jeffrey, 1967) of  $55.8$  to  $61.7^\circ$ . The best plane through any four atoms of the ring is given by II and is derived using the coordinates of C(1), C(3), C(4) and O(5); the remaining atoms C(2) and C(5) are out of this plane by  $-0.553$  and  $+0.681$  Å.

$$0.3226X + 0.8922Y + 0.3162Z = 3.456. \quad \text{II}$$

The hydrogen-bonding scheme in methyl  $\alpha$ -altroside, Fig. 2, contains several unusual features including two bifurcated hydrogen bonds. Relevant hydrogen–oxygen, oxygen–oxygen approach distances less than 3.25 Å are listed in Table 4 together with angles at the hydrogen-bonded protons. The structure contains two normal hydrogen bonds in the sense that the O–H...O angles are close to  $180^\circ$  and the H...O approach distances are substantially less than for a van der Waals contact (Pauling, 1960); the latter is more apparent when allowance is made for the observed short O–H distances. These two normal bonds involve O(4) acting as a donor to O(6'), and O(2) acting as a donor to O(3''). The two remaining hydroxyl oxygen atoms of the molecule, O(6) and O(3), act as donors

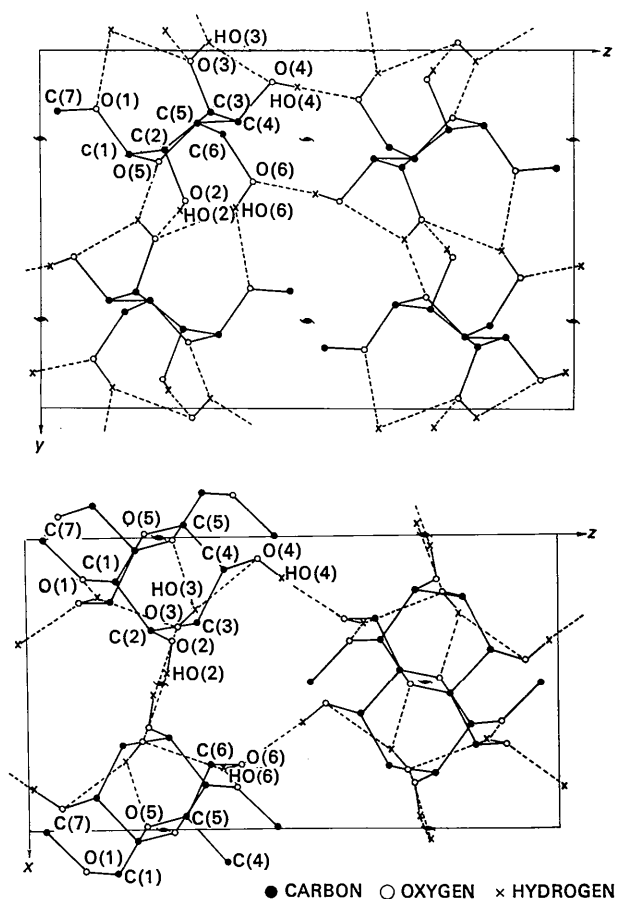


Fig. 2. Hydrogen bonding and packing.

Table 3. Bond lengths and angles

Bond lengths				Bond angles			
C(1)–C(2)	1.523 Å	HC(1)–C(1)	1.02 Å	Central atom	<i>i</i>	<i>j</i>	$\alpha_{ij}$
C(2)–C(3)	1.522	HC(2)–C(2)	0.97	C(1)	C(2)	O(1)	107.4°
C(3)–C(4)	1.521	HC(3)–C(3)	1.14		C(2)	O(5)	112.3
C(4)–C(5)	1.525	HC(4)–C(4)	1.04		O(1)	O(5)	112.1
C(5)–C(6)	1.495	HC(5)–C(5)	0.99		C(2)	HC(1)	112.8
		HC(6')–C(6)	1.02		O(1)	HC(1)	109.1
C(1)–O(1)	1.405	HC(6'')–C(6)	0.88		O(5)	HC(1)	103.2
C(2)–O(2)	1.437	HC(7')–C(7)	1.12	C(2)	C(1)	C(3)	113.2
C(3)–O(3)	1.436	HC(7'')–C(7)	0.97		C(1)	O(2)	106.6
C(4)–O(4)	1.426	HC(7''')–C(7)	0.95		C(3)	(2)	107.9
C(6)–O(6)	1.434	HO(2)–O(2)	0.88		C(1)	HC(2)	113.5
C(1)–O(5)	1.416	HO(3)–O(3)	0.83		C(3)	HC(2)	103.8
C(5)–O(5)	1.440	HO(4)–O(4)	0.81		O(2)	HC(2)	111.9
C(7)–O(1)	1.428	HO(6)–O(6)	0.85		C(2)	C(4)	112.0
					C(2)	O(3)	108.3
					C(4)	O(3)	110.4
					C(2)	HC(3)	103.4
					C(4)	HC(3)	119.4
					O(3)	HC(3)	102.4
					C(4)	C(3)	111.0
					C(4)	C(3)	109.8
					C(5)	O(4)	106.1
					C(3)	HC(4)	105.4
					C(5)	HC(4)	108.3
					O(4)	HC(4)	116.2
					O(1)	C(1)	113.2
					O(2)	C(2)	110.2
					O(3)	C(3)	108.2
					O(4)	C(4)	97.8
					O(5)	C(1)	113.9
					O(6)	C(6)	113.2

in bifurcated hydrogen bonds to O(1'') and O(3''), and O(4) and O(5'') respectively where the primes indicate symmetry related molecules. The intramolecular interaction of HO(3) with O(4) has an angle, O(3)–HO(3)–O(4) of 119° which is low for hydrogen bond formation although the HO(3)···O(4) contact is quite satisfactory. From a consideration of the hydrogen bond angles on HO(3) it would appear that O(5''), which constitutes the other arm of this bifurcated bond, exerts a dominant influence on HO(3) with the final position of the proton controlled more by the angle requirements of C(3)–O(3)–HO(3) than the presence of O(4). The significant difference between these hydrogen bond angles also casts doubt on whether this is a genuine example of either a bifurcated or an intermolecular hydrogen bond. With HO(6), however, these angles are equal and support the suggestion of a bifurcated bond. Furthermore this particular bond appears to play a key role in stabilizing the molecule in the C1 conformation as discussed below.

Table 4. Hydrogen-bond approach distances and angles

Oxygen–oxygen approach distances $\leq 3.25$ Å		
O(4)···O(6 <sup>I</sup> )	2.702 Å	
O(6)···O(1 <sup>III</sup> )	2.788	
O(2)···O(3 <sup>II</sup> )	2.868	
O(3)···O(5 <sup>IV</sup> )	2.939	
O(6)···O(3 <sup>III</sup> )	2.950	
O(3)···O(4)	2.713 (intramolecular)	
Hydrogen–oxygen approach distances and angles		
O(4)–HO(4)···O(6 <sup>I</sup> )	1.90 Å	172°
O(2)–HO(2)···O(3 <sup>II</sup> )	2.00	168
O(6)–HO(6)···O(3 <sup>III</sup> )	2.28	136
O(6)–HO(6)···O(1 <sup>III</sup> )	2.11	136
O(3)–HO(3)···O(5 <sup>IV</sup> )	2.29	135
O(3)–HO(3)···O(4)	2.22	119 (intramolecular)
Symmetry code:		
I	$\frac{1}{2} - x$	$\frac{1}{2} - y$
II	$1 - x$	$\frac{1}{2} + y$
III	$-x$	$\frac{1}{2} + y$
IV	$-x$	$-\frac{1}{2} + y$

Angyal, Pickles & Ahluwalia (1966) have estimated the energy of a 1-3 syndiaxial hydroxy-methoxy interaction, as for example between O(1) and O(3) of methyl  $\alpha$ -altropyranoside, to be 2.5 kcal.mole<sup>-1</sup>. The approach distance between O(1) and O(3) observed in the crystal is 2.94 Å which is greater than the van der Waals contact distance of 2.8 Å (Pauling, 1960). This suggests that the interaction between these two atoms is not significant and therefore it is not the major cause of the distortion of the molecule in this region. This contention is supported, furthermore, by the bonds C(1)-O(1) and C(3)-O(3) being almost exactly coplanar and not twisted away from precise *cis* alignment. It is suggested that the dominant interaction forcing the molecule away from a perfect *C1* conformation is the bond between O(2) and O(3'') counteracted partly by the bond between O(4) and O(6').

Contrary to expectations the 1,3 diaxial arrangement, in association with the O(6) proton, appears to assist actively in maintaining a *C1* conformation. Thus one may envisage that HO(6) interacts with O(1''') and O(3''') to localize the lone-pair electrons, which would be opposed by virtue of the disposition of C(7''') and HO(3'''), to form a genuine bifurcated bond and at the same time minimize any potential interaction between O(1''') and O(3'''). The separation of these two atoms appears too great, however, for a three centre bond to exist; consequently the observed planarity of C(1)-O(1)-C(3)-O(3) is probably fortuitous.

The authors are indebted to Dr A. McL. Mathieson of the Division of Chemical Physics, C.S.I.R.O., for his interest and encouragement, and for providing laboratory space and facilities. Also we wish to express our thanks to Dr N. K. Richtmeyer of the National Institute of Health, Maryland, for supplying seed crystals of methyl  $\alpha$ -altropyranoside.

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