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The Crystal Structure of the K Form of D-Mannitol

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The crystal structure of K-D-mannitol has been solved by use of a direct method procedure on a centrosymmetric projection and an interpretation of a Patterson–Harker section. The space group is $P2_12_12_1$, with four molecules in the unit cell of dimensions $a=8{\cdot}942$ (5), $b=18{\cdot}798$ (9) and $c=4{\cdot}893$ (4) Å. The molecules have the same conformation as in the B form with a carbon chain which is planar within 0·09 Å and a twofold axis of symmetry within 0·01 Å. The two polymorphs have nearly identical molecules, with similar systems of intermolecular hydrogen bonds in different steric arrangements.

Introduction

The crystal structures of the A′ and B forms of D-mannitol have been reported by Berman, Jeffrey & Rosenstein (1968)*. This third form was obtained accidentally from an attempted crystallization of a mannitol–boric acid complex and advantage has been taken of this circumstance to determine the structure. Since the acyclic sugar molecules might be expected to have greater conformational flexibility than the cyclic compounds, it is of interest to observe to what extent conformational variety does in fact occur when the same molecule appears in the different hydrogen-bonding environments of the three polymorphs. In the case of the A′ and B forms, it was found that the molecular conformations were the same, but this was not explored in detail because adequate crystals for a three-dimensional study were not obtained for the A′ form. This study provides a detailed comparison between the structures of the B and K forms.

Experimental

Crystals were obtained as colorless needles by slow evaporation of an aqueous solution of D-mannitol and boric acid in methanol. The crystal data are as follows:

$a=8{\cdot}942$ ($\sigma=0{\cdot}005$) Å
$b=18{\cdot}798$ ($\sigma=0{\cdot}009$)
$c=4{\cdot}893$ ($\sigma=0{\cdot}004$)
$Z=4$
$D_x=1{\cdot}471$ g.cm^{-3}
$D_m=1{\cdot}485$ g.cm^{-3} (by flotation)
$\mu_{\text{Cu }K\alpha}=11{\cdot}75$ cm^{-1}
M.W. 182·17

Space group, $P2_12_12_1$, from absences $h00$ for $h=2n+1$, $0k0$ for $k=2n+1$, $00l$ for $l=2n+1$.

This polymorph may be the same as the Γ form characterized by Rye & Sørum (1952) from powder data (see Berman, Jeffrey & Rosenstein, 1968). The lattice parameters were obtained from a series of general hkl diffractometer measurements using a least-squares program by Shiono (1966*a*). The three-dimensional intensity data were measured with a Picker four-angle automatic diffractometer in the $\theta/2\theta$ scanning mode using Cu $K\alpha$ radiation. The acicular crystal had dimensions $0{\cdot}03\times0{\cdot}05\times0{\cdot}5$ mm, and was mounted along the needle axis. Within the limit of $2\theta<130°$, 753 independent reflections were observed above background. The data were reduced to structure amplitudes without absorption corrections using a series of programs by Craven & Chu (1967).

Determination of the structure

The structure was solved in the [001] projection by means of the IBM 1620 sign correlation program of Beurskens (1963), which is based on a systematic use of correlations between sign relations as given by the Sayre equation. The normalized structure amplitudes were calculated with scale and temperature factors obtained by the method of Wilson (1942). The first trial structure gave an R value of 0·50 for the 182 $hk0$ reflections, which was refined by difference syntheses to 0·13. The z parameters of the atoms were determined without ambiguity from the Harker section, $P(\frac{1}{2}, v, w)$.

Refinement of the structure

The structure was refined in three-dimensions by the modified version (Shiono, 1966*b*) of the Busing, Martin & Levy (1962) full-matrix least-squares program for the IBM 7090 computer, with the Cruickshank (1961) weighting scheme. The function minimized was $\Sigma w(F_o-F_c)^2$, where $w=1/(A+BF+CF^2)$. The factors $A=1$, $B=0{\cdot}1$, $C=0{\cdot}01$ gave an essentially constant value of $\overline{w(F_o-F_c)^2}$ over all ranges of F. The fourteen hydrogen atoms were revealed unambiguously by difference Fourier syntheses. The final cycle of anisotropic least-squares varied all parameters except those of the

* We have changed the nomenclature for these polymorphs from lower to upper case Greek letters to avoid confusion with α and β which are commonly used in carbohydrate chemistry to denote particular molecular configurations.

hydrogen atoms, with no shift as much as σ, and gave an R value of 0·049. The final positional and thermal parameters are given in Table 1, and the structure factors in Table 2.

Description of the structure

The conformation of the molecule and the atomic numbering is shown in Fig. 1. The intramolecular distances and angles are given in Table 3. The average lengths of the C–C and C–O bonds are 1·519 and 1·426 Å respectively, and no bond length differs from the mean value by more than 2σ except the C(6)–O(6) bond, which had a trivially larger deviation. These values correspond closely with the mean values of 1·522 and 1·421 Å from some recent studies of the cyclic monosaccharides (Berman, Chu & Jeffrey, 1967). The corrections for 'riding' motion increase these lengths by about $0{\cdot}5\sigma$, as shown in Table 3. When compared with the same distances in the structure of the B form, the mean C–C distance is 0·003 Å shorter and the mean C–O distance is 0·012 Å longer. The thermal parameters in the two structures are so similar that the larger discrepancy cannot be explained by inadequate thermal corrections (*cf.* the thermal ellipsoids given in Table 4 with those given by Berman,

Table 1. *Fractional atomic coordinates and anisotropic thermal parameters in* K-D-*mannitol*

Key to atomic numbering is given in Fig. 1. The temperature factor expression used was:

$$\exp\left[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)\right].$$

The estimated standard deviations are given in parentheses.

Atom	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	0·4951 (5)	−0·0127 (2)	−0·1301 (9)	0·0117 (5)	0·0015 (1)	0·0329 (19)	0·0002 (2)	0·0005 (10)	0·0008 (4)
C(2)	0·4626 (4)	0·0516 (2)	0·0456 (8)	0·0089 (5)	0·0016 (1)	0·0169 (15)	0·0002 (2)	0·0023 (8)	0·0011 (3)
C(3)	0·4327 (4)	0·1184 (2)	−0·1204 (8)	0·0069 (4)	0·0018 (1)	0·0143 (15)	0·0001 (2)	−0·0002 (7)	0·0003 (3)
C(4)	0·4137 (4)	0·1849 (2)	0·0547 (8)	0·0075 (4)	0·0015 (1)	0·0158 (14)	0·0005 (2)	−0·0015 (7)	0·0005 (8)
C(5)	0·3950 (4)	0·2524 (2)	−0·1116 (8)	0·0088 (4)	0·0016 (1)	0·0158 (14)	−0·0003 (2)	−0·0029 (7)	0·0004 (3)
C(6)	0·3852 (4)	0·3195 (2)	0·0618 (9)	0·0094 (5)	0·0016 (1)	0·0299 (17)	0·0009 (2)	−0·0013 (9)	−0·0005 (4)
O(1)	0·6306 (3)	−0·0045 (1)	−0·2785 (6)	0·0119 (4)	0·0022 (1)	0·0189 (13)	0·0019 (1)	−0·0004 (6)	0·0007 (3)
O(2)	0·5822 (3)	0·0641 (1)	0·2314 (6)	0·0099 (4)	0·0024 (1)	0·0190 (12)	0·0016 (1)	−0·0008 (5)	0·0008 (3)
O(3)	0·3045 (3)	0·1073 (1)	−0·2905 (5)	0·0093 (3)	0·0019 (1)	0·0138 (10)	0·0001 (1)	−0·0012 (6)	−0·0007 (2)
O(4)	0·2835 (3)	0·1778 (1)	0·2212 (5)	0·0089 (3)	0·0019 (1)	0·0111 (9)	0·0008 (1)	0·0019 (5)	0·0014 (2)
O(5)	0·5149 (3)	0·2583 (1)	−0·3041 (5)	0·0096 (3)	0·0019 (1)	0·0166 (11)	−0·0009 (1)	−0·0006 (6)	0·0004 (2)
O(6)	0·5188 (3)	0·3307 (1)	0·2106 (6)	0·0109 (4)	0·0019 (1)	0·0167 (11)	−0·0014 (1)	−0·0004 (6)	−0·0003 (3)
H(O1)	0·611 (6)	0·016 (2)	−0·386 (10)						
H(O2)	0·670 (5)	0·053 (2)	0·143 (10)						
H(O3)	0·232 (5)	0·120 (2)	−0·194 (9)						
H(O4)	0·297 (5)	0·153 (2)	0·358 (9)						
H(O5)	0·594 (5)	0·277 (2)	−0·228 (9)						
H(O6)	0·500 (5)	0·313 (2)	0·350 (9)						
H(C1)	0·407 (5)	−0·027 (2)	−0·255 (10)						
H(C1′)	0·501 (5)	−0·054 (2)	−0·027 (9)						
H(C2)	0·383 (4)	0·044 (2)	0·191 (10)						
H(C3)	0·517 (4)	0·124 (2)	−0·244 (9)						
H(C4)	0·506 (4)	0·186 (2)	0·159 (8)						
H(C5)	0·306 (5)	0·253 (2)	−0·200 (9)						
H(C6)	0·288 (5)	0·316 (2)	0·190 (10)						
H(C6′)	0·368 (5)	0·359 (2)	−0·065 (10)						

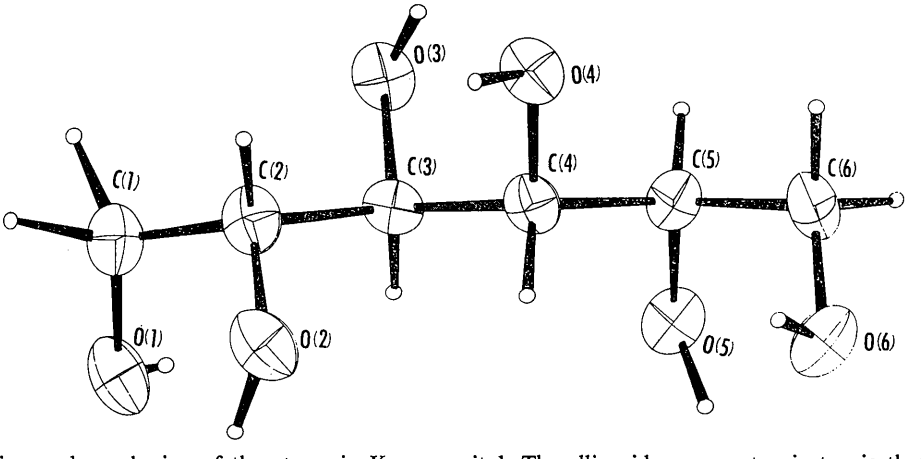

Fig. 1. Identification and numbering of the atoms in K-D-mannitol. The ellipsoids represent anisotropic thermal parameters.

Jeffrey & Rosenstein, 1968). It seems most likely that it is due to some unknown systematic errors in one or other of the structure determinations. The C–C–C bond angles are very constant at 113·4° and the C–C–O angles have a mean value of 110·2°, which is significantly closer to the ideal tetrahedral value. The same observation was made less precisely in the B structure.

The data on the conformation of the molecule with respect to the planarity of the carbon chain and the deviations from twofold axial symmetry normal to that plane are shown in Table 5. An interesting aspect of the detailed structure is a small, but significant, bowing of the chain, as revealed by the distances from the best plane. The same result was observed in the B form, as shown in Table 5. The molecule with the exception of the hydrogen atoms has very nearly twofold axial symmetry, as shown in Table 5 by the distances of the mid-points of the appropriate pairs of atoms from the molecular twofold axis. The conformation angles are given in the Newman projections in Fig. 2.

Table 2. *Observed and calculated structure factors*

Columns are: Index, $10|F_{obs}|$, $10|F_{calc}|$, $10A_{calc}$, $10B_{calc}$.
(* = unobserved).

Table 2 (*cont.*)

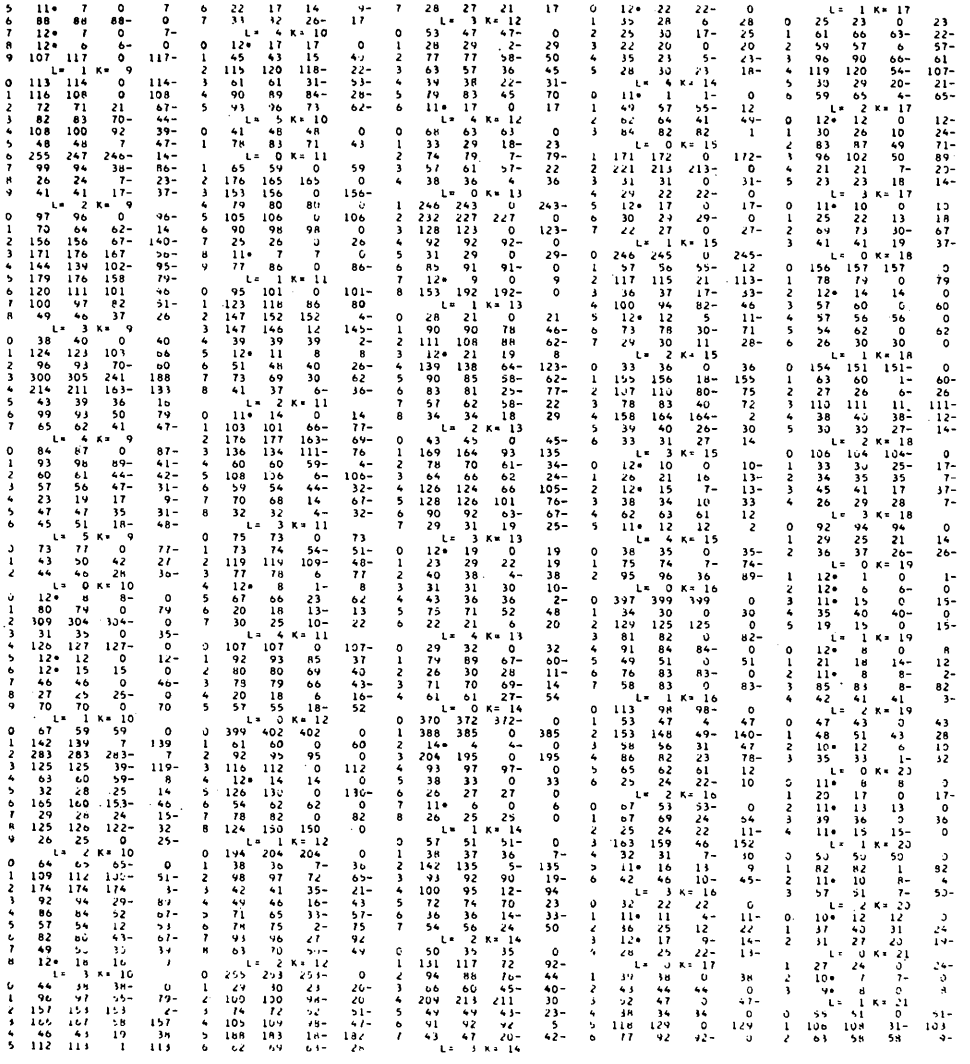

Table 3. *Intramolecular distances and angles in* K-D-*mannitol*

The estimated standard deviations given in parentheses refer to the last decimal positions of respective values.

i	*j*	D_{ij}	D_{ij}*
C(1)	C(2)	1·511 (6) Å	[1·518] Å
C(2)	C(3)	1·519 (5)	[1·522]
C(3)	C(4)	1·524 (5)	[1·524]
C(4)	C(5)	1·517 (5)	[1·518]
C(5)	C(6)	1·523 (5)	[1·529]
C(1)	O(1)	1·421 (5)	[1·422]
C(2)	O(2)	1·423 (5)	[1·430]
C(3)	O(3)	1·433 (4)	[1·435]
C(4)	O(4)	1·427 (4)	[1·431]
C(5)	O(5)	1·431 (4)	[1·435]
C(6)	O(6)	1·415 (5)	[1·415]
Mean C–C		1·519	
Mean C–O		1·426	

i	*j*	*k*	$\angle ijk$
C(1)	C(2)	C(3)	113·0 (3)°
C(2)	C(3)	C(4)	113·4 (3)
C(3)	C(4)	C(5)	113·4 (3)
C(4)	C(5)	C(6)	113·6 (3)
O(1)	C(1)	C(2)	111·6 (3)
C(1)	C(2)	O(2)	110·6 (3)
O(2)	C(2)	C(3)	109·7 (3)
C(2)	C(3)	O(3)	109·3 (3)
O(3)	C(3)	C(4)	110·9 (3)
C(3)	C(4)	O(4)	109·6 (3)
O(4)	C(4)	C(5)	109·1 (3)
C(4)	C(5)	O(5)	109·6 (3)
O(5)	C(5)	C(6)	110·2 (3)
C(5)	C(6)	O(6)	111·2 (3)
Mean C–C–C			113·4
Mean C–C–O			110·2

* Bond lengths corrected assuming 'riding' motion (Busing & Levy, 1964).

Table 4. *Principal axes of thermal ellipsoids*

The root mean square displacement U_i corresponds to the ith principal axis of the ellipsoid and θ_{ia}, θ_{ib}, θ_{ic} are angles between the ith axis and the crystallographic axes a, b, c.

	i	U_i	θ_{ia}	θ_{ib}	θ_{ic}
C(1)	1	0·1604 Å	93·33°	14·47°	104·07°
	2	0·2012	77·62	103·04	161·86
	3	0·2183	12·83	83·83	78·79
C(2)	1	0·1313	78·14	67·78	154·51
	2	0·1701	67·01	151·33	106·18
	3	0·1969	26·17	72·82	70·86
C(3)	1	0·1313	87·55	95·14	5·70
	2	0·1667	170·63	81·21	86·78
	3	0·1804	80·96	10·20	85·29
C(4)	1	0·1304	108·79	69·05	151·22
	2	0·1599	69·80	144·85	117·41
	3	0·1815	28·18	63·18	98·05
C(5)	1	0·1298	71·46	94·61	19·13
	2	0·1677	109·58	160·31	88·13
	3	0·1973	27·51	109·09	109·04
C(6)	1	0·1569	119·11	29·24	87·48
	2	0·1859	113·66	100·29	153·93
	3	0·2098	39·10	62·95	115·92
O(1)	1	0·1457	105·47	66·65	151·45
	2	0·1701	56·86	133·50	118·46
	3	0·2471	37·46	52·59	88·11
O(2)	1	0·1444	109·24	69·15	150·98
	2	0·1736	47·67	124·10	118·80
	3	0·2346	48·55	41·61	86·85
O(3)	1	0·1258	83·55	80·20	11·76
	2	0·1843	71·98	160·44	82·63
	3	0·1959	19·20	73·24	99·11
O(4)	1	0·1073	95·42	104·02	15·08
	2	0·1685	45·66	134·97	96·25
	3	0·2092	44·85	48·35	76·33
O(5)	1	0·1413	88·31	96·15	6·38
	2	0·1680	126·32	143·38	93·96
	3	0·2112	143·62	54·07	84·99
O(6)	1	0·1409	82·46	78·69	13·63
	2	0·1651	123·72	142·89	76·36
	3	0·2303	145·21	55·21	90·24

The dihedral angles of the C–C-bonds range from 51° to 65°. In general, the detailed structure of the molecule in the K form differs almost insignificantly from that in the B form despite the different hydrogen-bonding environment of the molecules. This suggests that the detailed shape of the molecule is determined almost entirely by intramolecular forces and that the effect of intermolecular forces on planarity and conformation angles is trivial in comparison.

The hydrogen-bonding is shown in Fig. 3. All the hydroxyl groups donate and accept one hydrogen bond with O(H)···O distances ranging from 2·716 to 2·835 Å. The angles at the donor oxygens vary between 111° and 128° and are invariably smaller than those at the corresponding acceptor oxygen (Table 6). For the two longest hydrogen bonds O(2)···O(1) and O(3)···O(6), the observed hydrogen atom positions deviate by as much as 0·4 Å from the line of the O···O centers towards the nearest intramolecular oxygen atoms, O(1) and O(4), respectively, possibly forming weak bifurcated hydrogen bonds. The intramolecular distances are 2·841 Å for O(2)···O(1) and 2·839 Å for O(3)···O(4). The other deviations of hydrogen atom positions from the line of O···O centers are less than 0·25 Å and are probably not significant.

The hydrogen-bonding scheme, illustrated in Figs. 3 and 4, consists of four-link infinite spirals about the screw axes, *i.e.* → O(1) → O(2) → O(1) → O(2) →, and four-link closed circuits, *i.e.* → O(6) → O(5) → O(4)x → O(3)x →. The molecules lie in planes approximately

Table 5. *Least squares plane and twofold axis in* K-D-*mannitol*

Equation for plane: $Ax+By+Cz=D$, where x, y, z are in Å and $A=0{\cdot}9876$, $B=0{\cdot}1565$, $C=-0{\cdot}0151$ and $D=4{\cdot}2543$. This plane makes an angle of 9° with (100).

Atoms included in plane	Distance from best plane K form	B form
C(1)	+0·090 Å	+0·065 Å
C(2)	−0·021	−0·010
C(3)	−0·076	−0·073
C(4)	−0·061	−0·036
C(5)	−0·015	+0·005
C(6)	+0·083	+0·048

Parametric equation of the best twofold axis in Å,

$$x = 4{\cdot}038+0{\cdot}988t$$
$$y = 2{\cdot}894+0{\cdot}153t$$
$$z = -0{\cdot}167+0{\cdot}002t$$

Atom pairs		Distance of mid-point of atom pairs from molecular twofold axis
C(1)	C(6)	0·005 Å
C(2)	C(5)	0·008
C(3)	C(4)	0·008
O(1)	O(6)	0·004
O(2)	O(5)	0·011
O(3)	O(4)	0·006

The angle between the plane and the axis is 89°6′.

Table 6. *Intermolecular distances and angles in* K-D-*mannitol*

Symmetry code

a	x	y	z
b	$1\frac{1}{2}-x$	$-y$	$-\frac{1}{2}+z$
c	x	y	$-1+z$
d	$-\frac{1}{2}+x$	$\frac{1}{2}-y$	$-z$
e	x	y	$1+z$
f	$\frac{1}{2}+x$	$\frac{1}{2}-y$	$-z$
g	$1\frac{1}{2}-x$	$-y$	$\frac{1}{2}+z$
h	$-\frac{1}{2}+x$	$\frac{1}{2}-y$	$1-z$
j	$\frac{1}{2}+x$	$\frac{1}{2}-y$	$1-z$

→: direction O–H···O bond.

i	j	k	l	D_{jk}	$\angle ijk$	$\angle jkl$
C(1)	O(1)→O(2)c	C(2)c		2·756 Å	111·2°	126·6°
C(2)	O(2)→O(1)g	C(1)g		2·802	127·7	136·8
C(3)	O(3)→O(6)d	C(6)d		2·835	125·5	153·2
C(4)	O(4)→O(3)e	C(3)e		2·739	119·2	119·4
C(5)	O(5)→O(4)f	C(4)f		2·716	126·7	139·9
C(6)	O(6)→O(5)e	C(5)e		2·737	111·2	128·2

parallel to (001). There are marked similarities to the molecular packing in the B form, which is also illustrated in Figs. 3 and 4. Both structures have the same number of hydrogen bonds per molecule and each hydroxyl group is involved in two bonds. In both unit cells, there is an infinite chain or spiral and a closed circuit of hydrogen bonds, which repeat after four links. The infinite chains involve only the oxygen atoms O(1), O(2) at one end of the molecule, while the remainder form the closed circuits in the sequence O(6), O(5), O(4), O(3). The donor direction of the closed circuits is reversed in the two structures. The hydrogen bonds in the K form are longer and make a wider range of C–O(H)–O angles than the B form; *i.e.* 2·716–2·835

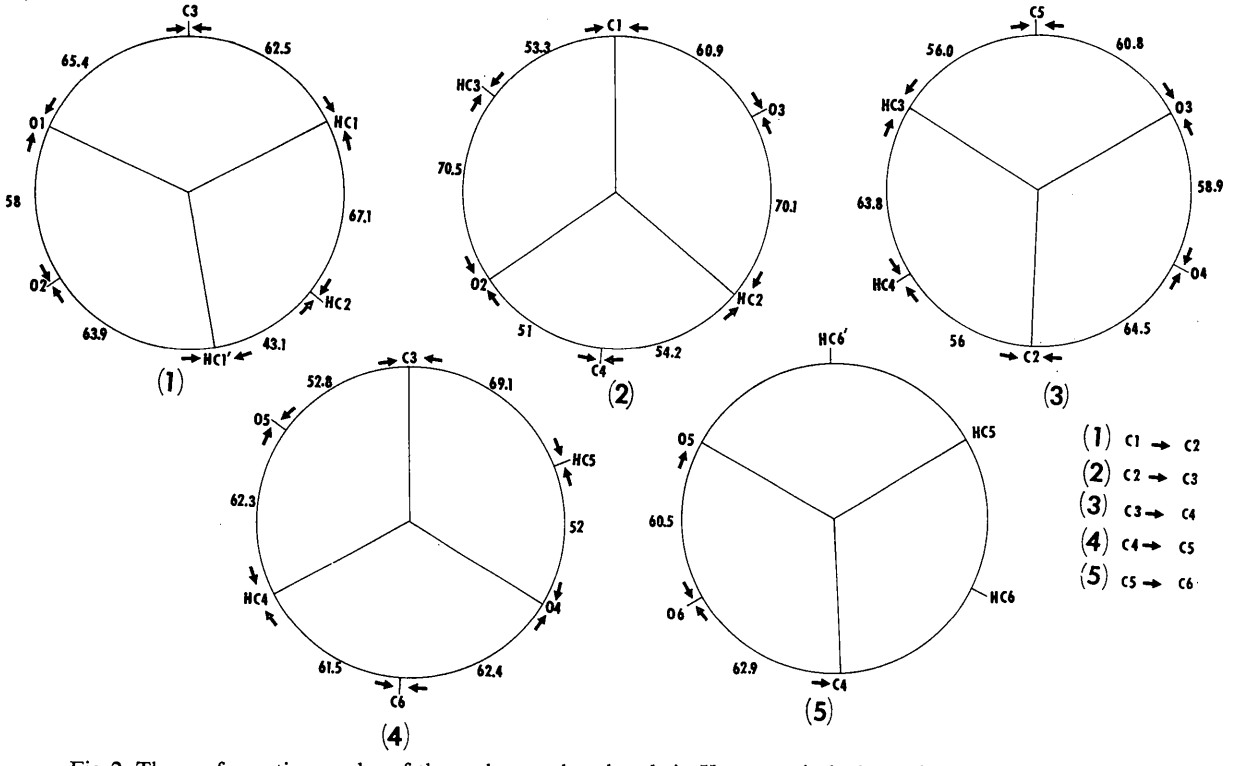

Fig. 2. The conformation angles of the carbon-carbon bonds in K-D-mannitol, shown in Newman projections.

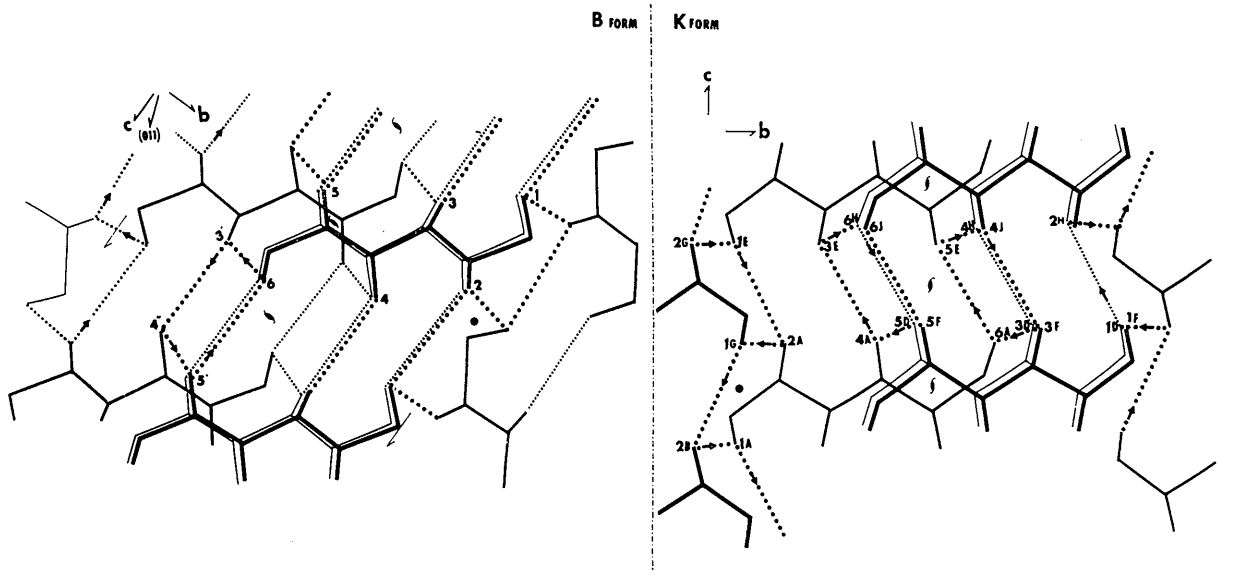

Fig. 3. The structures of the B and K forms of D-mannitol viewed down the *a* axis.

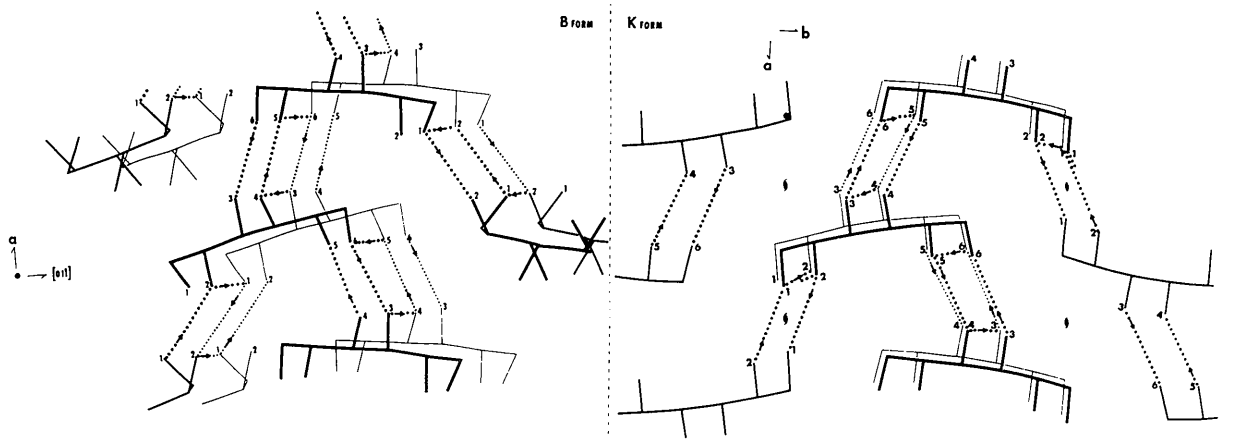

Fig. 4. The structures of the B and K forms of D-mannitol projected on the (01$\bar{1}$) and (001) planes, respectively.

versus 2·692–2·766 Å, 111·2–153·2 *versus* 108·3–124·9°. The unit cell volume of the K form is one per cent larger. Hence it is the metastable form, obtained only under special circumstances such as those described in this paper.

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