

## Effects of Calcium Interactions on Sugar Conformation: Crystal Structure of $\beta$ -D-Fructose-Calcium Bromide Dihydrate

BY WILLIAM J. COOK AND CHARLES E. BUGG

*Institute of Dental Research and Department of Biochemistry, University of Alabama in Birmingham, University of Alabama Medical Center, University Station, Birmingham, Alabama 35294, U.S.A.*

(Received 28 July 1975; accepted 9 October 1975)

**Abstract.** Monoclinic,  $P2_1$  (systematic absence  $0k0$   $k$  odd),  $a=8.102$  (3),  $b=11.892$  (2),  $c=7.090$  (1) Å,  $\beta=94.94$  (3)°. Two formula units per cell.  $D_m=2.02$ ,  $D_x=2.030$  g cm<sup>-3</sup>. Intensity data for 1171 reflections were collected with an automatic diffractometer. The structural parameters were refined by full-matrix least squares to an  $R$  of 0.039. Calcium ions are bound to all hydroxyl groups. The resultant sugar conformation is considerably different from that in the crystal structure of  $\beta$ -D-fructose.

**Introduction.** Recent crystallographic studies have suggested that calcium interactions with the hydroxyl groups of sugars can significantly affect sugar conformation (Cook & Bugg, 1973*a, b*, 1975). In this paper we describe the sugar conformation in a calcium-fructose complex and compare it with the conformation in the crystal structure of  $\beta$ -D-fructose (Rosenstein, 1968, and private communication). Crystals of  $C_6H_{12}O_6 \cdot CaBr_2 \cdot 2H_2O$  were obtained during efforts to crystallize a sucrose-calcium bromide complex. Sucrose was dissolved in a boiling, concentrated aqueous solution of calcium bromide, and crystals of the fructose complex grew as large prisms when the solution was slowly evaporated over a period of several weeks at room temperature. These crystals are nearly iso-

structural with those of  $\beta$ -D-fructose- $CaCl_2 \cdot 2H_2O$  (Craig, Stephenson & Stevens, 1974). Cell constants were obtained by least-squares analysis of  $2\theta$  values for 12 high-angle reflections (Cu  $K\alpha_1$ ,  $\lambda=1.54051$  Å) measured on the diffractometer. The density was measured by flotation in carbon tetrachloride-1,1,2,2-tetra-bromoethane.

Since the crystals are deliquescent, that used for data collection was mounted in a glass capillary tube. Three-dimensional X-ray intensity data for the 1171 symmetry-independent reflections with  $2\theta \leq 128^\circ$  were obtained with a Picker FACS-1 diffractometer (Ni-filtered Cu radiation, a scintillation counter, and a  $\theta$ - $2\theta$  scanning technique). The scanning speed was  $2^\circ$  min<sup>-1</sup> and a 20 s background measurement was performed at each terminus of the scans. Three strong reflections (500, 004 and 040) were monitored periodically during data collection; their intensities decreased by 23, 28, and 24%, respectively. The  $I_0$  values were scaled by a least-squares procedure in which the intensities of the standard reflections were used to calculate scale factors as a function of crystal exposure time (Ibers, 1969). Those reflections with scan counts below background levels were assigned intensities of 0.0 and were retained in all subsequent calculations. This introduced a bias in our refinement on  $F^2$ , but probably has a negligible

Table 1. *Non-hydrogen-atom parameters and their standard deviations*

Coordinates and thermal parameters have been multiplied by  $10^4$  and  $10^3$ , respectively. Temperature factors are coefficients in the expression  $T = \exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$ . The final value of the isotropic extinction parameter is  $g=0.010$  (2).

	$x$	$y$	$z$	$U_{11}$	$U_{22}$	$U_{33}$	$U_{12}$	$U_{13}$	$U_{23}$
Br(1)	7878 (1)	7500	7111 (1)	28 (1)	36 (1)	48 (1)	0 (1)	0 (1)	-5 (1)
Br(2)	1942 (1)	9403 (1)	7355 (2)	43 (1)	39 (1)	50 (1)	2 (1)	16 (1)	3 (1)
Ca	3096 (2)	6558 (2)	3191 (2)	31 (1)	33 (1)	25 (1)	-1 (1)	1 (1)	0 (1)
C(1)	5861 (11)	4482 (9)	7208 (12)	32 (4)	34 (5)	34 (4)	6 (4)	-1 (4)	-7 (4)
C(2)	4021 (11)	4790 (8)	7000 (11)	28 (4)	35 (5)	24 (4)	1 (4)	2 (3)	2 (3)
C(3)	3808 (10)	5939 (7)	7878 (10)	20 (4)	30 (5)	23 (3)	-2 (3)	-2 (3)	0 (3)
C(4)	2092 (11)	6182 (8)	8519 (11)	34 (5)	34 (5)	22 (4)	2 (4)	-1 (3)	4 (4)
C(5)	1342 (11)	5172 (9)	9421 (12)	24 (4)	55 (6)	25 (4)	-6 (4)	4 (3)	2 (4)
C(6)	1458 (11)	4175 (9)	8174 (12)	31 (4)	43 (6)	28 (4)	-10 (4)	-2 (4)	2 (4)
O(1)	6215 (8)	3493 (6)	6178 (8)	39 (3)	29 (3)	33 (3)	7 (3)	10 (3)	0 (3)
O(2)	3404 (8)	4835 (5)	5075 (8)	36 (3)	30 (3)	25 (3)	0 (3)	0 (2)	-3 (2)
O(3)	4122 (7)	6777 (5)	6500 (8)	23 (3)	29 (3)	32 (3)	-1 (2)	2 (2)	2 (2)
O(4)	2201 (8)	7073 (6)	9890 (8)	36 (3)	30 (3)	28 (3)	5 (3)	5 (2)	2 (2)
O(5)	2226 (9)	5023 (5)	11229 (8)	48 (4)	30 (4)	27 (3)	-10 (3)	-3 (3)	6 (3)
O(6)	3186 (7)	3923 (6)	7936 (8)	32 (3)	32 (3)	30 (3)	0 (3)	4 (2)	2 (2)
O(W1)	297 (8)	6676 (7)	3838 (10)	29 (3)	64 (5)	46 (4)	-1 (4)	10 (3)	-6 (4)
O(W2)	5757 (8)	6619 (7)	2229 (11)	29 (3)	42 (4)	62 (4)	2 (3)	4 (3)	-5 (3)

effect on the final results. Intensities were assigned variances,  $\sigma^2(I)$ , according to counting statistics plus a correction term  $(0.03S)^2$ ,  $S$  being the scan count. The intensities and their variances were corrected for Lorentz and polarization effects, and absorption corrections were applied with *ORABS* (Wehe, Busing & Levy, 1962). The data were scaled by a Wilson (1942) plot.

We arrived at a suitable trial structure by the heavy-atom method. Coordinates and anisotropic temperature parameters for the non-hydrogen atoms and Zachariasen's (1963) isotropic extinction parameter  $g$  [as formulated by Coppens & Hamilton (1970)] were refined by a modified version of *ORFLS* (Busing, Martin & Levy, 1962; Busing, 1971). The quantity minimized was  $\sum w(F_o^2 - F_c^2/k^2)^2$ , where  $k$  is a scale factor and the weight  $w$  is equal to  $1/\sigma^2(F_o^2)$ . Scattering factors for the non-hydrogen atoms were from *International Tables for X-ray Crystallography* (1962), and anomalous dispersion correction factors for these atoms were from Cromer & Liberman (1970). Scattering factors for the H atoms were from Stewart, Davidson & Simpson (1965). Coordinates for those H atoms bonded to C atoms were calculated by assuming tetrahedral bonding with C-H bond distances of 0.95 Å. All H atoms bonded to O atoms were located in difference Fourier maps that were calculated during the latter stages of refinement. H atoms were assigned the approximate isotropic temperature factors of the atoms to which they are bonded and were included in structure-factor calculations but not in the least-squares refinement. During the last cycle of refinement, no parameter shifted more than one-fifth of its estimated standard deviation. The final  $R$  index  $\{\sum ||F_o| - |F_c|| / \sum |F_o|\}$  is 0.039, and the goodness-of-fit  $\{[\sum w(F_o^2 - F_c^2)/(m-s)]^{1/2}\}$ , where  $m$  is the number of reflections used and  $s$  the number of parameters refined, is 2.61. In a final difference map, which was calculated with the H atoms omitted from the calculated structure factors, the electron densities at H atom positions had an average

value of  $0.8 \text{ e } \text{\AA}^{-3}$  and ranged from 0.6 to  $0.9 \text{ e } \text{\AA}^{-3}$ . The remainder of the map showed several peaks and troughs ranging from 0.9 to  $1.4 \text{ e } \text{\AA}^{-3}$  in the vicinities of the bromide ions; no other peaks or troughs exceeded  $0.5 \text{ e } \text{\AA}^{-3}$ .

**Discussion.** Table 1 lists the non-hydrogen-atom parameters and their estimated standard deviations. Hydrogen-atom parameters are given in Table 2.\* The crystal-packing scheme, hydrogen-bonding pattern and fructose conformation are shown in Fig. 1. All H atoms that are covalently bonded to O atoms participate in hydrogen bonding. The calcium ion is bound

\* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31456 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

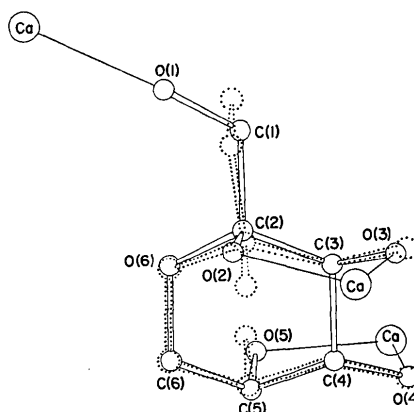


Fig. 2. Conformation of fructose in the crystal structure of the calcium bromide complex (solid lines) as compared with that in the crystal structure of  $\beta$ -D-fructose (dotted lines). The molecules are oriented so that the C(3)-C(4) and C(4)-C(6) vectors lie in the plane of the paper. The C(3)-C(4) bonds are exactly superimposed.

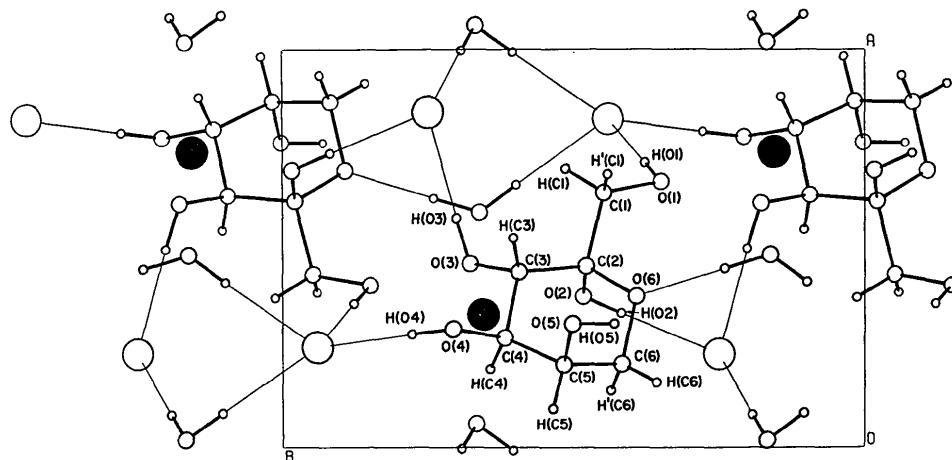


Fig. 1. Crystal packing and hydrogen-bonding scheme as viewed perpendicular to the  $ab$  plane. Heavy lines represent covalent bonds and fine lines represent hydrogen bonds. Calcium ions are represented by solid black circles and bromide ions by large open circles. This drawing and Fig. 2 were prepared by using the computer program *ORTEP* (Johnson, 1965).

to three symmetry-related fructose molecules. One fructose molecule is coordinated to the calcium ion through the O(2) and O(3) hydroxyl groups, another through the O(4) and O(5) hydroxyl groups, and a third molecule binds through its O(1) hydroxyl group. The Ca is thus surrounded by a coordination polyhedron composed of seven O atoms: five from hydroxyl groups and two from water molecules. The seven O atoms assume a pentagonal bipyramidal arrangement, with Ca-O distances ranging from 2.32 to 2.47 Å.

The bond angles and conformational torsion angles are listed in Tables 3 and 4, respectively, along with the corresponding values for  $\beta$ -D-fructose. In Fig. 2 the fructose moiety from the calcium bromide complex is superimposed on that from the uncomplexed

Table 2. *Hydrogen-atom parameters*

Values have been multiplied by  $10^3$ . Positional parameters were either calculated or determined from difference Fourier maps. Each H atom was assigned the approximate isotropic temperature factor of the non-hydrogen atom to which it is bonded.

	x	y	z	$U_{iso}$
H(C1)	649	513	675	27
H'(C1)	622	441	851	27
H(C3)	459	604	895	43
H(C4)	139	644	744	18
H(C5)	22	536	959	27
H(C6)	95	358	871	39
H'(C6)	89	436	696	39
H(O1)	677	378	512	39
H(O2)	303	419	444	30
H(O3)	526	702	669	25
H(O4)	213	778	915	26
H(O5)	220	431	1172	29
H(W1)	-41	693	478	42
H'(W1)	-35	604	350	42
H(W2)	644	599	236	36
H'(W2)	611	740	218	36

Table 3. *Bond angles for the fructose molecules in the crystal structure of  $\beta$ -D-fructose.  $\text{CaBr}_2 \cdot 2\text{H}_2\text{O}$  and  $\beta$ -D-fructose (the estimated standard deviations are about  $0.5^\circ$  and  $0.6^\circ$  respectively)*

	Fructose- $\text{CaBr}_2 \cdot 2\text{H}_2\text{O}$	Fructose
C(2)-C(1)-O(1)	112.6°	110.2°
C(1)-C(2)-C(3)	108.6	112.8
C(1)-C(2)-O(2)	111.3	110.3
C(1)-C(2)-O(6)	106.2	103.6
C(3)-C(2)-O(2)	108.6	107.7
C(3)-C(2)-O(6)	112.6	111.7
O(2)-C(2)-O(6)	109.5	110.6
C(2)-C(3)-C(4)	115.5	110.2
C(2)-C(3)-O(3)	108.3	110.8
C(4)-C(3)-O(3)	106.8	108.7
C(3)-C(4)-C(5)	112.6	109.9
C(3)-C(4)-O(4)	109.7	110.0
C(5)-C(4)-O(4)	107.6	109.1
C(4)-C(5)-C(6)	109.5	110.6
C(4)-C(5)-O(5)	106.9	110.4
C(6)-C(5)-O(5)	112.6	107.1
C(5)-C(6)-O(6)	110.1	111.2
C(2)-O(6)-C(6)	113.8	114.2

Table 4. *Torsion angles for the fructose molecules in the crystal structures of  $\beta$ -D-fructose.  $\text{CaBr}_2 \cdot 2\text{H}_2\text{O}$  and  $\beta$ -D-fructose (the estimated standard deviations are about  $0.6^\circ$  and  $0.7^\circ$  respectively)*

The angles are defined according to Klyne & Prelog (1960).

	Fructose- $\text{CaBr}_2 \cdot 2\text{H}_2\text{O}$	Fructose
O(1)-C(1)-C(2)-C(3)	-171.2°	57.3°
O(1)-C(1)-C(2)-O(2)	-51.8	177.8
O(1)-C(1)-C(2)-O(6)	67.4	-63.7
C(1)-C(2)-C(3)-C(4)	-156.4	-169.2
C(1)-C(2)-C(3)-O(3)	83.9	70.4
O(2)-C(2)-C(3)-C(4)	82.4	68.8
O(2)-C(2)-C(3)-O(3)	-37.3	-51.6
O(6)-C(2)-C(3)-C(4)	-39.0	-52.9
O(6)-C(2)-C(3)-O(3)	-158.8	-173.3
C(2)-C(3)-C(4)-C(5)	39.4	52.3
C(2)-C(3)-C(4)-O(4)	159.3	172.4
O(3)-C(3)-C(4)-C(5)	160.0	173.9
O(3)-C(3)-C(4)-O(4)	-80.2	-66.0
C(3)-C(4)-C(5)-C(6)	-49.8	-54.9
C(3)-C(4)-C(5)-O(5)	72.4	63.4
O(4)-C(4)-C(5)-C(6)	-170.8	-175.6
O(4)-C(4)-C(5)-O(5)	-48.6	-57.2
C(4)-C(5)-C(6)-O(6)	61.3	56.7
O(5)-C(5)-C(6)-O(6)	-57.4	-63.7
C(5)-C(6)-O(6)-C(2)	-63.6	-58.4
C(1)-C(2)-O(6)-C(6)	169.7	177.9
C(3)-C(2)-O(6)-C(6)	50.9	56.2
O(2)-C(2)-O(6)-C(6)	-70.0	-63.8

structure, in order to depict the major conformational changes. Calcium interactions appear to be responsible for a number of significant distortions in the fructose conformation. The most pronounced change is in the orientation of the hydroxymethyl group, which is rotated  $131^\circ$  about the C(1)-C(2) bond from the orientation found in the uncomplexed fructose. Smaller, but significant, conformational changes are also induced at the two sites where calcium ions are chelated by pairs of hydroxyl groups. The O(2)-C(2)-C(3)-O(3) and O(4)-C(4)-C(5)-O(5) angles have changed by about  $14^\circ$  and  $9^\circ$ , respectively. Concomitantly, there are several significant changes in bond angles, the largest occurring in the C(2)-C(3)-C(4) and the C(6)-C(5)-O(5) angles, which have increased by more than  $5^\circ$  in the calcium complex. All of these changes appear to be attributable to hydroxyl-calcium interactions. O(1) has moved to an orientation that permits binding to a calcium ion, and the O(2)-O(3) and O(4)-O(5) hydroxyl groups seem to be drawn toward the calcium ions to which they are chelated. The net result of the conformational changes is that the O(2)-O(3) and the O(4)-O(5) spacings are about  $0.2 \text{ \AA}$  shorter in the calcium complex, a finding that is consistent with the distortions observed in other carbohydrate complexes where calcium ions are chelated by pairs of hydroxyl groups (Cook & Bugg, 1973a, b, 1975).

We thank Dr Bob Rosenstein for his unpublished parameters for  $\beta$ -D-fructose, and Miss Catherine Sims and Miss Mary Ann Comer for assistance with the

preparation of this manuscript. This work was supported by N.I.H. grants CA-12159 and DE-02670.

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## 1-Benzyl-2-phenyl-3-hydroxy-4,5-dimethylphosphol-2-ene 1-Oxide

BY DICK VAN DER HELM,\* D. M. WASHECHECK, JOHN E. BURKS AND S. E. EALICK

*Department of Chemistry, University of Oklahoma, Norman, Oklahoma 73069, U.S.A.*

(Received 23 September 1975; accepted 24 September 1975)

**Abstract.**  $C_{19}H_{21}O_2P$ , m.p. 181–183°, orthorhombic, space group  $Pc2_1b$ ,  $a=8.1319$  (6),  $b=8.5671$  (7),  $c=24.081$  (3) Å,  $Z=4$ ,  $M=312.33$ ,  $D_x=1.236$ ,  $D_m=1.236$  g cm<sup>-3</sup>. The title compound exists in the enol form having a C(2)–C(3) bond length of 1.357 Å. The stereochemistry at P and C(5) is *trans* as is the stereochemistry at C(4) and C(5). A strong hydrogen bond is formed between the P=O and O–H related by the twofold screw axis.

**Introduction.** The title compound represents a novel class of 2-phospholene-3-ole structures which may serve as starting materials for C–P heterocycles with possible biological activity. Certain phospholenes have shown biological activity [Vizel, Zvereva, Ivanovskaya, Studentsova, Dunaev & Berim (1965); Arbuzav, Vizel, Zvereva, Studentsova & Garaev (1966)] and the fact that alkylation appears to be sterically influenced (Purdum & Berlin, 1974) should stimulate interest. A preliminary report of this structure has been published (Washecheck, van der Helm, Purdum & Berlin, 1975).

The compound was recrystallized from ethanol–water mixture. A prismatic crystal, approximately 0.5 × 0.3 × 0.15 mm, was used for data collection and unit-cell determination. The unit-cell dimensions were determined at 27°C from the +2 $\theta$  and –2 $\theta$  values of 30 reflections distributed through all octants of recip-

rocal space. The data showed definite systematic absences of 0k0,  $k=2n+1$  and 00l,  $l=2n+1$  with very weak or zero intensities, and inconsistent from crystal to crystal for  $hk0$ ,  $k=2n+1$  and  $0kl$ ,  $l=2n+1$  indicating a probable space group of  $Pc2_1b$ ,  $Pcmb$  or  $P22_12_1$ . Space group  $Pc2_1b$  was later confirmed by the structure solution when an attempted refinement in space group  $P22_12_1$  failed. The intensities of 1852 reflections [1766 reflections had  $I > 2\sigma(I)$ ] with  $2\theta < 150^\circ$  were measured using Cu  $K\alpha$  radiation ( $\lambda=1.5418$  Å) and  $\theta$ – $2\theta$  scans on a Nonius CAD-4 automatic diffractometer. Absorption corrections ( $\mu=14.7$  cm<sup>-1</sup>) and Lorentz and polarization corrections were applied. The program used for the absorption corrections was that of Coppens, Leiserowitz & Rabinovich (1965) and employs the method of Gaussian integration. In this case 216 sampling points were used and the correction factor ranged from 0.5779 to 0.8245.

The structure was solved using conventional Patterson and Fourier techniques. The hydrogen atoms were located in a difference Fourier map based on the refined positions of the P, O and C atoms. The structure was refined using block-diagonal least-squares techniques (Ahmed, 1966) with anisotropic temperature factors for the non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms. The refinement was terminated when all shifts for the non-hydrogen atoms were less than 0.6 of the corresponding estimated standard deviation. The error in an observation of unit weight,  $[\sum w(F_o - F_c)^2 / (m - n)]^{1/2}$ , where  $m$  = the number

\* Supported, in part, by N. I. H. Development Award K4-GM-42572.