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Interactions of Calcium Ions with Carbohydrates: Crystal Structure of Calcium DL-Glycerate Dihydrate

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The crystal structure of calcium DL-glycerate dihydrate has been determined by the heavy atom method. The crystal is monoclinic, space group $P2_1/c$, with unit cell dimensions: $a=14.40$, $b=7.63$, $c=10.40$ Å, and $\beta=98.8°$. Two independent glycerate anions have different conformations. β-Hydroxy oxygen in one conformer is trans-gauche to α-carboxy carbon and α-hydroxy oxygen, while that in the other conformer is gauche-gauche. Ca–O interactions and hydrogen bonds stabilize the crystal structure. The calcium ion is bound to three glycerate anions and two water molecules, the two glycerate anions chelating the calcium ion with the α-carboxy oxygen and α-hydroxy oxygen, and third glycerate anion bonding to the calcium ion with β-hydroxy oxygen. Seven oxygens surround a calcium ion in a distorted pentagonal biprism arrangement with Ca–O distances ranging from 2.32 to 2.47 Å.

A ^1H NMR study on lanthanoid complexes of polyhydroxy α-carboxylic acids in an aqueous solution indicates that the ligand anion has a conformation suitable for the complex formation with the cation and usually chelates the cation with α-carboxy oxygen, α-hydroxy oxygen, and β-hydroxy oxygen.[1,9] The same type of 'three O atoms' chelation to a calcium ion has been observed in the crystal structures of Ca-arabonate·$5H_2O$[11] and CaBr-lactobionate·$4H_2O$.[12] However, such a chelate form may not be always necessary for a stable calcium binding to β-hydroxy carboxylic acid in the crystal state, since the calcium binding features in Ca-tartrate·$3H_2O$[20] and Ca-glucarate·$4H_2O$[10] differ from that mentioned above. The calcium ion is generally coodinated with seven to nine oxygens in a crystalline state, and the oxygen polyhedra observed in a number of calcium carbohydrate crystals[8-32] are largely distorted from the idealized form. In the present investigation we were, therefore, interested in the conformation of the glycerate anion and in the chelating feature of the anion with the calcium ion; the steric arrangement of the ligand oxygens around the calcium ion in the crystal structure received special attention.

Experimental

Colorless monoclinic crystals of calcium glycerate dihydrate $Ca(C_3H_5O_4)_2 \cdot 2H_2O$ were obtained by slow evaporation of the saturated aqueous solution. Prelimilary experiments indicated that the space group is $P2_1/c$, from the systematic absences of $h0l$ and $0k0$ for l and k odd, and that the unit cell dimensitions are $a=14.40(7)$, $b=7.63(4)$, $c=10.40(4)$ Å, and $\beta=98.8(3)°$, from Weissenberg photographs calibrated by NaCl standard powder lines. $V=1129$ Å^3, $Z=4$, and $D_x=1.68$ g/cm^3. Equi-inclination Weissenberg photographs were taken by rotating the crystal about the b- and c-axes, using nickel-filtered Cu $K\alpha$ radiation. Intensity data were collected on a SYNTEX AD-1 densitometer controlled by a NOVA 1200 computer acting in cooperation with a DIABLO-31 disk drive. Structure factors of 1150 independent reflections were obtained through the usual data reduction procedure.

Positional parameters of the calcium ion were determined from sharpened Patterson maps and those of carbon and oxygen atoms were determined from the Fourier maps synthesized with phases of the calcium ion. Six cycles of block-diagonal least-squares refinement with the anisotropic thermal parameters gave an R-value of 0.14.

TABLE 1. ATOMIC PARAMETERS AND THEIR ESTIMATED STANDARD DEVIATIONS
The values have been multiplied by 10^4. Temperature factors are in the form
$T^{-1}=\exp(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Ca	2712(2)	498(4)	1357(3)	22(1)	85(5)	49(2)	5(3)	12(1)	−2(4)
C(1)	1694(10)	4143(18)	585(14)	36(7)	79(28)	79(16)	−17(12)	20(9)	−14(17)
C(2)	1534(10)	4109(18)	2040(14)	39(7)	83(29)	63(15)	5(12)	20(8)	16(16)
C(3)	491(10)	4456(24)	2091(15)	38(8)	168(35)	86(17)	13(16)	18(9)	42(23)
O(1a)	2000(7)	2811(13)	132(9)	62(7)	113(22)	54(10)	27(10)	26(7)	−12(12)
O(1b)	1547(77)	5607(14)	25(9)	55(6)	105(20)	61(10)	−3(11)	22(6)	7(13)
O(2)	1773(7)	2382(14)	2495(9)	52(6)	107(20)	68(11)	27(10)	35(7)	12(13)
O(3)	339(7)	4443(20)	3432(11)	36(6)	360(37)	85(12)	−5(13)	27(7)	−24(20)
C(4)	3897(9)	−830(19)	−886(12)	36(7)	98(29)	36(11)	−16(11)	12(7)	−6(15)
C(5)	4066(9)	−2417(20)	−10(13)	26(6)	103(27)	52(14)	16(12)	10(8)	−14(17)
C(6)	3804(9)	−4104(20)	−742(14)	26(6)	140(33)	64(15)	−3(12)	12(8)	−15(18)
O(4a)	3371(7)	342(13)	−603(9)	48(6)	93(19)	70(10)	19(9)	28(6)	7(13)
O(4b)	4317(7)	−839(14)	−1895(9)	44(6)	154(24)	59(10)	−20(10)	25(6)	−3(13)
O(5)	3549(6)	−2161(13)	1067(8)	36(5)	143(22)	37(9)	23(9)	15(5)	−3(12)
O(6)	2909(6)	−4006(13)	−1510(9)	28(5)	104(20)	70(10)	−12(8)	15(6)	2(11)
O(7)	1322(6)	−1110(13)	655(11)	29(5)	122(21)	111(13)	−12(8)	19(7)	−9(14)
O(8)	3987(7)	2286(14)	2103(11)	34(5)	99(21)	121(14)	5(9)	17(7)	−23(14)

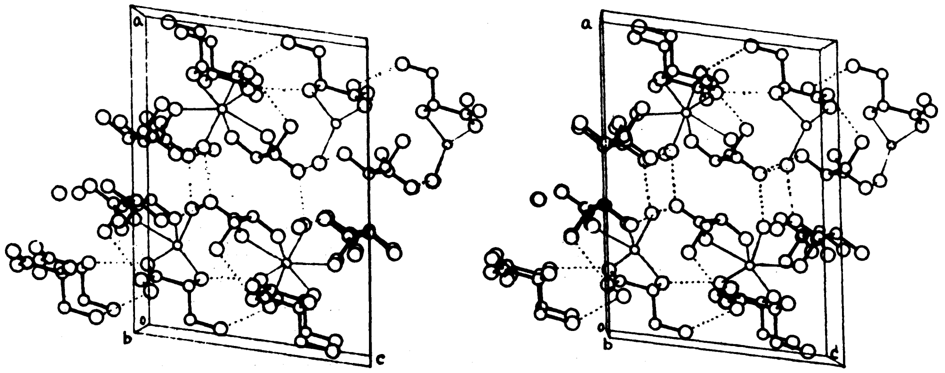

Fig. 1. Stereo-representation of the crystal structure of calcium DL-glycerate dihydrate. Ca, C, and O atoms are represented by the small, middle, and large circles, respectively. The hydrogen bonds and the Ca–O contacts are indicated by the dotted and full lines.

The hydrogen atom positions were assumed from the difference Fourier maps synthesized at this stage. After the Zachariazen extinction correction was applied for the reflection data, three more cycles of full-matrix least-squares refinement including the hydrogen atoms in the structure factor calculations reduced the R-value to 0.095. Atomic scattering factors were obtained from the International Tables for X-Ray Crystallography IV.[6] All computations for the structure analysis were undertaken by using a KPAX program system which included the UNICS programs on a FACOM M-190 in the Data Processing Center of Kyoto University.

The final atomic parameters and their estimated standard deviations are given in Table 1, and the observed and calculated structure factors at the final stage are listed in Table 2.[7]

Results and Discussion

Crystal Packing. Calcium-oxygen interactions and hydrogen bonds stabilize the crystal structure. Figure 1 shows the crystal packing and Table 3 lists the hydrogen-bond distances. All hydrogen atoms of hydroxyl groups and water molecules participate in the hydrogen bonds. The O atoms related to O(4b) and O(8) by 2_1 symmetry through 1/2, 0, 1/4, and 1/2, 0, 3/4 form an infinite hydrogen-bond chain along the b-axis. O(3), O(7), and their centrosymmetrically related O atoms form a square linkage of hydrogen-bonds about the $\bar{1}$ site, 0, 0, 0, and 0, 1/2, 1/2. Three glycerate anions and two water molecules are bound to a calcium ion, the two glycerate anions chelating the calcium ion with α-carboxy and α-hydroxy oxygens, and the one glycerate anion bonding to the calcium ion through the β-hydroxy oxygen. Figure 2 shows the environment of the calcium ion, which is surrounded by seven oxygens in a distorted pentagonal biprism arrangement, five glycerate oxygens being approximately coplanar (Table 4). The Ca–O distances range from 2.32 to 2.47 Å. The O–Ca–O angles within the pentagonal plane range from 65 to

Table 3. Hydrogen-bond distances

Donor Acceptor	Distance	Symmetry operation for acceptor O
O(2)···O(1a)	2.72 Å	$x, 1/2-y, 1/2+z$
O(3)···O(7)	2.74	$-x, 1/2+y, 1/2-z$
O(5)···O(4b)	2.71	$x, -1/2-y, 1/2+z$
O(6)···O(1b)	2.73	$x, -1+y, z$
O(7)···O(3)	2.82	$x, 1/2-y, -1/2+z$
O(7)···O(1b)	2.62	$x, -1+y, z$
O(8)···O(4b)	2.72	$1-x, -y, -z$
O(8)···O(4b)	2.92	$x, 1/2-y, 1/2+z$

Table 4. Least-squares plane of five oxygens around calcium ion and atomic deviations

The plane is defined by $Ax+By+Cz=D$ where x, y, and z are in Å along the axes a and b and the normal to the ab plane. An asterisk indicates an atom not used in the plane calculation.

$A=0.7703$, $B=0.5345$, $C=0.3471$, and $D=3.521$.

Atom	Deviation (Å)
Ca	−0.007
O(1a)	0.124
O(2)	−0.002
O(4a)	−0.217
O(5)	0.218
O(6′)	−0.117
O(7)*	2.355
O(8)*	−2.326

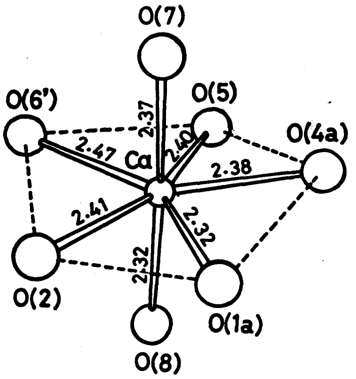

Fig. 2. The calcium ion coordination shell. Atom O(6′) is generated from O(6) by the symmetry operation $x, -1/2-y, 1/2+z$. The estimated standard deviation of a Ca–O distance is 0.02 Å.

80°, while the O–Ca–O angles out of the plane range from 85 to 99°. The O(7)–Ca–O(8) angle is 175°. The estimated standard deviations of the O–Ca–O angles are less than 1°.

Geometry of the Glycerate Anions. The conformations of the two crystallographically independent glycerate anions differ from each other (Fig. 3). The bond lengths and angles, and the torsion angles about the C–C bond for each conformer are given in Tables 5 and 6. The C(3)–O(3) bond is trans to C(1)–C(2) about the C(2)–C(3) bond in one conformer, while C(6)–O(6) is gauche to C(4)–C(5) about C(5)–C(6) in the second conformer. Similar conformational dimorphism has been observed in the crystals of potassium salts of gluconic acid[8] and of calcium and potassium salts of glucaric acid.[9,10] Although in these crystals each conformer is crystallized in different crystal forms, the two conformers in the present case are crystallized together into one crystal structure. The ^{1}H NMR studies of glyceric acid in an aqueous solution[1,2] showed that the two β-protons are asymmetric in an unprotonated carboxyl state and the glycerate anion has two or more different conformations in the solution. The two conformers observed here may be therefore energetically very close to each other. For both conformers, α-hydroxy oxygen lies approximately on the same plane of the carboxyl group; the atomic deviations from the least-squares plane of the carboxyl group are given in Table 7. The nonbonding distances between α-hydroxy oxygen and one of the carboxy oxygen are 2.55 Å for O(1a)···O(2) and 2.57 Å for O(4a)···O(5). The stability of such a planar α-hydroxy carboxyl arrangement was discussed by Newton and Jeffrey.[3]

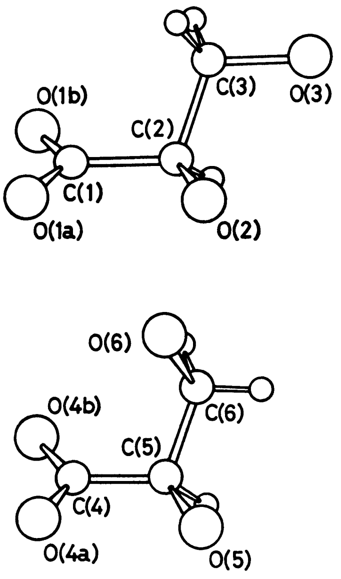

Fig. 3. Two conformations of glyceric anions. Both conformers are shown in the D-isomers.

TABLE 5. BOND LENGTHS AND ANGLES, AND THEIR ESTIMATED STANDARD DEVIATIONS

Bond length		Bond angle	
C(1)–C(2)	1.57(2) Å	C(1)–C(2)–C(3)	109(1)°
C(2)–C(3)	1.54(2)	O(1a)–C(1)–O(1b)	127(1)
C(1)–O(1a)	1.24(2)	O(1a)–C(1)–C(2)	118(1)
C(1)–O(1b)	1.27(2)	O(1b)–C(1)–C(2)	114(1)
C(2)–O(2)	1.43(2)	C(1)–C(2)–O(2)	106(1)
C(3)–O(3)	1.46(2)	C(3)–C(2)–O(2)	110(1)
		C(2)–C(3)–O(3)	109(1)
C(4)–C(5)	1.52(2)	C(4)–C(5)–C(6)	112(1)
C(5)–C(6)	1.52(2)	O(4a)–C(4)–O(4b)	125(1)
C(4)–O(4a)	1.25(2)	O(4a)–C(4)–C(5)	119(1)
C(4)–O(4b)	1.30(2)	O(4b)–C(4)–C(5)	109(1)
C(5)–O(5)	1.46(2)	C(4)–C(5)–O(5)	108(1)
C(6)–O(6)	1.41(2)	C(6)–C(5)–O(5)	113(1)
		C(5)–C(6)–O(6)	112(1)

TABLE 6. TORSION ANGLES ABOUT THE C–C BONDS

Bond	Angle
O(1a)–C(1)–C(2)–C(3)	−119.8°
O(1b)–C(1)–C(2)–C(3)	64.7
O(1a)–C(1)–C(2)–O(2)	−2.2
O(1b)–C(1)–C(2)–O(2)	−177.6
C(1)–C(2)–C(3)–O(3)	−179.5
O(2)–C(2)–C(3)–O(3)	65.4
O(4a)–C(4)–C(5)–C(6)	−122.8
O(4b)–C(4)–C(5)–C(6)	56.3
O(4a)–C(4)–C(5)–O(5)	1.4
O(4b)–C(4)–C(5)–O(5)	−179.4
C(4)–C(5)–C(6)–O(6)	48.2
O(5)–C(5)–C(6)–O(6)	−73.2

TABLE 7. LEAST-SQUARES PLANE OF FIVE ATOMS OF CARBOXYL AND α-HYDROXYL GROUPS, AND ATOMIC DEVIATIONS

The plane is defined by $Ax+By+Cz=D$ where x, y, and z are in Å along the axes a and b and the normal to the ab plane. An asterisk indicates an atom not used in the plane calculation.

$A=0.908$ $A=0.715$
$B=0.289$ $B=-0.462$
$C=0.302$ $C=0.525$
$D=1.045$ $D=7.229$

Atom	Deviation (Å)	Atom	Deviation (Å)
C(1)	0.026	C(4)	−0.003
C(2)	0.001	C(5)	0.009
C(3)*	1.280	C(6)*	1.185
O(1a)	−0.007	O(4a)	0.004
O(1b)	−0.014	O(4b)	−0.004
O(2)	−0.006	O(5)	−0.006
O(3)*	1.260	O(6)*	2.399
Ca*	−0.630	Ca*	0.511

The Polyhedron of Oxygen Atoms about a Calcium Ion. Oxygen-polyhedra about a cation in inorganic crystals can be generally classified into a limited number of typically regular forms, depending on a coordination number; for instance, cube, square antiprism, and dodecahedron are usual forms for eight-coordination, and pentagonal biprism, monocapped octahedron, and monocapped trigonal biprism for seven-coordination.[4] The square antiprism for eight-coordination is the most usual form observed to data in the calcium carbohydrate crystals.[10–32] The pentagonal biprism, as observed in the present crystal, has been found in the crystal structures of α-D-xylose $CaCl_2 \cdot 3H_2O$,[13] β-D-fructose $CaBr_2 \cdot 2H_2O$,[14] and α,α′-D-trehalose $CaBr_2 \cdot H_2O$;[15] all seven-coordinations about a calcium ion in the carbohydrate crystals are in this form. The pentagonal biprism may be therefore the most favored arrangement of oxygens about a calcium ion for the seven-coordination. This fact is evidenced by the Doyl-Britten calculations of repulsive potential energy between ligand atoms of simple seven-coordination models.[5] The Ca–O distance, averaged for those in 22 structures observed hitherto,[10–32] is 2.445 Å for Ca–O (carboxy oxygen), 2.488 Å for Ca–O (hydroxy oxygen), and 2.442 Å for Ca–O (water oxygen), the Ca–O (hydroxy oxygen) being slightly larger than the others. Thus, the partial charge and the dipole moment on the ligand oxygen apparently influence the Ca–O distance. The large distortion of the actual oxygen-polyhedron about a calcium ion may be due to such different Ca–O interactions which depend on the ligand oxygens, in addition to a steric restriction by covalent bonds bridged between two or more ligand oxygens and to the effect of crystal field, especially of the hydrogen-bonds which formed around the oxygen-polyhedron.

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References

1) T. Taga, Y. Kuroda, and M. Ohashi, *Bull. Chem. Soc. Jpn.*, in press.

2) D. T. Sawyer and J. R. Brannan, *Anal. Chem.*, **38**, 192 (1966).

3) M. D. Newton and G. A. Jeffery, *J. Am. Chem. Soc.*, **99**, 2413 (1977).

4) A. F. Wells, "Structural Inorganic Chemistry," Clarendon Press, Oxford (1975), pp. 60—70.

5) D. Britton, *Can. J. Chem.*, **41**, 1632 (1963).

6) "International Table for X-Ray Crystallography IV," Kynoch Press, Birmingham (1974), p. 71.

7) Table 2 is kept in the office of the Chemical Soiety of Japan, 1-5 Kanda-Surugadai, Chiyoda-ku, Tokyo 101, (Document No. 7817).

8) N. C. Panagiotopolous, G. A. Jeffrey, S. J. La Palaca, and W. C. Hamilton, *Acta Crystallogr., Sect. B*, **30**, 1421 (1974).

9) T. Taga, Y. Kuroda, and K. Osaki, *Bull. Chem. Soc. Jpn.*, **50**, 3083 (1977).

10) T. Taga and K. Osaki, *Bull. Chem. Soc. Jpn.*, **49**, 1517 (1976).

11) S. Furberg and S. Helland, *Acta Chem. Scand.*, **16**, 2373 (1962).

12) W. J. Cook and C. E. Bugg, *Acta Crystallogr., Sect. B*, **29**, 215 (1973).

13) G. F. Richards, *Carbohydr. Res.*, **26**, 448 (1073).

14) W. J. Cook and C. E. Bugg, *Acta Crystallogr., Sect. B*, **32**, 656 (1976).

15) W. J. Cook and C. E. Bugg, *Carbohydr. Res.*, **31**, 265 (1973).

16) I. Nitta and K. Osaki, *X-Ray*, **5**, 37 (1948).

17) C. Sterling, *Acta Crystallogr.*, **18**, 917 (1965).

18) M. P. Gupta, S. M. Prasad, R. G. Sahu, and B. N. Sahu, *Acta Crystallogr., Sect. B*, **28**, 135 (1972).

19) C. I. Branden and B. O. Soderberg, *Acta Chem. Scand.*, **20**, 730 (1966).

20) G. K. Ambady, *Acta Crystallogr., Sect. B*, **24**, 1548 (1968).

21) V. A. Uchtman and R. P. Oerter, *J. Am. Chem. Soc.*, **95**, 1802 (1973).

22) B. Sheldrick, *Acta Crystallogr., Sect. B*, **30**, 2056 (1974).

23) R. Norrestam, P. E. Werner, and M. V. Glehn, *Acta Chem. Scand.*, **22**, 1395 (1968).

24) A. A. Balchin and C. E. Carlisle, *Acta Crystallogr.*, **19**, 103 (1965).

25) J. P. Glusker, J. A. Minkin, and C. A. Casciato, *Acta Crydtallogr., Sect. B*, **27**, 1284 (1971).

26) S. E. B. Gould, R. O. Gould, C. A. Rees, and W. E. Scott, *J. Chem. Soc., Perkin Trans. 2*, 237 (1975).

27) S. Thanomkul, J. A. Hjortas, and H. Sorum, *Acta Crystallogr., Sect. B*, **32**, 920 (1976).

28) W. J. Cook and C. E. Bugg, *Acta Crystallogr., Sect. B*, **29**, 2404 (1973).

29) D. C. Craig, N. C. Stephenson, and J. D. Stevens, *Carbohydr. Res.*, **22**, 494 (1972).

30) C. E. Bugg, *J. Am. Chem. Soc.*, **95**, 908 (1973).

31) W. J. Cook and C. E. Bugg, *Acta Crystallogr., Sect. B*, **32**, 656 (1976).

32) D. C. Craig, N. C. Stephenson, and J. D. Stevens, *Cryst. Struct. Commun.*, **3**, 195 (1974).