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The crystal structure of lithium L-ascorbate dihydrate

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ABSTRACT

The crystal structure of lithium L-ascorbate dihydrate is triclinic, $P1$; with a = 5.964(9), b = 5.299(9), c = 7.760(15) Å; α = 100.82(9), β = 109.78(9), γ = 92.02(9)°. The planar fragment of the ascorbate anion is a part of the five-membered ring [C-1,C-2,C-3(O-3),C-4], and O-4 deviates by 0.053(2) Å from this plane. Deprotonated O-3 is an acceptor of three hydrogen bonds, but does not interact with Li^+. The coordination number of the Li^+ is 5 and it is bonded to two water molecules and three hydroxyl oxygen atoms of two ascorbate anions: O-2 and the *gauche* O-5,6 of the side chain.

INTRODUCTION

L-Ascorbic acid (vitamin C) forms salts with Na^+, Ca^{2+}, and Tl^+, which are fairly stable in the solid state. The transport of vitamin C in humans is sodium dependent[1]. Ascorbic acid is not stable in aqueous solution, and heavy metal cations, as well as K^+ and Mg^{2+}, accelerate its oxidation. Thus, of the metal cations, Na^+, K^+, Mg^{2+}, and Ca^{2+}, important in biological processes[2], K^+ and Mg^{2+}, which are present in larger proportions inside the cell, catalyse the oxidation of ascorbic acid and therefore do not form stable salts, whereas Na^+ and Ca^{2+} give relatively stable salts.

The molecular and crystal structures of L-ascorbic acid[3], sodium ascorbate[4], calcium ascorbate dihydrate[5], and thallium ascorbate[6] have been determined by X-ray analysis. In each of these salts, the ascorbate is monodeprotonated at HO-3, but the interactions with the cations differ significantly. It has been suggested that Mg^{2+} and Li^+ compete for biologically important ligands[2].

The preparation of lithium L-ascorbate dihydrate and its crystal structure are now reported.

EXPERIMENTAL

Preparation. — Lithium carbonate (109 mg, 1.48 mmol) was added to 0.74M L-ascorbic acid (4 mL, 2.96 mmol), and the mixture was stirred at room temperature until the evolution of CO_2 ceased. To this solution (pH 5.6) was added 2-propanol

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dropwise to saturation, and then crystallisation at 2° gave lithium ascorbate dihydrate, m.p. 112° (dec.).

Crystal data. — $C_6H_7O_6^{-}Li^{+}\cdot 2H_2O$, $M_w = 218.09$, triclinic system, space group $P1$, unit-cell parameters: $a = 5.964(9)$, $b = 5.299(9)$, $c = 7.760(15)$ Å; $\alpha = 100.82(9)$, $\beta = 109.78(9)$, $\gamma = 92.02(9)°$; $V = 225.4(7)$ Å^3; $Z = 1$, $D_x = 1.607$ g.cm^{-3}, $D_m = 1.599$ g.cm^{-3} (flotation in bromobenzene–dibromoethane), Mo-K_α radiation ($\lambda = 0.71069$ Å), $\mu = 1.41$ cm^{-1}.

Diffraction data. — A crystal, 0.06 × 0.2 × 0.6 mm, was sealed in a capillary and used for intensity measurements on a Syntex P2$_1$ diffractometer with Mo-K_α radiation. Unit-cell parameters were determined by a least-squares method from 15 reflections centered on the diffractometer. The $\theta/2\theta$ scan technique with variable scan speed was used. Two standard reflections showed no variation of intensity. Of 2180 reflections measured in the 2θ range 4–60° and index range, h $-8 \rightarrow 7$, k $-7 \rightarrow 7$, l $-10 \rightarrow 10$, 1619 were unique and Friedel pairs were not merged.

Solution of the structure and refinement. — Positions of the C and O atoms were found by direct methods (program SHELXS86[7]) and the remaining atoms were located in a difference Fourier map. Positional and anisotropic thermal parameters of non-H atoms were refined. Initially, the riding model was applied to the H-atom coordinates (with bond length constraints: C–H 1.08 and O–H 0.97 Å); then, in the final calculations, those coordinates were kept fixed, whereas individual isotropic thermal factors of the H atoms were refined. The full-matrix least-squares refinement of 145 parameters, including isotropic extinction parameters, converged at $R = 0.040$ and $R_w = 0.0382$ for 1565 observed reflections [$F_o \geq 4\sigma(F_o)$]. The function minimised was $\Sigma w(|F_o| - |F_c|)^2$, where $w = \sigma^{-2}(F_o)$. The extinction parameter, x, was refined to $6.3(4) \times 10^{-6}$ where $F_{corr} = F(1 - x F^2/\sin\theta)$. The final residual electron density was $-0.34 < \Delta\rho < 0.30$ eÅ^{-3}. Calculations were carried out using the SHELX76 system[8]. Scattering factors were taken from International Tables for X-ray Crystallography[9].

RESULTS AND DISCUSSION

The final atomic parameters for lithium L-ascorbate dihydrate are listed in Table I*. The conformation and atomic numbering of the anion are shown in Fig. 1. The molecular dimensions, *i.e.* anion and cation–anion bond lengths and angles, and the principal torsion angles of the ascorbate anion, are given in Table II. The lithium coordination mode is illustrated in Fig. 2 and the hydrogen-bond geometry is described in Table III.

Ascorbate anion. — The ascorbate anion is monovalent with HO-3 deprotonated. The bond lengths indicate that the negative charge is distributed over the fragment O-1 = C-1–C-2 = C-3–O-3. Similar effects have been found in other metal[3–6] salts and the

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* Lists of structure factors, anisotropic thermal parameters, and least-squares plane calculations are deposited with, and can be obtained from Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/491/*Carbohydr. Res.*, 226 (1992) 43–48.

TABLE I

Atomic coordinates (× 10^4 for non-H atoms and × 10^3 for H-atoms) and isotropic temperature factors (Å^2) for lithium ascorbate dihydrate

Atom	x/a	y/b	z/c	$U^a_{eq/iso}$
Li	3567(10)	5513(11)	5292(8)	0.031(1)*
O-1	3060(0)	5000(0)	325(0)	0.036(1)*
O-2	3869(6)	2264(6)	3454(4)	0.029(1)*
O-3	7731(6)	−1165(7)	3000(4)	0.033(1)*
O-4	5995(6)	2925(6)	−261(4)	0.031(1)*
O-5	4491(5)	−2291(6)	−2022(4)	0.030(1)*
O-6	7151(5)	−2957(6)	−4195(4)	0.031(1)*
C-1	4505(7)	3448(7)	740(5)	0.027(1)*
C-2	5001(7)	1986(7)	2157(5)	0.026(1)*
C-3	6736(7)	431(7)	2036(5)	0.024(1)*
C-4	7434(7)	940(7)	408(5)	0.026(1)*
C-5	6971(7)	−1379(7)	−1167(5)	0.024(1)*
C-6	7791(7)	−732(7)	−2696(5)	0.029(1)*
O-1W	868(7)	3712(7)	5707(5)	0.044(1)*
O-2W	2045(5)	7551(6)	3322(4)	0.030(1)*
H-20	334	61	363	0.05(1)
H-50	412	−321	−117	0.04(1)
H-60	717	−250	−534	0.04(1)
H-4	932	163	86	0.03(1)
H-5	788	−295	−63	0.02(1)
H-61	683	89	−306	0.09(2)
H-62	966	0	−227	0.03(1)
H-1W1	−24	425	602	0.11(2)
H-1W2	34	197	498	0.09(2)
H-2W1	41	798	300	0.05(1)
H-2W2	223	643	225	0.07(1)

^{a*}, $U_{eq} = 1/3\,[U_{11}(a^*a)^2 + U_{22}(b^*b)^2 + U_{33}(c^*c)^2 + 2(U_{12}\,a^*b^*ab\cos\gamma + U_{13}\,a^*c^*ac\cos\beta + U_{23}\,b^*c^*bc\cos\alpha)]$.

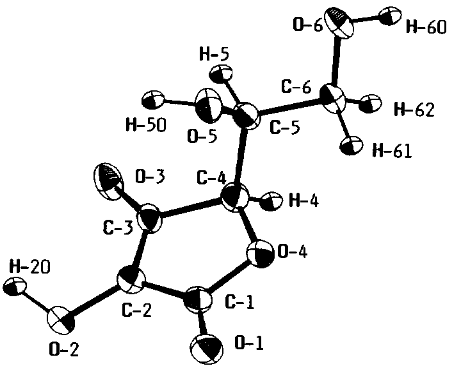

Fig. 1. Perspective view of the ascorbate anion with atomic numbering.

TABLE II

Molecular geometry of lithium ascorbate dihydrate

Bond lengths (Å)			
O-1–C-1	1.218(4)	Li...O-2	2.074(5)
O-2–C-2	1.379(3)	Li...O-1W	1.991(6)
O-3–C-3	1.265(4)	Li...O-2W	2.019(6)
O-4–C-1	1.369(3)	Li...O-5*	2.067(5)
O-4–C-4	1.442(4)	Li...O-6*	2.137(6)
O-5–C-5	1.423(4)		
O-6–C-6	1.429(4)		
C-1–C-2	1.418(4)		
C-2–C-3	1.362(4)	*Symmetry code:*	
C-3–C-4	1.522(4)	(*) $x, y-1, z-1$	
C-4–C-5	1.504(4)		
C-5–C-6	1.516(4)		
Valence angles (°)			
C-1–O-4–C-4	108.8(3)	0.5*...Li...O-2	150.4(3)
O-1–C-1–O-4	118.8(3)	O-6*...Li...O-2	91.3(2)
O-1–C-1–C-2	131.4(4)	O-6*...Li...O-5*	78.7(2)
O-4–C-1–C-2	109.8(3)	O-1W...Li...O-2	92.0(2)
O-2–C-2–C-1	122.1(4)	O-1W...Li...O-5*	88.1(2)
O-2–C-2–C-3	127.9(4)	O-1W...Li...O-6*	158.7(3)
C-1–C-2–C-3	110.0(4)	O-2W...Li...O-2	96.2(2)
O-3–C-3–C-2	131.8(4)	O-2W...Li...O-5*	112.2(3)
O-3–C-3–C-4	121.6(4)	O-2W...Li...O-6*	94.6(2)
C-2–C-3–C-4	106.6(3)	O-2W...Li...O-1W	105.9(3)
O-4–C-4–C-3	104.7(3)		
O-4–C-4–C-5	109.6(3)		
C-3–C-4–C-5	114.3(3)		
O-5–C-5–C-4	112.1(3)		
O-5–C-5–C-6	106.8(3)		
C-4–C-5–C-6	110.9(3)		
O-6–C-6–C-5	107.9(3)		
Torsion angles (°)			
Exocyclic		*Endocyclic*	
O-1–C-1–O-4–C-4	−176.7(3)	C-1–O-4–C-4–C-3	−3.4(4)
O-1–C-1–C-2–O-2	−3.8(7)	O-4–C-1–C-2–C-3	−2.6(5)
O-2–C-2–C-1–O-4	175.7(3)	O-4–C-4–C-3–C-2	1.8(4)
O-2–C-2–C-3–O-3	1.5(8)	C-1–C-2–C-3–C-4	0.4(4)
O-3–C-3–C-2–C-1	179.6(4)	C-2–C-1–O-4–C-4	3.7(4)
O-3–C-3–C-4–O-4	−177.5(4)		
O-3–C-3–C-4–C-5	62.5(5)		
O-4–C-4–C-5–O-5	−54.6(4)		
O-4–C-4–C-5–C-6	64.7(4)		
C-3–C-4–C-5–C-6	−178.1(3)		
C-3–C-4–C-5–O-5	62.6(4)		
O-5–C-5–C-6–O-6	−53.6(4)		
O-6–C-6–C-5–C-4	−176.1(3)		

TABLE III

Hydrogen bonds

Donor-H······Acceptor	D-H(Å)	H··A(Å)	D··A(Å)	D-H··A(°)
O-2–H-2O ·· O-2W (*x*, −1+*y*,*z*)	0.97	1.71	2.659(3)	165
O-5–H-5O ·· O-1 (*x*, −1+*y*,*z*)	0.97	1.87	2.838(3)	174
O-6–H-6O ·· O-3 (*x*,*y*, −1+*z*)	0.97	1.70	2.650(3)	166
O-1W–H-1W1 ·· O-6 (−1+*x*, 1+*y*, 1+*z*)	0.82	2.17	2.894(3)	147
O-1W–H-1W2 ·· O-3 (−1+*x*,*y*,*z*)	0.97	2.19	3.091(3)	155
O-2W–H-2W1 ·· O-3 (−1+*x*, 1+*y*, *z*)	0.97	1.68	2.626(3)	166
O-2W–H-2W2 ·· O-1 (*x*,*y*,*z*)	0.97	1.78	2.726(3)	166

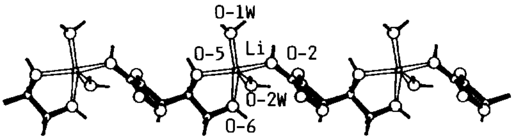

Fig. 2. The Li$^+$ cation coordination sphere.

TABLE IV

Torsion angles (°) of the five-membered ring in the ascorbic acid molecule and the ascorbate anion

Compound	*Torsion angle*					
	C1C2C3C4	*C2C3C4O4*	*C3C4O4C1*	*C4O4C1C2*	*O4C1C2C3*	*Ref.*
Ascorbic acid						3
molecule A	−1.3	0.8	0.1	−0.9	1.4	
molecule B	−2.4	4.8	−5.4	4.3	−1.2	
Serine/ascorbic acid	2.3	−4.3	4.6	−3.4	0.6	10
Na ascorbate	−9.3	11.5	−9.0	3.5	4.1	4
Ca ascorbate						5
anion A	−5.8	7.6	−6.7	3.5	1.6	
anion B	2.4	−5.7	6.9	−5.8	2.0	
Tl ascorbate						6
anion A	−0.2	0.8	−1.1	1.1	−0.7	
anion B	5.9	−2.7	−1.1	4.5	−7.1	
Arginine ascorbate	−6.9	7.5	−5.3	1.3	3.8	11
Li ascorbate	0.4	1.8	−3.4	3.7	−2.6	

L-arginine complex[11] with ascorbic acid. The planar part of the five-membered ring is the C-1,C-2,C-3(O-3),C-4 fragment and O-4 deviates from this plane by 0.053(2) Å.

The enofuranose ring and the ethanediol side chain are flexible and distortions depend on the environment in the crystal. Deviations of the enofuranose ring from planarity are small but significant. The comparison of dihedral angles (Table IV) indicates that the ascorbate anion in the present structure adopts one of the less-distorted ring conformations.

It seems that the − *gauche* conformation about the C-5–C-6 single bond in the side chain is one of the preferred orientations of the two neighboring hydroxyl groups of the ascorbate residue. This conformation occurs in crystal structures of Na^+ (ref. 4), Tl^+ (anion A) (ref. 6), L-arginine[11], and Li^+ ascorbates, and also in L-serine/L-ascorbic acid co-crystals[10]. The *trans* conformation was observed for the ascorbic acid[3] and the anion B of the Tl^+ salt[6], while the + *gauche* conformation was found only in Ca^{2+} salt[5].

Cation–anion interactions. — The analysis of crystal structures of sodium[4], calcium dihydrate[5], thallium[6], and lithium dihydrate salts of ascorbic acid clearly indicates that the metal-cation coordination ability changes both coordination numbers and sites: Na^+ 6 and O-1,2,3,5,6; Ca^{2+} 8 with O-5,6 for anion A and O-1,3,5,6 for anion B; Tl^+ 3 and 4 with O-1,3 for anion A and O-2,3 for anion B.

The lithium coordination number is 5, and the Li^+ bonds to two water molecules and three hydroxyl oxygen atoms of two ascorbate anions, namely, O-2 and − *gauche* oriented O-5,6 of the side chain. Whereas O-3 is an acceptor of three hydrogen bonds, there are no direct interactions with Li^+. The coordination polyhedron about Li^+ is a distorted tetragonal pyramid. The Li^+–O distances are in agreement with values found for other salts with the penta-coordinated Li^+; *e.g.*, values observed in crystals of the Li^+ salts of hydrogen oxalate monohydrate[12], glycolate[13], hydrogen malate[14], hydrogen oxydiacetate[15], ammonium tartrate monohydrate[16], and formate monohydrate[17] were in the range 1.926(2)–2.357(3) Å.

Hydrogen bonding. — The anion (except O-4) and water oxygen atoms are hydrogen-bond donors and/or acceptors (Table III). The interionic Li^+–ascorbate anion bonds form chains (Fig. 2) which are hydrogen bonded to give a three-dimensional network in the crystal structure.

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