MONDAL, P. (1973). Ph.D. Thesis, London Univ.

MOORE, A. E. (1966). *Mag. Concr. Res.* **18** (55), 59–64.

MURAKAMI, K., TANAKA, H. & NAKURA, Y. (1968). *Chem. Ind.* pp. 1769–1770.

NURSE, R. W., WELCH, J. H. & MAJUMDAR, A. J. (1965). *Trans. Brit. Ceram. Soc.* **64**, 409–418.

ORDWAY, F. (1952). *Proc.* III*rd Int. Symp. Chem. Cem.* pp. 91–111. London: Cement & Concrete Association.

PONOMAREV, V. I., KHEIKER, D. M. & BELOV, N. V. (1971). *Sov. Phys. Crystallogr.* **15**, 995–998.

REGOURD, M., CHROMY, S., HJORTH, L., MORTUREUX, B. & GUINIER, A. (1973). *Rev. Mat. Constr.* No. 682, 7–14.

STEELE, F. A. & DAVEY, W. P. (1929). *J. Amer. Chem. Soc.* **51**, 2283–2293.

WHITAKER, A. (1965). Ph.D. Thesis, London Univ.

WIEBENGA, E. H. & SMITS, D. W. (1950). *Acta Cryst.* **3**, 265–267.

The Structure of an Ascorbate Precursor: 2-Keto-L-gulonic Acid Monohydrate

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The crystal structure of 2-keto-L-gulonic acid monohydrate $C_6H_{10}O_7.H_2O$ has been determined by X-ray diffraction with an automatic diffractometer and Mo $K\alpha$ radiation. The space group is $P2_12_12_1$ with $a = 16.469$ (2), $b = 7.853$ (1), $c = 6.808$ (1) Å. The parameters were refined to $R = 0.044$ and R(weighted) = 0.028 for 1393 reflexions. The average standard deviations are 0.0026 Å and 0.2° for non-hydrogen atoms. The molecular and crystal structure resembles that of α-sorbose, although the hydrogen-bond system is different. The α-anomeric $C(2)$–$O(2)H$ bond length is 1.381 Å, and the combined effect of this and the adjacent COOH group gives rise to a difference of 0.022 Å in the C–O bonds of the pyranoid ring. The carboxyl group is almost coplanar with the anomeric hydroxyl substituent. All the oxygen atoms participate in hydrogen bonding, and the water molecule connects four different sugar molecules, both within and between the helical chains. The relationships to the bonding properties of L-ascorbic acid are discussed.

Introduction

The production of L-ascorbic acid (vitamin C) starting with D-glucose has L-sorbose (I) and 2-keto-L-gulonic acid (II/III) as the most important intermediates. The latter compound is readily converted to L-ascorbic acid by means of acids, but in alkaline media the process is rather slow and unwilling. Formulation of the structure as an open chain (II) comprising a free carbonyl group has been questioned by Reichstein (1936) who instead proposed a structure involving a pyranoid lactol ring (III) which would explain the stability towards alkali.

CH₂OH ... (molecular structure diagrams I, II, III)
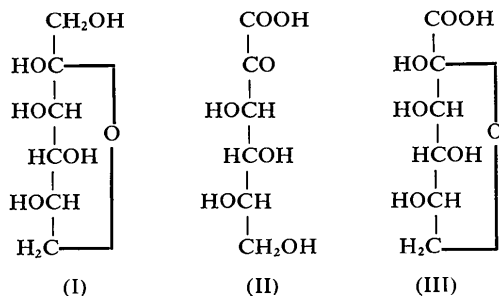
The conversion of 2-keto-L-gulonic acid to L-ascorbic acid proceeds according to Euler & Eistert (1957) by the opening of the pyranoid ring, formation of an oxonium cation, enolization and lactonization. A corresponding process is presumably also taking place *in vivo* during the formation of vitamin C. L-Ascorbic acid may thus be described as the γ-lactone of the enediolic form of (II).

Our investigation was undertaken to establish the molecular structure and conformation of this acid and to compare the results with the values found by Kim & Rosenstein (1967) for the α-anomer of L-sorbose, and also to study its relationship to L-ascorbic acid.

Experimental

Commercially available 2-keto-L-gulonic acid monohydrate, $C_6H_{10}O_7.H_2O$ (Merck), was recrystallized from water, giving a m.p. of 162°C. A transparent, colourless prismatic specimen with the dimensions $0.17 \times 0.06 \times 0.028$ cm was used for the collection of X-ray data. The space group was identified as $P2_12_12_1$ from systematic absences on Weissenberg photographs. The crystal was mounted on an automatic Picker four-angle diffractometer with the c axis slightly inclined to the φ axis of the goniometer. The diffractometer was operated in the usual ω–2θ mode, with Mo $K\alpha$ radiation ($\lambda = 0.7107$ Å). By restricting $2\theta_{max}$ to 70°, 2159 reflexions were considered, but only 1393 were clearly above the background. The stability of

the crystal was checked by means of three reference reflexions, but no sign of disintegration was observed. The scan speed was $\frac{1}{2}°$ min^{-1}, and the background counts lasted for 30 s on each side of the Bragg peak.

The conversion of the observed intensities to structure factors was performed by programs devised for the CDC 3300 computer by Dahl, Gram, Groth, Klewe & Rømming (1972), whereas the subsequent analyses and refinements were performed by programs adapted for CYBER 74 by P. Groth (1973) and by E. Bye at our department.

The effects of absorption and anomalous scattering for this compound are very small, and were neglected in our calculations.

Crystal data

$C_6H_{10}O_7.H_2O$, $a=16·469$ (2), $b=7·853$ (1), $c=6·808$ (1) Å; $M=212·16$; $V=880·49$ (1) Å^3. Space group $P2_12_12_1$, $Z=4$, $d_{obs}=1·60$, $d_{calc}=1·600$ g cm^{-3}.

Structure determination

This structural problem provides an example of straightforward solution by means of direct methods. The computer program *MULTAN* (Germain, Main & Woolfson, 1971) yielded a sufficient number of phases to identify all the 14 'heavy' atoms of the molecules in the asymmetric unit. Subsequent Fourier refinement established the identity of the individual atoms and the conformation of the six-membered ring system. The conventional residual R was at this stage 0·18, but was improved to 0·11 by the use of least-squares refinement. Only a limited number of reflexions were included, and we initially used isotropic temperature parameters. Inclusion of anisotropic thermal parameters and 1393 structure factors did not readily improve the residual below 0·09. The contribution from the hydrogen atoms was thus believed to be significant. Once they were localized from difference Fourier maps, full-matrix least-squares refinement including all atoms was performed. We used isotropic thermal

parameters for the hydrogen atoms, and the refinement was terminated when the residuals had reached $R=0·044$ and R(weighted)$=0·028$. There was no residual electron density above 0·4 e Å^{-3}.

The atomic form factors for carbon and oxygen were from Hanson, Herman, Lea & Skillman (1964) and for hydrogen from Stewart, Davidson & Simpson (1965). Fractional atomic coordinates and their thermal parameters are given in Tables 1 and 2, respectively and the observed and calculated structure factors in Table 3.

Table 1. *Fractional coordinates for the atoms in 2-keto-L-gulonic acid monohydrate*

Standard deviations are in parentheses. The values are multiplied by 10^4 for the heavy atoms and by 10^3 for the hydrogen atoms. W indicates water atoms. Hydrogen atoms are identified by the atoms to which they are attached.

	x	y	z
O(1A)	3099 (1)	−2183 (2)	5444 (3)
O(1B)	3895 (1)	−1661 (3)	2878 (2)
O(2)	4728 (1)	0757 (2)	4884 (2)
O(3)	3279 (1)	2200 (2)	4318 (2)
O(4)	2958 (1)	3681 (2)	8136 (2)
O(5)	4249 (1)	2942 (2)	10937 (2)
O(6)	4278 (1)	−0761 (2)	7618 (2)
OW	1682 (1)	3250 (2)	4529 (3)
C(1)	3687 (1)	−1389 (3)	4533 (3)
C(2)	4066 (1)	0026 (3)	5798 (3)
C(3)	3420 (1)	1398 (3)	6149 (3)
C(4)	3664 (1)	2652 (3)	7749 (3)
C(5)	3942 (1)	1715 (3)	9580 (3)
C(6)	4593 (1)	0444 (3)	9038 (3)
O(1A)H	283 (1)	−272 (3)	472 (4)
O(2)H	500 (1)	−002 (3)	456 (4)
O(3)H	285 (1)	248 (4)	435 (4)
O(4)H	309 (1)	455 (3)	856 (4)
O(5)H	412 (1)	266 (3)	1201 (3)
C(3)H	294 (1)	082 (3)	656 (3)
C(4)H	409 (1)	343 (2)	726 (3)
C(5)H	347 (1)	114 (3)	1013 (3)
C(6)H$_e$	474 (1)	−024 (3)	1016 (3)
C(6)H$_a$	508 (1)	109 (2)	848 (3)
OWH$_1$	140 (2)	258 (4)	386 (4)
OWH$_2$	151 (2)	308 (4)	556 (4)

Table 2. *Thermal parameters for the atoms in 2-keto-L-gulonic acid monohydrate*

Standard deviations are in parentheses. Temperature factors are in the form $T=\exp(-B_{11}h^2-B_{22}k^2-B_{33}l^2-B_{12}hk-B_{13}hl-B_{23}kl)$, and the values are multiplied by 10^5. For the hydrogen atoms the isotropic B values are given.

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
O(1A)	00329 (7)	01395 (33)	01276 (40)	−00615 (26)	−00016 (30)	−00508 (65)
O(1B)	00348 (7)	02244 (42)	01357 (42)	−00618 (30)	00291 (29)	−01550 (76)
O(2)	00177 (6)	01047 (28)	01392 (39)	00003 (23)	00217 (25)	−00085 (62)
O(3)	00267 (7)	01687 (35)	01089 (39)	00554 (28)	−00086 (30)	00377 (62)
O(4)	00223 (6)	00682 (25)	01532 (40)	−00037 (21)	00105 (26)	−00407 (61)
O(5)	00360 (7)	01133 (30)	00866 (37)	−00413 (25)	−00006 (29)	−00359 (59)
O(6)	00207 (5)	00841 (23)	00971 (33)	−00036 (21)	−00158 (23)	00026 (52)
OW	00280 (7)	01018 (29)	01087 (40)	−00201 (24)	−00003 (30)	00207 (63)
C(1)	00180 (8)	00887 (35)	01154 (49)	00112 (28)	−00178 (35)	−00114 (82)
C(2)	00163 (7)	00815 (33)	00862 (44)	00014 (27)	00015 (32)	00018 (70)
C(3)	00153 (7)	00899 (35)	00805 (44)	00017 (29)	00008 (29)	−00022 (71)
C(4)	00162 (7)	00731 (32)	00957 (46)	−00063 (26)	00107 (33)	00019 (71)
C(5)	00193 (8)	00870 (36)	00928 (45)	−00215 (28)	00037 (33)	00076 (75)
C(6)	00191 (9)	01025 (41)	00988 (49)	−00043 (31)	−00227 (35)	−00006 (79)

Table 2 (cont.)

	B_{iso}		B_{iso}
O(1A)H	2·5 (0·6)	C(4)H	0·5 (0·4)
O(2)H	2·0 (0·6)	C(5)H	1·5 (0·4)
O(3)H	2·8 (0·7)	C(6)H$_e$	1·9 (0·5)
O(4)H	2·1 (0·6)	C(6)H$_a$	1·1 (0·4)
O(5)H	1·8 (0·5)	OWH1	5·0 (0·8)
C(3)H	0·6 (0·4)	OWH2	3·1 (0·7)

Discussion

Molecular geometry

A view of the structure is shown in Fig. 1. The positive direction of the c axis is above the paper, constituting a left-handed system where the choice of axes conforms to the absolute configuration of 2-keto-L-gulonic acid. The molecule is the α-anomer with a chair-form pyranose ring and the substituents have the conformation 2a3e4e5e as shown in Fig. 2. The numbering of the atoms is in accordance with that in L-sorbose and L-ascorbic acid.

The C–C bond lengths range from 1·511 to 1·539 Å with a mean of 1·525 Å and average standard deviation $\bar{\sigma} = 0\cdot0027$ Å. We have noted that the bonds at the anomeric carbon atom C(2) are longer than the rest by up to 10$\bar{\sigma}$.

The C–O bonds excluding the carboxyl group range from 1·381 to 1·449 Å with $\bar{\sigma} = 0\cdot0024$ Å which indicates significant deviations from the mean of 1·423 Å. In this case the anomeric carbon atom not only provides a particularly short axial bond (1·381 Å), but also a difference in the C–O bonds in the ring (1·449 *versus* 1·427 Å). This is contrary to the empirical rule (Robertson & Sheldrik, 1965; Chu & Jeffrey, 1967; Kim & Jeffrey, 1967) that such a difference only occurs if the hydrogen atom at the anomeric C–OH group is substituted. The discordance may be explained by the presence of the carboxyl group at C(2). Support for this view is found in the bonding distances of sialic acid (Flippen, 1973) although the magnitude of σ precluded significance in that case.

Whereas the internal carbon valences are close to tetrahedral with a mean of 110·5° ($\bar{\sigma} = 0\cdot2°$), the external C–C–O angles vary from 106·3° to 112·7° which are significantly different from the mean of 109·7°. The equatorially bonded OH substituents are all distorted in the same sense with respect to an ideal tetrahedral arrangement as may be inferred from Fig. 2.

The average value of the conformational angles within the ring (56·3°) is smaller than that for the substituents (64·1°) as shown in Table 4. It seems

Table 3. Observed and calculated structure factors

The first entry is h, the second is $10F_{obs}$ and the third is $10F_{calc}$. The F_{obs} are corrected for absorption.

reasonable to interpret this effect as due the relatively larger repulsive effect from the OH substituents.

Table 4. *Selected conformation angles in 2-keto-L-gulonic acid*

The pyranoid ring		The substituents	
O(6)–C(2)–C(3)–C(4)	−52·0°	C(1)–C(2)–C(3)–O(3)	+68·8°
C(2)–C(3)–C(4)–C(5)	+49·9	O(2)–C(2)–C(3)–O(3)	−52·8
C(3)–C(4)–C(5)–C(6)	−52·9	O(3)–C(3)–C(4)–O(4)	−68·2
C(4)–C(5)–C(6)–O(6)	+59·3	O(4)–C(4)–C(5)–O(5)	+68·5
C(5)–C(6)–O(6)–C(2)	−64·2	C(6)–O(6)–C(2)–O(2)	−62·2
C(6)–O(6)–C(2)–C(3)	+59·3	C(6)–O(6)–C(2)–C(1)	+175·9

Conformational angle A(1)–A(2)–A(3)–A(4) is viewed down the A(2)–A(3) bond with a clockwise angle of A(1) to A(4) taken to be positive.

Most of our results agree well with those observed in α-sorbose, except, perhaps for the C(4)–O(4)H bond which is relatively long (1·440 Å) in 2-keto-L-gulonic acid. In the latter, however, two strong hydrogen bonds are observed at O(4) (2·624 and 2·657 Å).

The carboxyl group is almost coplanar with C(2)–O(2) and with C=O *cis* to that group, as indicated by the torsional angle O(1)C(1)C(2)O(2) which is only 7·9°.

Thermal analysis

The thermal motion of these molecules is moderate, with slightly larger amplitudes for the external oxygen atoms than for the ring atoms. Rigid-body analyses (Schomaker & Trueblood, 1968) proved that only the pyranoid ring could be correlated satisfactorily with a rigid-body model. The corrections to bond lengths and angles were all within their standard deviations, and are not included in our presentation.

Relation to L-ascorbic acid

The acid-catalysed conversion to L-ascorbic acid has as the net result the breaking of the C(2)–O(6) bond, elimination of water between O(1)H of the carboxyl group and the O(4)H substituent and establishment of the C(2)=C(3) double bond.
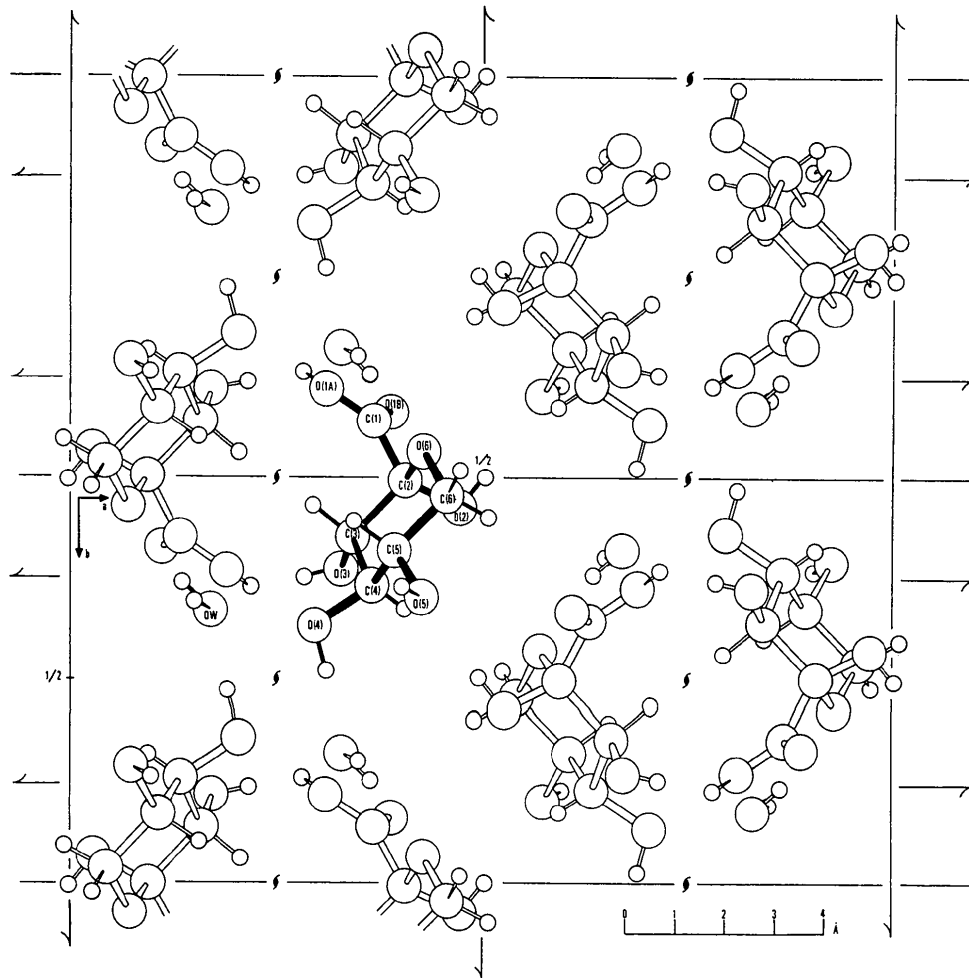

Fig. 1. View of the structure of 2-keto-L-gulonic acid hydrate along [001]. The reference molecules are indicated by solid lines. The positive direction of c is above the paper.

For atoms which have retained their hybridization during this conversion, the interatomic bond lengths in ascorbic acid (Hvoslef, 1968) and in 2-keto-L-gulonic acid compare as follows (ascorbic acid mentioned first): C(4)–C(5): [1·521, 1·518 Å], C(5)–C(6): [1·521, 1·511 Å], C(1)=O(1): [1·216, 1·197 Å], C(4)–O(4): [1·444, 1·440 Å], C(5)–O(5): [1·427, 1·427 Å], C(6)–O(6): [1·431, 1·449 Å].

For the bonds adjacent to C(2) and C(3) for which changes in bond character occur, the following contractions are observed; C(1)–C(2): 0·087 Å, C(2)–C(3): 0·195 Å, C(2)–O(2): 0·020 Å, C(3)–O(3): 0·090 Å, C(3)–C(4): 0·029 Å. As expected, the effect of hybridi-

zational change is clearly largest for the bonds constituting the conjugated O(1)=C(1)–C(2)=C(3)–O(3)H system of L-ascorbic acid.

Hydrogen bonding

The crystal structure of 2-keto-L-gulonic acid bears great resemblance to that of α-sorbose. Not only are the space groups identical, but also the molecular orientations about the screw axes are very much alike. The region of the disordered OH substituent in α-sorbose is, however, replaced by the carboxyl group and a water molecule and the effect is an entirely different hydrogen-bond network. In 2-keto-L-gulonic acid very extensive interaction is described by the sequence:

$$O(2)\text{--}H\cdots O(5)\text{--}H\cdots O(3)\text{--}H \qquad H_1\cdots O(6)$$
$$O(W)$$
$$O(1A)\text{--}H\cdots O(4)\text{--}H \qquad H_2\cdots O(1B)$$

as shown in Fig. 3, and it generates helical interactions running along the screw axes. The important function of the water molecules is to reinforce the helix running along [001], thereby tying different layers of molecules together, and also interconnecting stacks of helices of this type along [010] by a relatively strong bond (2·657 Å). The interconnection along the a axis is, however, relatively weak (2·834 Å).

The relative strengths of the different hydrogen bonds may be inferred from Table 5 which includes all bonding distances and angles involving hydrogen atoms.

The equatorial OH substituents participate both as donors and as acceptors of hydrogen bonds, whereas O(1) and O(2) are donors only. It is noted that the

Fig. 2. *ORTEP* plot of the asymmetric unit of 2-keto-L-gulonic acid monohydrate (Johnson, 1965). Distances (Å) and angles (°) for non-hydrogen atoms are included in the drawing. Average standard deviations are 0·0026 Å and 0·2°. The thermal ellipsoids are at 50 % probability. The angle O(1B)C(1)C(2) is 122·7°.

Table 5. *Distances* (Å) *and angles* (°) *involving hydrogen atoms*

Average standard deviations are 0·02 Å and 1·3° for bonds involving hydrogen atoms and 0·003 Å for the donor–acceptor distances. (W) denotes the water atoms. H_a and H_e indicate axially and equatorially bonded hydrogen atoms, respectively. Hydrogen atoms are identified by the atom to which they are attached.

	Acceptor symmetry code			O–H	H···O	O···O	O–H···O	C–O–H
O(1A)–H···O(4)′	$\frac{1}{2}-x,$	$\bar{y},$	$-\frac{1}{2}+z$	0·79	1·846	2·624	169·2	111·8
O(2)—H···O(5)‴	$1-x,$	$-\frac{1}{2}+y,$	$\frac{3}{2}-z$	0·78	2·054	2·834	173·9	104·2
O(3)—H···O(W)	$x,$	$y,$	z	0·74	2·017	2·760	177·7	105·6
O(4)—H···O(W)′	$\frac{1}{2}-x,$	$1-y,$	$\frac{1}{2}+z$	0·78	1·878	2·657	174·8	109·9
O(5)—H···O(3)*	$x,$	$y,$	$1+z$	0·80	2·123	2·861	154·3	108·2
O(W)–H₁··O(6)′	$\frac{1}{2}-x,$	$\bar{y},$	$-\frac{1}{2}+z$	0·83	2·006	2·831	170·9	
O(W)–H₂··O(1B)*	$\frac{1}{2}-x,$	$\bar{y},$	$\frac{1}{2}+z$	0·77	2·042	2·768	157·3	

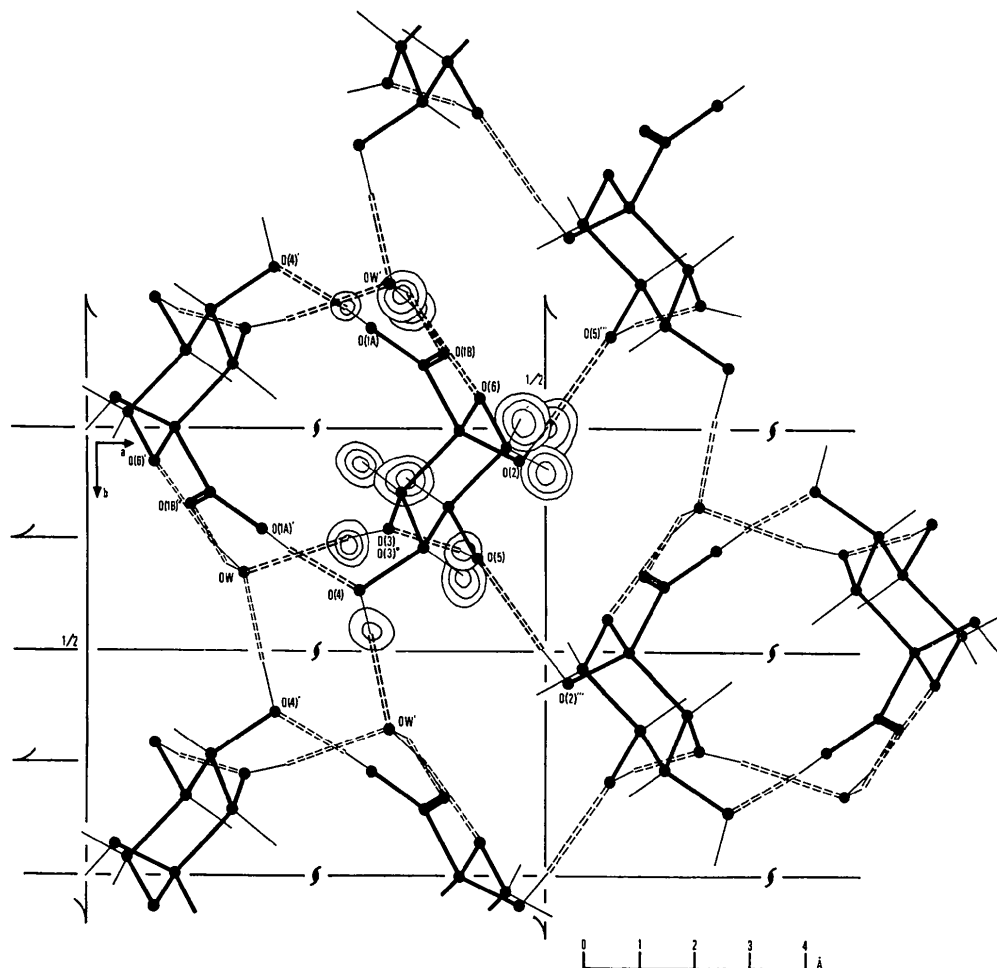|	C–H	C(2)–C(3)–H	O(3)–C(3)–H	C(4)–C(3)–H	
C(3)–H	0·95	106·4	109·7	108·6	
C(4)–H	0·99	C(3)–C(4)–H 110·7	O(4)–C(4)–H 106·4	C(5)–C(4)–H 111·1	
C(5)–H	0·99	C(4)–C(5)–H 107·8	O(5)–C(5)–H 109·9	C(6)–C(5)–H 110·8	
C(6)–Hₐ	0·98	C(5)–C(6)–H 108·7	O(6)–C(6)–H 110·7	Hₑ—C(6)–Hₐ 111·7	H₁–O(W)–H₂ 99·2°
C(6)–Hₑ	1·02	110·5	105·3	–	

Fig. 3. Hydrogen-bond network in 2-keto-L-gulonic acid as seen along [001]. A composite three-dimensional difference electron density map corresponding to one asymmetric unit is included in the drawing. Contours are at intervals of 0·1 e Å^{-3}, starting at 0·3 e Å^{-3}. Atoms marked by primes and asterisks belong to non-reference molecules.

latter oxygen atom gives rise to a weak hydrogen bond, perhaps due to the very short C–O bond distance.

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References

CHU, S. S. C. & JEFFREY, G. A. (1967). *Acta Cryst.* **23**, 1038–1049.

DAHL, T., GRAM, F., GROTH, P., KLEWE, B. & RØMMING, C. (1970). *Acta Chem. Scand.* **24**, 2232–3.

EULER, H. & EISTERT, B. (1957). *Chemie und Biochemie der Reduktone und Reduktonate.* Stuttgart: Enke Verlag.

FLIPPEN, J. L. (1973). *Acta Cryst.* **B29**, 1881–1885.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* **A27**, 368–376.

GLUSKER, J. P., MINKIN, J. A. & SOULE, F. B. (1972). *Acta Cryst.* **B28**, 2499–2505.

GROTH, P. (1973). *Acta Chem. Scand.* **27**, 1837.

HANSON, H. P., HERMAN, F., LEA, J. D. & SKILLMAN, S. (1964). *Acta Cryst.* **17**, 1040–1044.

HVOSLEF, J. (1968). *Acta Cryst.* **B24**, 23–35.

JOHNSON, C. K. (1965). *ORTEP.* Oak Ridge National Laboratory Report ORNL-3794 (revised).

KIM, S. H. & JEFFREY, G. A. (1967). *Acta Cryst.* **22**, 537–545.

KIM, S. H. & ROSENSTEIN, R. D. (1967). *Acta Cryst.* **22**, 648–656.

REICHSTEIN, T. (1936). *Festschrift für E. C. Barell,* p. 118. Basel.

ROBERTSON, J. H. & SHELDRICK, B. (1965). *Acta Cryst.* **19**, 820–826.

SCHOMAKER, V. & TRUEBLOOD, K. N. (1968). *Acta Cryst.* **B24**, 63–76.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.