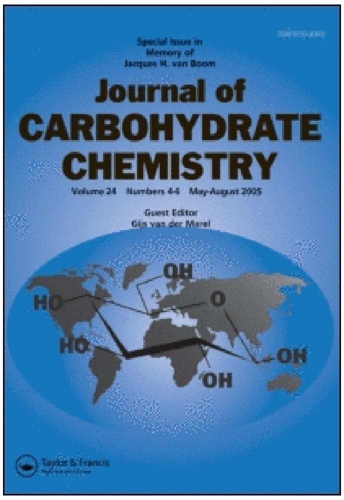

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COMMUNICATION

CRYSTAL STRUCTURE OF D-ERYTHROASCORBIC ACID

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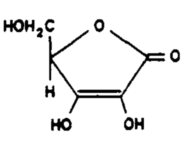
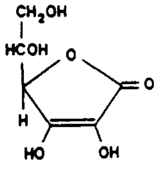
D-*Glycero*-2-pentenono-1,4-lactone (D-erythroascorbic acid, EAA) is present in yeasts and fungi where little or no L-ascorbic acid (AA) is found.[1,2] Higher organisms all contain AA in active and growing cells. AA is thought to have evolved to protect living cells from lethal levels of active-oxygen species.[3] AA is required also for optimal activity of enzymes that catalyze hydroxylation reactions.[4,5] The role of EAA in yeasts



EAA



AA

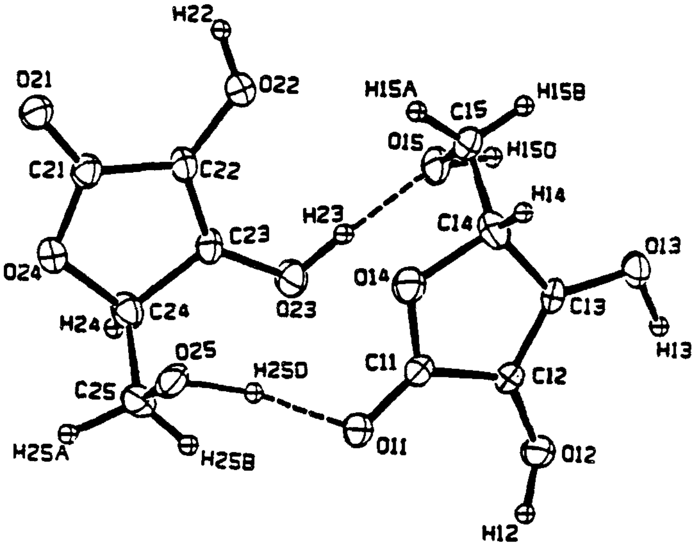


FIG. 1. ORTEP drawing and hydrogen bonding (---) between molecules 1 and 2 of EAA.

and fungi is unknown. Frank A. Loewus (personal communication) has found that plant-pathogenic fungi catabolize EAA to oxalate, an acid involved in the invasion of the host. Chemical syntheses[6-8] of EAA have been reported in recent years. Herein, we present information on the conformation of EAA.

The crystal of EAA ($C_5H_6O_5$ MW=146.10) belongs to the orthorhombic crystal system, space group $P2_12_12_1$, and has unit cell dimensions a= 9.7442(6) Å, b=14.844(2) Å, c=8.4775(9)Å, with V=1226.2(2), Z=8, and D_{calc}=1.583 g/cm^3. All 911 measured reflections were used to determine and to refine the structure to R=0.048.

Two slightly different molecules 1 and 2 were found in the crystallographic asymmetric unit (Figs 1 and 2). When comparing the two molecules there was ~3° difference in the rotation about the C-4 to C-5 bond. Neither molecule contained a coplanar ring structure (Tables 1 and 2). Two intermolecular hydrogen bonds are proposed, one between the 5-OH and 1-carbonyl, and the other between the 3- and 5-OH (Fig 1). The 5-OH of EAA in both molecules is in a gauche position with respect to O-4. Thus EAA, like AA,[9, 10] has the 5-OH oriented atop the lactone ring. The close proximity of the 2-, 3-, and 5-hydroxyls in EAA and AA may be important to their strong complexing with ferric ion.[11]

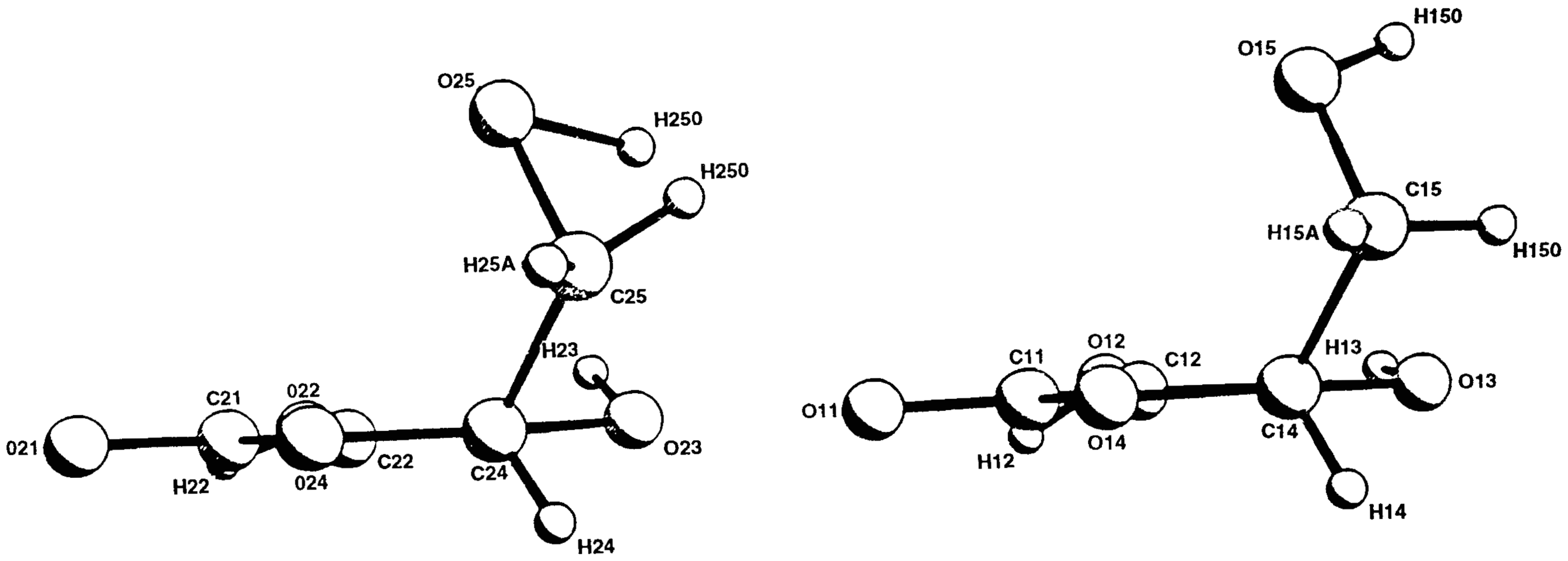


FIG. 2. Structure of molecules 1 and 2 projected parallel to the lactone ring.

Table 1. Selected Bond Lengths (Å) and Valency Angles (°) of Molecules 1 and 2 of EAA and AA. The estimated standard deviations are in parentheses.

	Molecule of EAA		AA[a]
	1	2	
C1=O1	1.218(7)	1.208(7)	1.216
C2-O2	1.333(7)	1.370(7)	1.361
C3-O3	1.325(7)	1.333(7)	1.326
C1-O4	1.331(7)	1.335(7)	1.355
C4-O4	1.470(7)	1.442(8)	1.444
C5-O5	1.426(8)	1.435(9)	1.427
C2=C3	1.347(8)	1.339(8)	1.338
C1-C2	1.436(8)	1.427(8)	1.452
C3-C4	1.481(8)	1.494(8)	1.493
C4-C5	1.506(9)	1.523(9)	1.521
C1-C2-C3	106.6(5)	108.1(5)	107.8
C2-C3-C4	110.4(5)	108.9(5)	109.5
C1-C2-O2	126.6(5)	124.2(6)	124.6
O2-C2-C3	126.7(5)	127.2(5)	-
C2-C3-O3	130.7(5)	132.6(5)	133.5
O3-C3-C4	118.8(5)	118.5(5)	117.1
C3-C4-C5	114.3(5)	115.8(5)	114.8

[a] Data from Ref. 9.

Table 2. Selected Torsion Angles (°) of Molecules 1 and 2 of EAA and Their Standard Deviations.

	1	2
O4-C1-C2-O2	-175.8(5)	-175.0(5)
O4-C1-C2-C3	1.9(8)	-2.0(8)
O4-C4-C3-O3	-179.2(5)	177.6(5)
O4-C4-C3-C2	2.3(6)	-0.5(6)
O4-C4-C5-O5	-68.8(6)	-65.7(7)
O2-C2-C3-O3	-3.0(1)	-4.0(1)
O5-C5-C4-C3	46.5(7)	49.9(7)
C1-O4-C4-C5	121.2(5)	122.7(6)

Table 3. Fractional coordinates and equivalent isotropic thermal parameters*

Atom	x	y	z	B_{eq}·Å
O(11)	1.1199(5)	0.7627(3)	1.359(5)	4.2(2)
O(12)	1.0631(5)	0.7847(3)	1.7036(5)	3.7(2)
O(13)	2.1560(4)	0.6082(3)	1.8418(5)	3.3(2)
O(14)	1.1834(4)	0.6243(3)	1.4233(5)	3.5(2)
O(15)	0.9668(4)	0.5082(3)	1.5614(5)	3.5(2)
C(11)	1.1378(7)	0.7059(4)	1.4613(7)	3.2(3)
C(12)	1.1160(6)	0.7140(4)	1.6282(7)	2.7(2)
C(13)	1.1545(5)	0.6350(4)	1.6927(6)	2.6(2)
C(14)	1.1972(6)	0.5708(4)	1.5684(8)	3.3(3)
C(15)	1.1097(7)	0.4874(4)	1.5580(8)	3.4(3)
H(12)	1.087(7)	0.844(5)	1.673(8)	4.0(2)
H(13)	1.106(6)	0.664(4)	1.905(7)	4.0(1)
H(14)	1.292(5)	0.554(3)	1.580(5)	0.6(8)
H(15A)	1.143(8)	0.456(5)	1.45(1)	6.0(2)
H(15B)	1.122(6)	0.452(4)	1.653(8)	3.0(1)
H(15O)	0.921(6)	0.500(4)	1.680(7)	3.0(1)
O(21)	0.9215(5)	0.4593(3)	0.8707(5)	3.6(2)
O(22)	0.9617(5)	0.4353(3)	1.2146(5)	3.5(2)
O(23)	0.8644(4)	0.6168(3)	1.3486(5)	3.6(2)
O(24)	0.8466(4)	0.5960(3)	0.9305(5)	3.5(2)
O(25)	1.0531(4)	0.7159(2)	1.0564(5)	3.5(2)
C(21)	0.8952(6)	0.5150(4)	0.9701(7)	2.9(3)
C(22)	0.9058(6)	0.5077(4)	1.1375(7)	3.0(3)
C(23)	0.8672(5)	0.5865(4)	1.2006(6)	2.7(2)
C(24)	0.8255(7)	0.6489(4)	1.0711(8)	3.4(3)
C(25)	0.9088(8)	0.7354(4)	1.0570(9)	3.9(3)
H(22)	0.959(7)	0.380(5)	1.181(9)	5.0(2)
H(23)	0.94(1)	0.571(6)	1.41(1)	8.0(2)
H(24)	0.738(6)	0.665(3)	1.085(7)	3.0(1)
H(25)	0.878(6)	0.767(4)	0.944(8)	3.0(1)
H(25B)	0.94(1)	0.779(7)	1.13(1)	11.0(3)
H(25O)	1.03(1)	0.727(8)	1.21(2)	14.0(4)

*)$B_{eq} = 8/3\Sigma_i\Sigma_j U_{ij} a^*_i a^*_j a_i a_j$

The ^{1}H NMR spectrum of EAA gave $J_{4,5}$ and $J_{4,5'}$ at pH 2 of 2.75 Hz and 3.66 Hz, respectively, and 2.44 Hz and 4.89 Hz at pH 7. In the three possible rotamers of the C-4 to C-5 bond in EAA, only the rotamer with O5 positioned over the middle of the lactone ring possesses two gauche conformations between H-4 and H-5, and H-4 and H-5'. The other two rotamers have one antiparallel conformation of vicinal protons, which should produce one ^3J coupling of approximately[10] 7-10 Hz. Thus, the side-chain conformation of EAA in aqueous solution at pH 2-7 appears almost the same as in the crystal.

EXPERIMENTAL

D-Erythroascorbic acid was prepared and crystallized from acetonitrile by the method of Shao et al.[6] All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated CuKα radiation ($\lambda = 1.5418$Å) and a 12KW rotating anode generator. The intensities of three representative reflections were measured after every 150 reflections and remained constant, indicating the stability of the crystal. Data were collected at a temperature of 23 ± 1 °C using the ω-2θ scan technique to a maximum 2θ value of 112.4°. All data were corrected for Lorentz and polarization effects. The structure was solved by direct methods.[12,13] The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located in the difference maps and were introduced into refinement with isotropic thermal parameters. Refinement was carried out by a full-matrix least squares, minimizing $\sum w(|Fo|-|Fc|)^2$, where w is $1/T\ (Fo)^2$. Neutral atom scattering factors were taken from Cromer and Waber.[14] The final atomic parameters are given in Table 3. All calculations were performed using the TEXSAN crystallographic software package of Molecular Structure Corporation, Woodlands, TX. Atomic coordinates have been deposited with the Cambridge Crystallographic Data Center, University Chemical Laboratory, Lensfield Rd, Cambridge CB2 1EW, U.K.

^{1}H NMR spectra were run in D_2O at 27.0 °C on a Varian 400 MHz Unity Plus Instrument. A D_2O solution of EAA was adjusted with a pH electrode to pH 7 by adding NaOD. Chemical shifts were referenced to HDO at δ 4.80 ppm from DSS. Coupling constants were the line splittings in the spectra. The chemical shifts (ppm) and couplings (Hz) were as follows at pH 2: δ 3.86 (dd, 1H), $J_{4,5'} = 3.66$, $J_{5,5'}$ 13.12, H-5'; δ 4.06 (dd, 1H), $J_{4,5} = 2.75$, $J_{5,5'} = 13.66$, H-5; δ 4.94 (dd, 1H), $J_{4,5} = 2.75$, $J_{4,5'} = 3.66$, 4-H; and at pH 7: δ 3.76 (dd, 1H), $J_{4,5'} = 4.89$, $J_{5,5'} = 12.82$, H-5'; δ 3.99 (dd, 1H), $J_{4,5} = 2.44$, $J_{5,5'} = 12.52$, H-5; δ 4.54 (dd, 1H), $J_{4,5'} = 4.89$, $J_{4,5} = 2.44$, H-4. Lit.[7], ^{1}H NMR (D_2O, pH 8), δ 3.72 (H-5'), δ 3.97 (H-5), and δ 4.50 (H-4).

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