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Refinement of the Structure of Potassium Hydrogen Isocitrate Lactone

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Abstract. This is a refinement of a previous structure determination from projection data [Glusker, Patterson, Love & Dornberg (1963). *Acta Cryst.* **16**, 1102] of potassium hydrogen isocitrate lactone, derived from naturally occurring (+)-isocitric acid. The crystals are orthorhombic, space group $P2_12_12_1$, $Z=4$, F.W. 212.20 $a=9.064$ (2), $b=12.708$ (2), $c=6.653$ (1) Å, $V=766.3$ (3) Å^3. $D_x=1.839$, $D_{\text{meas}}=1.838$ g cm^{-3}, λ(Mo $K\alpha$)= 0.7107 Å. The final residual $R=0.046$. All hydrogen atoms were located and were refined isotropically. The study shows that the carboxyl group adjacent to the ring oxygen atom is the one that is predominantly ionized.

Experimental. Crystals were provided by Drs H. B. Vickery and D. G. Wilson of the Connecticut Agricultural Experiment Station. They were derived from (+)-isocitric acid extracted from leaves. An approximately spherical crystal, 0·28 mm diameter, was used to collect 3-dimensional data on a Syntex automated diffractometer with monochromatic Mo $K\alpha$ radiation using the θ–2θ scan technique. Intensities were measured for 1371 reflections (those in the range $\sin\theta/\lambda=$ 0 to 0·715 Å^{-1}). Values for $\sigma(F)$ were derived from counting statistics and measured instrumental uncertainties. The formula used was $\sigma(F)=(F/2)\{\sigma^2(I)/I^2+\delta^2\}^{1/2}$ where $\sigma(I)$ is derived from counting statistics alone and δ is the measured instrumental uncertainty. There were 322 reflections for which the measured intensity, I_{obs}, was less than 2·33 $\sigma(I)$ and these were considered to be unobserved. For these 'unobserved reflections', when $I\geq\sigma(I)$, the measured value of I was used in computing F and when $I<\sigma(I)$, F was computed using the value $0{\cdot}77\sigma(I)$. The intensity data were converted to structure amplitudes by application of Lorentz and polarization factors and a spherical absorption correction (Johnson, 1963), with μ[Mo $K\alpha$] $=6{\cdot}87$ cm^{-1}, and placed on an approximate absolute scale by means of a Wilson plot.

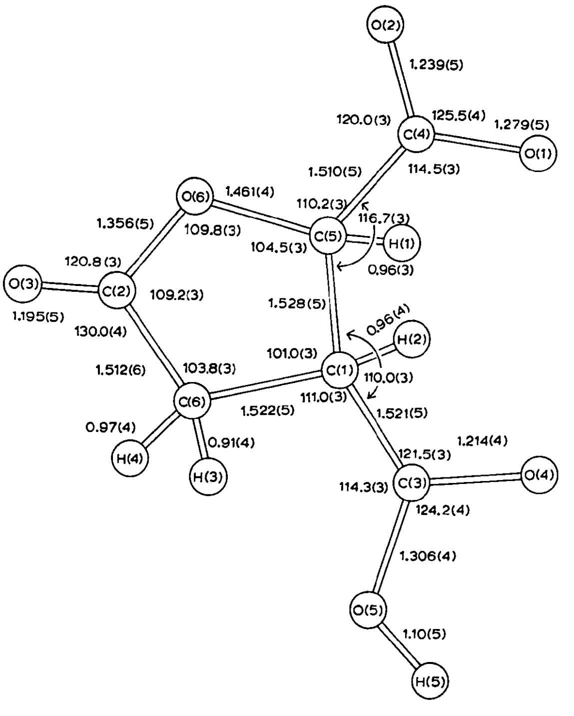

Fig. 1. Angles and distances in the hydrogen isocitric lactone ion. Estimated standard deviations are given in parentheses for the last digit quoted.

Structure determination and refinement. The structure had been previously determined from projection data in this laboratory (Glusker, Patterson, Love & Dornberg, 1963). The published coordinates were used as a

Table 1. *Final atomic parameters*

Positional parameters are given as fractions of cell edges × 10^4 (× 10^3 for hydrogen). Anisotropic temperature factors are expressed as $\exp[-\frac{1}{4}(h^2a^{*2}B_{11}+k^2b^{*2}B_{22}+l^2c^{*2}B_{33}+2hka^*b^*B_{12}+2hla^*c^*B_{13}+2klb^*c^*B_{23})]$ and isotropic temperature factors as $\exp(-B\sin^2\theta/\lambda^2)$ with B values given in Å^2. For the non-hydrogen atoms, the B values given are the average of $B_{11}+B_{22}+B_{33}$.

The standard deviations for each parameter, determined from the inverted full matrix, are given in parentheses and apply to the last specified digits.

	x	y	z	B
K	9168 (1)	2361 (1)	1699 (1)	2·85
O(1)	2759 (3)	3242 (2)	4519 (4)	2·46
O(2)	2150 (3)	3172 (2)	1262 (4)	3·31
O(3)	5715 (3)	5637 (2)	−1360 (4)	3·13
O(4)	6164 (4)	3245 (2)	2122 (4)	3·57
O(5)	6210 (3)	3388 (2)	5458 (4)	2·40
O(6)	4009 (3)	4756 (2)	0344 (3)	2·07
C(1)	5023 (4)	4750 (3)	3617 (5)	1·79
C(2)	5250 (4)	5349 (3)	0229 (6)	2·10
C(3)	5865 (4)	3715 (3)	3657 (5)	1·94
C(4)	2778 (4)	3587 (3)	2713 (6)	2·11
C(5)	3585 (4)	4617 (3)	2446 (5)	1·75
C(6)	5817 (5)	5561 (3)	2327 (6)	2·38
H(1)	291 (3)	517 (3)	280 (5)	0·8 (9)
H(2)	487 (4)	499 (3)	496 (5)	2·3 (9)
H(3)	682 (5)	552 (3)	240 (6)	3·4 (10)
H(4)	553 (4)	627 (3)	263 (6)	2·0 (8)
H(5)	688 (5)	267 (4)	550 (8)	6·1 (13)

Table 1 (*cont.*)

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
K	2·92 (3)	3·08 (3)	2·56 (3)	−0·28 (3)	−0·55 (3)	−0·23 (3)
O(1)	2·56 (9)	2·45 (12)	2·36 (10)	−0·74 (9)	−0·05 (9)	0·44 (10)
O(2)	3·42 (13)	4·07 (12)	2·43 (10)	−1·66 (13)	0·39 (12)	−0·57 (13)
O(3)	3·58 (13)	3·55 (12)	2·27 (12)	−0·60 (13)	0·39 (12)	0·78 (10)
O(4)	4·70 (16)	3·75 (12)	2·27 (12)	2·03 (13)	−0·34 (12)	−0·68 (10)
O(5)	2·46 (13)	2·71 (12)	2·04 (10)	0·74 (9)	−0·12 (9)	0·64 (10)
O(6)	1·97 (9)	2·71 (12)	1·54 (8)	−0·32 (9)	−0·22 (9)	0·44 (10)
C(1)	2·30 (13)	1·61 (12)	1·45 (14)	−0·05 (13)	−0·07 (12)	−0·10 (10)
C(2)	2·20 (13)	1·81 (12)	2·28 (15)	0·14 (13)	−0·05 (14)	0·37 (13)
C(3)	1·45 (13)	2·20 (12)	2·18 (15)	0·09 (13)	0·05 (14)	−0·10 (13)
C(4)	1·58 (13)	2·26 (12)	2·48 (15)	0·05 (13)	0·53 (14)	0·17 (13)
C(5)	1·77 (13)	1·94 (12)	1·54 (12)	0·18 (13)	0·29 (12)	0·20 (13)
C(6)	2·76 (16)	2·07 (12)	2·32 (14)	−0·83 (18)	−0·29 (16)	0·41 (13)

starting point for the refinement. All hydrogen atoms were located on a difference map. The structure was refined by full-matrix least-squares calculations with the hydrogen atoms treated isotropically and all others anisotropically. The weights used were $1/[\sigma^2(F_o)]$ with unobserved reflections assigned zero weight. The quantity minimized was $\sum\omega||F_o|-|F_c||^2$. The final refinement resulted in a residual, R, of 0·046 and a weighted R value of 0·037 for observed data. The final coordinates are listed in Table 1. A Table of calculated and observed structure factors is available.*

The atomic scattering factors used for potassium ions and oxygen and carbon atoms were those in *International Tables for X-ray Crystallography* (1962) and for hydrogen atoms those of Stewart, Davidson & Simpson (1965). The components of anomalous dispersion correction that were used for the potassium ion, $\Delta f'=0{\cdot}179$, $\Delta f''=0{\cdot}250$ respectively, are those listed by Cromer & Liberman (1970). Computer programs used in this determination were *CLINUS*, a version of the least-squares program *ORFLS* of Busing, Martin & Levy (1962) at Brookhaven National Laboratory (Hamilton, 1972, unpublished), and the X-ray System (Stewart, Kruger, Ammon, Dickinson & Hall, 1972).

Discussion. This refinement of a previously reported structure from this laboratory (Glusker *et al.*, 1963) was carried out in order to provide better interatomic distances and angles, and to determine the location of the hydrogen atom in the hydrogen bond. The coordinates agree within three standard deviations listed in the paper by Glusker *et al.* (1963) except for the x values for K, O(4), O(5) and C(5), where the differences are 4–7 $\sigma(x)$.

The study has shown, by the location of the hydrogen atom H(5), that the carboxyl group adjacent to the oxygen atom of the lactone ring, C(4) O(2) O(1), is the one that is predominantly ionized, as shown in Fig. 1. However, the two carbon oxygen distances (1·239 and 1·279 Å) differ by 8σ so that there may possibly be disorder of the hydrogen atom H(5), such that it may be attached to O(1) in some unit cells. The hydrogen bond between two different lactone ions is fairly short (2·502 Å) although probably not symmetrical since the distances O(1)···H(5) and O(5)–H(5) differ by 6σ.

One potassium ion forms a tridentate chelate with one anion through O(2), O(4) and O(6) and a bidentate chelate through O(1) and O(5) of another anion. Some distances involved are given in Table 2.

Table 2. *Interatomic distances* (Å)

Symmetry code

Superscript	Atom at
None	$x, \quad y, \quad z$
I	$\frac{1}{2}+x, \frac{1}{2}-y, 1-z$
II	$1+x, \quad y, \quad z$
III	$\frac{1}{2}+x, \frac{1}{2}-y, \quad -z$
IV	$1\frac{1}{2}-x, 1-y, \frac{1}{2}+z$

K···O(1$^{\rm I}$)	2·924 (3)	K···O(2$^{\rm II}$)	2·907 (3)
K···O(2$^{\rm III}$)	2·772 (3)	K···O(3$^{\rm IV}$)	2·855 (3)
K···O(4)	2·959 (4)	K···O(4$^{\rm III}$)	3·213 (3)
K···O(5$^{\rm I}$)	2·812 (3)	K···O(6$^{\rm III}$)	3·017 (3)
Hydrogen bond			
O(5)—H(5)	1·10 (5)	O(5)···O(1$^{\rm I}$)	2·502 (4)
H(5)···O(1$^{\rm I}$)	1·41 (5)	Angle O(5)–H(5)···O(1$^{\rm I}$) = 178 (5)°	

In the anion the bond length C(2)–O(6) is significantly shorter than that for O(6)–C(5) (difference of 0·105 Å = 20–25σ) as found in similar lactones (Glusker, Minkin & Casciato, 1971; Glusker, Minkin & Soule, 1972). The oxygen atom O(6) is 0·497 Å from the plane of the adjacent carboxyl group C(4) O(1) O(2). The shapes of the lactones, derived from (*a*) (−)-hydroxycitric acid (Glusker *et al.*, 1971), (*b*) (+)-isocitric acid (this paper) and (*c*) (+)-allohydroxycitric acid (Glusker *et al.*, 1972), are shown in Fig. 2 which illustrates each anion with respect to the plane [O(3) C(2) O(6) C(6)] of the carbonyl group. In Table 3, numerical values and further information on the conformations of the lactone ions are given. It can be seen that (*a*) and (*b*) are remarkably similar, apart from absolute configuration, even though the hydroxyl group is not present in (*b*) (the isocitrate

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* The table has been deposited with the National Lending Library, England, as Supplementary Publication No. SUP 30055. Copies may be obtained from the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. *Conformations of three lactone ions*

The atoms in garcinia acid [the lactone of (−)-hydroxycitric acid] and hibiscus acid [the lactone of (+)-allohydroxycitric acid] have been renumbered to conform with those of the isocitrate lactone.

(*a*) Torsion angles

	Garcinia acid	Isocitrate lactone	Hibiscus acid
O(1) C(4) C(5) O(6)	−160·6°	159·7°	−179·9°
O(2) C(4) C(5) O(6)	23·0	−23·4	0·2
O(4) C(3) C(1) H(2) (or OH)	−174·9	178·6	171·5
O(5) C(3) C(1) H(2) (or OH)	7·6	−0·8	−10·2

(*b*) Spatial arrangement of substituents

	Garcinia acid	Isocitrate lactone	Hibiscus acid
α COOH	equatorial	equatorial	equatorial
β COOH	axial	axial	equatorial
β OH	equatorial		axial

(*c*) Deviations in Å of the ring and hydroxyl group from the plane of the carbonyl group

Plane	Deviation of atom	Garcinia acid	Isocitrate lactone	Hibiscus acid
O(1) O(2) C(4) C(5)	O(6)	0·473	0·497	0·002
O(4) O(5) C(3) C(1)	OH	0·139	-	−0·214

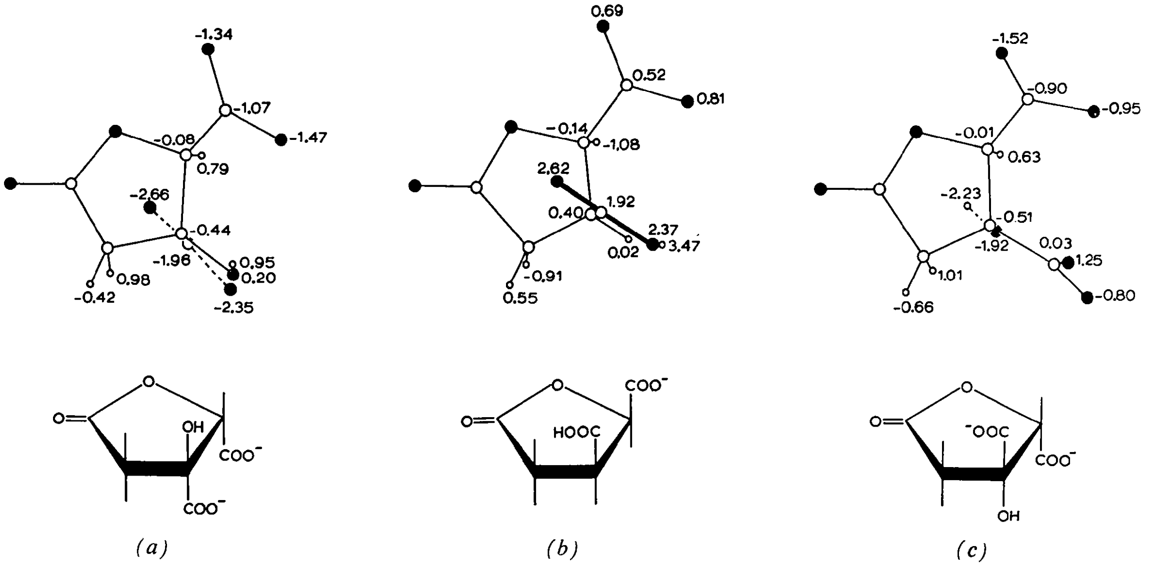

Fig. 2. Lactone ions drawn with respect to the plane of the carbonyl group [O(3) C(2) O(6) C(6)]. The numbers refer to distances, in Å, above and below this plane. (*a*) The lactone from (−)-hydroxycitric acid (garcinia acid). (*b*) The lactone from (+)-isocitric acid. (*c*) The lactone from (+)-allohydroxycitric acid (hibiscus acid). Oxygen atoms are black and carbon and hydrogen atoms white with hydrogen atoms smaller.

lactone anion). In (*c*) the carboxyl group adjacent to the hydroxyl group is in an 'equatorial-like' rather than the 'axial-like' conformation of (*a*) and (*b*).

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