Carbohydrate Research, 108 (1982) 205–211
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

THE CRYSTAL STRUCTURE OF GALACTARIC ACID (MUCIC ACID) AT −147°: AN UNUSUALLY DENSE, HYDROGEN-BONDED STRUCTURE

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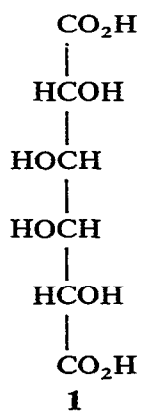
(Received March 31st, 1982; accepted for publication, April 21st, 1982)

ABSTRACT

Galactaric acid, $C_6H_{10}O_8$, (CAS Reg. No. 526-99-8), is triclinic, $P\bar{1}$, with cell dimensions at −147° [and 20°], a = 4.900(1) [4.918(1)], b = 5.728(1) [5.816(1)], c = 6.784(1) [6.849(1)] Å, α = 92.32(2) [92.31(2)], β = 93.74(2) [94.16(2)], γ = 93.08(2) [93.49(2)]°, V = 189.5 Å^3, Z = 1, D_x = 1.831 [1.800], D_m = [1.790] g.cm^{-3}, molecular symmetry $\bar{1}$. The structure was solved by the direct method, MULTAN, and refined to R = 0.034, R_w = 0.039 for 787 reflections with $F_{obs} > 3\sigma(F_{obs})$. The crystal structure has a system of strong, intermolecular hydrogen-bonds, which accounts for the high crystal density and low solubility in water.

INTRODUCTION

Galactaric acid (**1**; mucic acid) has an unusually low solubility in water for an unsubstituted carbohydrate. This property is accompanied by a relatively high melting-point, 206°, and a high crystal density for a carbohydrate, where the densities generally lie between 1.4 and 1.6 g.cm^{-3}. In contrast, D-mannaric and D-glucaric acid are very soluble in water, as are the pentaric acids. D-Glucaric acid (**2**; saccharic acid), m.p. 125°, is, in fact, deliquescent, making it difficult to crystallize, and it is generally characterized as one of its salts. The present crystal-structure analysis was conducted in order to determine the intermolecular forces associated with the low aqueous solubility and high crystal-density of galactaric acid.



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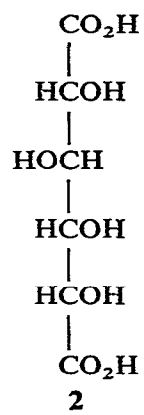

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EXPERIMENTAL

Prismatic crystals of galactaric acid were obtained by slow cooling of a hot, aqueous solution. The crystal selected for investigation had the (100), (010), and (001) faces most prominently developed. Their respective distances from a common, internal origin were 0.20, 0.10, and 0.07 mm, resulting in a maximum, mean free-path-length, in the crystal of 0.022 cm ($\mu_{MoK\alpha} = 1.89\ cm^{-1}$).

Intensities of 881 independent reflections with $\theta < 27.5°$ were measured at $-147(5)°$ on a CAD-4 diffractometer, using graphite-monochromated MoKα radiation and a $\theta - 2\theta$ scan. Unit-cell dimensions were obtained at 20° and −147° from least-squares analyses of 25 reflections with $21° < \theta < 25°$. Lorentz polarization and absorption corrections were applied to the data.

The structure determination was by means of MULTAN 78 (ref. 1), using 128 structure amplitudes with $E > 1.49$. All non-hydrogen atoms appeared in the E-maps, and the hydroxyl-hydrogen atoms were located from subsequent, three-dimensional, Fourier-difference maps. The methylene-hydrogen atom positions were generated by using tetrahedral carbon geometry and a C–H bond-length of 0.96 Å.

The atomic parameters were refined by using full-matrix least-squares, minimizing $\Sigma w(|F_o| - k|F_c|)^2$, where $w^{-1} = \sigma^2(|F_o|)$, and $\sigma^2(|F_o|)$ was obtained from counting statistics. Reflections with $|F_o| < 3\sigma(|F_o|)$ were given zero weight in the refinement. Standard atomic-scattering factors were used for the carbon and oxygen atoms[2] and the hydrogen atoms[3]. Anomalous-dispersion corrections of $\Delta f' = 0.00$, $\Delta f'' = 0.10$ were applied to the oxygen atoms[2]. An isotropic, extinction parameter, g, for a type I crystal with a Lorentzian mosaicity distribution[4] was included, and refined in the final cycles. The value obtained for g was 88(33) rad^{-1}, so that the worst-affected reflection had $|F_o| = 0.96\ |F_c|$. The non-hydrogen atoms were given anisotropic thermal parameters, and the hydrogen atoms, isotropic thermal parameters, all of which were refined independently. The final, discrepancy factors for the 787 observed reflections were $R(F) = 0.034$, $R_w(F) = 0.039$, and GoF = 2.56, where GoF is the "goodness of fit" given by $[\Sigma w(|F_o| - |F_c|)^2/(n - m)]^{\frac{1}{2}}$, where n is the number of reflections, and m (=85) the number of refinable parameters.

Atomic parameters for the atoms in the asymmetric unit are given in Table I*. The atomic notation** and thermal ellipsoids[5] of the molecule are shown in Fig. 1. Bond lengths, valence angles, and torsional angles are listed in Table II.

DISCUSSION

The molecular structure and conformation, shown in Fig. 1, showed no un-

*Tables of structure factors are deposited with and can be obtained from: Elsevier Scientific Publishing Company, BBA Data Deposition, P. O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/227/*Carbohydr. Res.*, 108 (1982) 205–211.

**Because of the symmetry of the molecule, it proved convenient not to employ the customary numbering for the carbon atoms.

TABLE I

ATOMIC PARAMETERS[a] ($\times 10^4$ FOR THE NON-HYDROGEN ATOMS, $\times 10^3$ FOR THE HYDROGEN ATOMS) FOR THE CRYSTAL STRUCTURE OF GALACTARIC ACID AT −147°

	x/a	y/b	z/c	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O-1A	8408(2)	2115(2)	4635(2)	129(6)	110(5)	147(5)	−8(4)	−64(4)	6(4)
O-1B	7254(2)	5565(2)	3510(2)	116(6)	98(5)	132(5)	−12(4)	−25(4)	−13(4)
O-2	2836(2)	3635(2)	1458(2)	85(6)	125(5)	168(6)	32(4)	−42(4)	−17(4)
O-3	7890(2)	2018(2)	−313(2)	95(6)	101(5)	159(5)	−23(4)	24(4)	4(4)
C-1	6907(3)	3467(2)	3560(2)	81(7)	117(7)	84(6)	1(6)	16(5)	−7(5)
C-2	4673(3)	2077(2)	2304(2)	74(7)	93(6)	99(7)	−8(5)	−14(5)	−6(5)
C-3	6060(3)	632(2)	735(2)	74(7)	75(6)	101(6)	−11(5)	−14(5)	2(5)
H-2	377(4)	106(3)	317(2)	7(4)					
H-3	713(4)	−53(3)	141(2)	9(4)					
H-O-1A	979(6)	297(4)	531(3)	41(7)					
H-O-2	129(7)	297(5)	100(4)	57(8)					
H-O-3	723(6)	311(5)	−76(4)	50(8)					

[a]Parameters for the symmetry-related atoms in the same molecule are given by: $1-x/a$, $-y/b$, $-z/c$. For the non-hydrogen atoms, the temperature factor is: $T = \exp[-2\pi(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$. For the hydrogen atoms: $T = \exp(-8\pi^2 U \sin^2\theta/\lambda^2)$. Estimated standard deviations are given in parentheses.

expected features. The torsional angles along the straight chain differ slightly from exact linearity, with C-1–C-2–C-3–C-3′ = −174°. The carboxylic acid group is almost planar, with H-O-1A–O-1A–C-1–O-1B = −1.8°. The characteristic, planar conformation of an α-hydroxy carboxylic acid group[6] is also observed, with O-1A, O-1B, C-1, C-2, O-2 in a plane, with maximum deviations of 0.096 Å for C-2 and

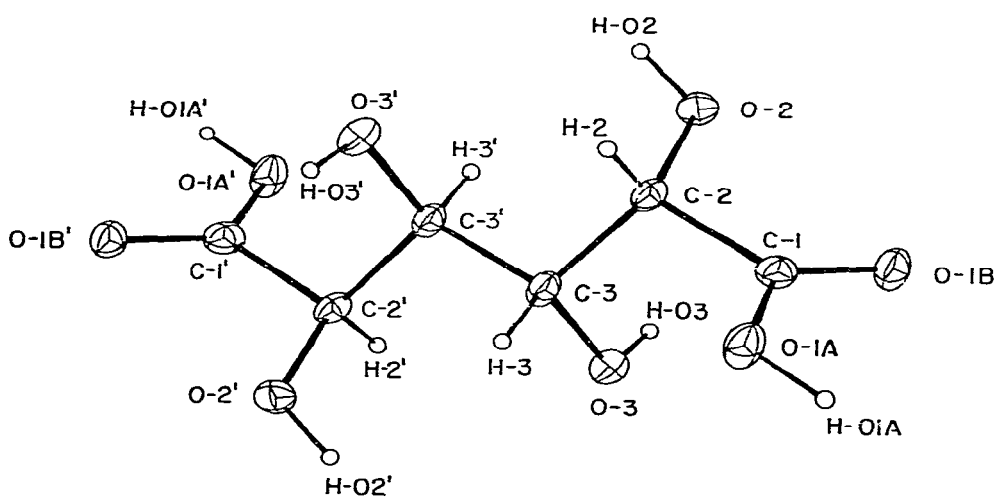

Fig. 1. Atomic notation and thermal ellipsoids at 70% probability for galactaric acid at −147°.

TABLE II

BOND LENGTHS, VALENCE ANGLES, AND PRINCIPAL TORSIONAL ANGLES FOR GALACTARIC ACID[a]

(i) Bond Lengths (Å)			
O-1A–C-1	1.308(2)	C-3–C-3′	1.524(2)
O-1B–C-1	1.207(2)	H-O-1A–O-1A	0.90(2)
O-2–C-2	1.413(2)	H-O-2–O-2	0.86(3)
O-3–C-3	1.412(2)	H-O-3–O-3	0.78(3)
C-1–C-2	1.513(2)	H-2–C-2	0.95(2)
C-2–C-3	1.538(2)	H-3–C-3	0.98(2)
(ii) Valence Angles (°)			
O-1A–C-1–O-1B	125.4(1)	C-2–C-3–C-3′	111.1(1)
O-1A–C-1–C-2	111.8(1)	C-2–C-3–O-3	112.3(1)
O-1B–C-1–C-2	122.8(1)	C-3′–C-3–O-3	108.9(1)
C-1–C-2–C-3	107.6(1)	H-3–C-3–O-3	107.5(1.1)
C-1–C-2–O-2	109.1(1)	H-3–C-3–C-2	108.2(1.1)
C-3–C-2–O-2	112.5(1)	H-3–C-3–C-3′	108.8(1.1)
H-2–C-2–O-2	110.8(1.0)	H-O-1A–O-1A–C-1	110.4(1.6)
H-2–C-2–C-1	106.6(1.0)	H-O-2–O-2–C-2	113.9(1.9)
H-2–C-2–C-3	110.1(1.0)	H-O-3–O-3–C-3	113.4(2.0)

(iii) Principal Torsional Angles (°)	
H-O-1A–O-1A–C-1–O-1B	−1.8(1.7)
O-1A–C-1–C-2–C-3	−68.2(2)
O-1A–C-1–C-2–O-2	169.6(1)
O-1B–C-1–C-2–O-2	−12.1(2)
O-1B–C-1–C-2–C-3	110.2(2)
C-1–C-2–C-3–C-3′	−174.0(1)
C-1–C-2–C-3–O-3	−51.8(2)
O-2–C-2–C-3–O-3	68.3(2)
C-2–C-3–C-3′–O-3′	−55.8(1)

[a]The primed notation refers to the atom related by the center of symmetry at the midpoint of the C-3–C-3′ bond. E.s.d. values are given in parentheses.

0.077 Å for O-2. The orientation of the hydroxyl group is staggered, with C-3–C-2–O-2–H-O-2 = +77°, C-2–C-3–O-3–H-O-3 = −71°. The C-1–C-2 (sp^2-sp^3) bond to the carboxylate group is shorter than the C-2–C-3, C-3–C-3′ (sp^3–sp^3) bonds.

The molecules are linked in the crystal structure by strong hydrogen bonds which involve all of the functional groups, as shown in Fig. 2. The carboxylic acid groups form characteristic, hydrogen-bond dimers across the centers of symmetry, which link the molecules end-to-end in chains. The hydroxyl groups hydrogen-bond into equally characteristic squares, which link the dimerized, molecular chains laterally. There is, in addition, a weak, bifurcated interaction from one hydroxyl, O-3···H, to the carboxylate oxygen, O-1B, on an adjacent chain. This system of bonds forms a layered arrangement of hydrogen bonds, as illustrated in the stereo-views in Fig. 3. The hydroxyl-oxygen atoms, which form the square, and the carboxy-late atoms, which form the dimers (shown most clearly in Fig. 3a), lie in two planes

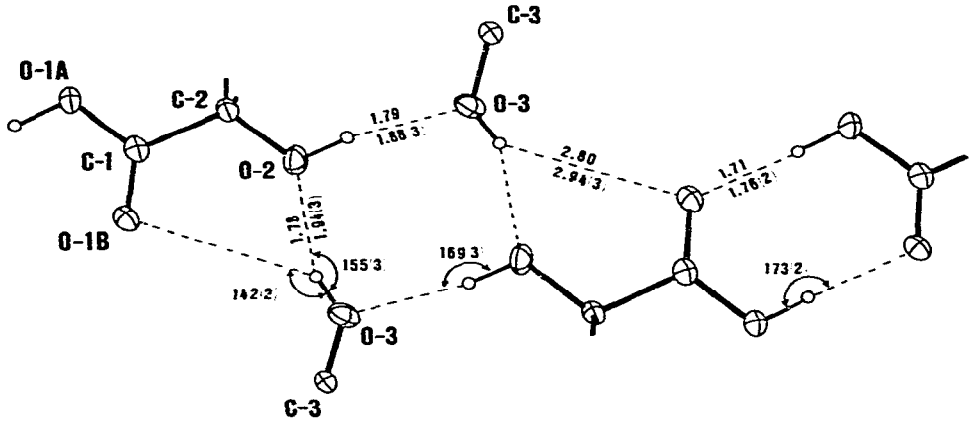

Fig. 2. Intermolecular hydrogen-bonding in the crystal structure of galactaric acid. [Observed values are given, with standard deviations in parentheses; those without standard deviations are normalized so that the O–H covalent-bond distances are the neutron diffraction value of 0.97 Å.]

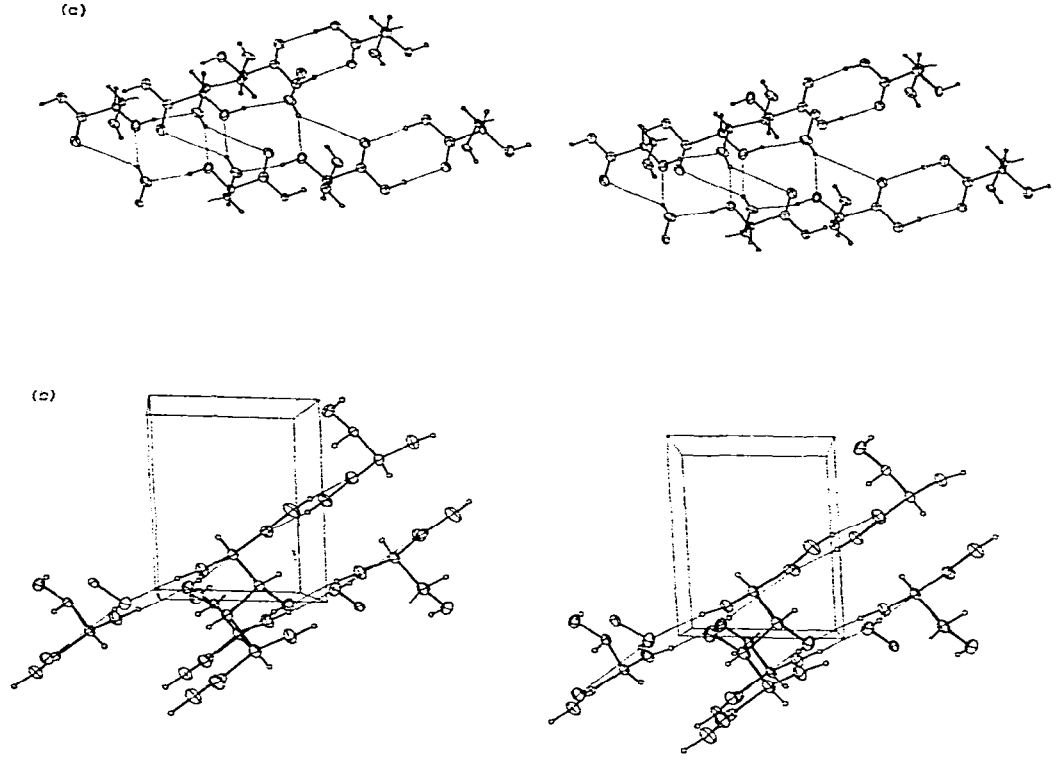

Fig. 3. Stereoviews of the crystal structure of galactaric acid. The thin lines are hydrogen bonds. (a) View down [010]. (b) View down [2$\bar{1}\bar{2}$].

inclined at 6° to each other and separated by 0.50 Å. These planes form the layers which are approximately parallel to the $(10\bar{2})$, shown edgewise in Fig. 3b. The layers are linked by the chains of molecules formed by the dimerized carboxylic acid groups, so that the separation of the layers is only 2.48 Å.

The hydrogen bonding of the carboxylic acid dimer is the same as that observed in the gas-phase, formic acid dimer[7], and in many other carboxylic acids, *e.g.*, benzoic[8], propanoic[9], butanoic[10], and pentanoic (valeric)[11] acid. It forms strong hydrogen bonds having H···O distances of ~1.70 Å, and is one of the two modes of hydrogen bonding commonly observed in carboxylic acids[12]. The alternative mode is that in which the carboxylic acid groups hydrogen-bond to form infinite chains.

The "square" system of hydrogen bonds is also common, being observed in pentaerythritol[13], and in 1,6-anhydro-β-D-mannopyranose[14], for example. The hydrogen-bond geometry is shown in Fig. 2. Using normalized, covalent O–H distances, the O–H···O hydrogen bonds have H···O lengths that are shorter than the standard value of 1.807 Å, the mean H···O distance for a cooperative O–H···O hydrogen bond obtained from a survey of neutron-diffraction, carbohydrate structures[15]. The weak, bifurcated, hydrogen-bond length of 2.80 Å is comparable to those observed between hydroxyl groups and carboxylate oxygen atoms in neutron-diffraction studies of the amino acids[16].

Both the carboxylic acid dimer and the four-hydroxyl, square system are examples of cyclic cooperative, or non-additive, hydrogen bonding, which has increased stability over alternative patterns involving isolated bonds, or finite or infinite chains[17]. The stability of cyclic, "homodromic" systems of hydrogen bonds has been pointed out by Saenger[18] in relation to the hydrogen bonding in the cyclomaltohexaose hydrates.

It is the combination of these two energetically favorable, hydrogen-bonding schemes in the same crystal structure, together with the exceptionally close stacking of the hydrogen-bonded layers, that is responsible for the high crystal density in this structure.

The low solubility in cold water can be explained in terms of an exceptionally large, crystal-lattice energy. This must exceed both that of the solvated molecules and the difference in entropy between the solid and solution states.

The pentitols and hexitols, which have hydrogen-bonded crystal structures involving all of the hydroxyl groups, have densities ranging from 1.47 to 1.54 $g.cm^{-3}$, and are all very soluble in water. The aliphatic dicarboxylic acids, in which only the carboxylic acid groups are hydrogen-bonded, have much lower densities, 1.1 to 1.2 $g.cm^{-3}$.

The lower members of the aldaric acids also have high densities, but this is not accompanied by low aqueous solubility. Glyceraric acid, $HO_2C–CHOH–CO_2H$ has a density of 1.84 $g.cm^{-3}$. In its crystal structure[19], the molecules are linked in chains by carboxylic acid dimer hydrogen-bonding, but these chains are separated by 4.4 Å, with no strong hydrogen-bonding between them. In fact, the hydroxyl

groups in that structure do not appear to be involved in other than weak interactions to neighboring carboxylic oxygen atoms at O···O separations of > 3 Å.

In tetraric acid crystals, which have densities of 1.65 to 1.75 g.cm^{-3}, the carboxylic acid dimer hydrogen-bonding is found on one side of the molecules only, both in the anhydrous, triclinic erythraric (*meso*) form and in the monoclinic *meso* monohydrate[20]. The other *meso* forms that have been analyzed[20], and D-threaric acid[21], have the alternative, infinite-chain type of hydrogen-bonding between the carboxylic acid groups.

Galactaric acid therefore seems to be unique, both in the combination of high density and low aqueous solubility, and in the exceptionally strong system of hydrogen bonds in its crystal structure.

ACKNOWLEDGMENTS

The authors are grateful to Dr. Martin Seidman of the A. E. Staley Company for bringing this interesting problem to our attention. This research was supported by the National Institutes of Health, U.S. Public Health Service, Grant No. GM-24526.

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