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The crystal structure of the molecular cocrystal *L*-malic acid *L*-tartaric acid (1/1)

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The synthesis and X-ray single crystal structure determination of the molecular cocrystal *L*-malic acid *L*-tartaric acid (1/1) **1**, the first example of a dimeric cocrystal incorporating two aliphatic carboxylic acids, are reported. $[\text{C}_4\text{H}_6\text{O}_5][\text{C}_4\text{H}_6\text{O}_6]$, triclinic, $P1$, $a = 4.835(1)$, $b = 6.488(1)$, $c = 9.227(1)$ Å, $\alpha = 73.83(1)$, $\beta = 88.32(1)$, $\gamma = 77.32^\circ$, $V = 271.06(8)$ Å³, $Z = 1$, $D_{\text{calc}} = 1.741$ Mg m⁻³, $T = 123(2)$ K, $\mu(\text{Mo-K}\alpha) = 0.169$ mm⁻¹. A total of 1238 reflections were measured and 1181 unique reflections were used in the refinement. The final parameters for observed data were $R = 0.030$, $R^2_w = 0.085$ and $R = 0.033$, $R^2_w = 0.134$ for all data. The competition between complimentary hydrogen-bond sites of the two acids, which results in the unexpected heteromeric complex, is discussed, and the observed packing arrangements, and the structural consequences arising from the presence of the extended hydrogen-bond networks, are examined in detail.

INTRODUCTION

L-tartaric acid and *L*-malic acid are two naturally occurring, chiral, dicarboxylic acids which have been closely linked to a range of important scientific discoveries during the last 150 years. From Pasteur's separation of crystalline enantiomers,¹ via chiral synthesis² and solid-state physics (ferroelectricity and nonlinear optics),³ to recent efforts in crystal engineering,⁴ the structure and properties of tartaric acid have provided considerable material for multidisciplinary research. Malic acid, an important contributor to several areas of biochemistry (e.g. the citric acid cycle and carbohydrate research), has also been employed as a building block of predictable anionic hydrogen-bonded motifs in crystal engineering.⁵ The endurance of the broad academic interest in these compounds is illustrated by the fact that, in the last four years, 336 and 296 papers have been abstracted under the keywords tartaric acid and malic acid, respectively. Much of this attention has its origin in the structures and hydrogen-bonding abilities of the two acids, both in solution and in the solid state.

The different 'versions' of tartaric acid, (the racemate, the two pure enantiomers and the *meso* compound), have previously been subjected to crystallographic examinations (X-ray and neutron) and the crystallographic literature also contains numerous examples of inorganic and organic salts of both the monovalent and the divalent anion.⁶ Although malic acid is, chemically, very similar, it has traditionally been very difficult to grow reasonably sized crystals of either malic acid itself, or of salts thereof.⁷ Despite these differences in crystal-growing ability, extant organic salts of hydrogentartrates and hydrogenmalates display considerable structural similarities. In most such salts, the anions create infinite, 2-D, layers, held together by two, or more, O-H ... O interactions. Neighbouring anions are invariably linked in a head-to-tail fashion into infinite chains via a short O-H ... O hydrogen bond.^{5,8} The consistency of these anionic networks (even in the presence of very different cations), has provided a basis for reliable 'scaffolding' for several new nonlinear optical materials.

The close resemblance between the structural behaviour of the two acids, both as molecular solids and in ionic compounds, in addition to their similar chemical properties, e.g. solubilities, pK_a-values, inspired our efforts to combine both molecules within the same framework in a molecular cocrystal.

RESULTS AND DISCUSSION

During our attempts at preparing a cocrystal of malic acid and tartaric acid, a range of experimental conditions (ratios and solvents) were used, but in most cases the product was simply a physical mixture of the two acids (as determined by X-ray powder diffraction). However, by mixing equimolar solutions (ethanol-water; 1:1) of the two acids, followed by slow evaporation of the

solvent, colourless rhombohedral crystals (mp. 161–162°C) were obtained. The powder X-ray diffraction pattern did not correspond to that of either of the starting materials, and the elemental analysis confirmed the presence of both acids. The crystal structure of this material was then determined using X-ray diffraction.

The single-crystal study showed that the rhombohedral crystals were indeed the desired compound, *L*-malic acid *L*-tartaric acid (1/1). Fractional atomic coordinates are listed in Table 1, and relevant bond distances and bond angles are presented in Table 2. The triclinic structure is held together by a complex network comprising seven unique hydrogen bonds, Table 3. There are no unexpected intramolecular geometric features; both acids display *trans* configurations of the C–C–C–C backbone (177.8° [malic acid], 177.2° [tartaric acid]), Fig. 1. There are, furthermore, no dramatic deviations from coplanarity between the carbonyl groups and the α -hydroxy group (9.4 to -15.93°). The most important intermolecular interactions are the four O...O hydrogen bonds which generate the two dimeric head-to-head motifs, $R_2^2(8)$,⁹ between neighbouring malic acid and tartaric acid molecules, Fig. 2. These interactions result in infinite, straight, chains composed of alternating malic acid and tartaric acid entities. The geometries of these

Table 1 Atomic coordinates [$\times 10^4$] and equivalent isotropic displacement parameters [$\text{Å}^2 \times 10^3$] for *L*. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U(\text{eq})$
O(11A)	1289(5)	5650(4)	11177(2)	19(1)
O(12A)	3259(5)	3613(4)	13421(2)	14(1)
C(1A)	3280(8)	4141(5)	12032(4)	12(1)
C(2A)	5621(9)	3145(6)	11164(4)	17(1)
C(3A)	4380(8)	2257(5)	9991(4)	15(1)
O(3A)	2707(6)	762(4)	10631(3)	21(1)
C(4A)	6805(7)	1348(5)	9103(3)	12(1)
O(41A)	7885(5)	2906(3)	8198(2)	17(1)
O(42A)	7614(5)	-618(4)	9220(3)	15(1)
O(11B)	2107(5)	7701(4)	7885(3)	18(1)
O(12B)	2491(6)	11204(4)	6867(2)	14(1)
C(1B)	3254(8)	9246(5)	6997(3)	13(1)
C(2B)	5634(8)	8289(5)	6107(4)	12(1)
O(2B)	7094(5)	9914(4)	5316(3)	14(1)
C(3B)	4416(8)	7256(5)	5022(3)	12(1)
O(3B)	2333(5)	8768(3)	4006(2)	14(1)
C(4B)	6843(8)	6426(5)	4102(4)	13(1)
O(41B)	8814(5)	4882(4)	4955(2)	16(1)
O(42B)	6935(5)	7167(4)	2732(2)	15(1)
H(11A)	-171(5)	6200(4)	11820(2)	23
H(21A)	6436(9)	4456(6)	10623(4)	20
H(22A)	6961(9)	2035(6)	11823(4)	20
H(3A)	3162(8)	3471(5)	9218(4)	18
H(30A)	3971(6)	-362(4)	11414(3)	25
H(41A)	9348(5)	2275(3)	7824(2)	20
H(11B)	771(5)	8364(4)	8398(3)	21
H(2B)	6949(8)	7085(5)	7014(4)	15
H(20B)	5888(5)	10959(4)	4825(3)	17
H(3B)	3642(8)	6167(5)	5616(3)	15
H(30B)	818(5)	9053(3)	4591(2)	17
H(41B)	10438(5)	4350(4)	4401(2)	20

Table 2 Bond lengths [Å] and angles [°] for *L*

<i>O(11A)</i> - <i>C(1A)</i>	1.307(4)	<i>O(12A)</i> - <i>C(1A)</i>	1.231(4)
C(1A)-C(2A)	1.501(5)	C(2A)-C(3A)	1.549(4)
C(3A)-O(3A)	1.393(5)	C(3A)-C(4A)	1.518(4)
C(4A)-O(42A)	1.224(4)	C(4A)-O(41A)	1.314(4)
O(11B)-C(1B)	1.320(4)	O(12B)-C(1B)	1.215(4)
C(1B)-C(2B)	1.517(5)	C(2B)-O(2B)	1.418(5)
C(2B)-C(3B)	1.542(4)	C(3B)-O(3B)	1.402(4)
C(3B)-C(4B)	1.519(4)	C(4B)-O(42B)	1.225(4)
C(4B)-O(41B)	1.310(4)		
O(12A)-C(1A)-O(11A)	123.0(3)	O(12A)-C(1A)-C(2A)	123.2(3)
O(11A)-C(1A)-C(2A)	113.7(3)	C(1A)-C(2A)-C(3A)	110.2(3)
O(3A)-C(3A)-C(4A)	113.4(3)	O(3A)-C(3A)-C(2A)	113.1(3)
C(4A)-C(3A)-C(2A)	108.3(3)	O(42A)-C(4A)-O(41A)	124.7(3)
O(42A)-C(4A)-C(3A)	123.0(3)	O(41A)-C(4A)-C(3A)	112.3(3)
O(12B)-C(1B)-O(11B)	125.2(4)	O(12B)-C(1B)-C(2B)	123.2(3)
O(11B)-C(1B)-C(2B)	111.6(3)	O(2B)-C(2B)-C(1B)	111.0(3)
O(2B)-C(2B)-C(3B)	111.4(3)	C(1B)-C(2B)-C(3B)	109.4(3)
O(3B)-C(3B)-C(4B)	107.5(2)	O(3B)-C(3B)-C(2B)	113.0(2)
C(4B)-C(3B)-C(2B)	107.5(3)	O(42B)-C(4B)-O(41B)	125.0(4)
O(42B)-C(4B)-C(3B)	123.1(3)	O(41B)-C(4B)-C(3B)	111.9(3)

four hydrogen bonds ($r[\text{O} \cdots \text{O}] < 2.69 \text{ Å}$, $\angle (\text{DH} \cdots \text{A}) > 165^\circ$) provide evidence for the relative strength of these selective hydrogen bonds. As expected, neighbouring chains are crosslinked *via* an O...O interaction between hydroxy groups of adjacent tartaric acid molecules, to form a 2-D, flat, layer, Fig. 2. Neighbouring layers are, in turn, crosslinked *via* two hydrogen bonds, Fig. 3, resulting in a compact 3-D structure ($D_{\text{calc}} = 1.74 \text{ g cm}^{-3}$). There are no hydrogen-bond interactions between adjacent malic acid molecules, but tartaric acid molecules are linked through one hydrogen bond involving the 'surplus' hydroxy moiety. In comparison, the crystal structure of *L*-tartaric acid¹⁰ itself displays a complex 3-D network but without the commonly occurring (among carboxylic acids) head-to-head motif. The structure of *L*-malic acid¹¹ (hydrogen atoms were not located) displays a 3-D network incorporating the hydrogen-bonded head-to-head motif, with an overall packing which is very similar to that observed in **1**.

The appearance of a cocrystal is rarely the result of a straightforward mixture of two, or more, components. In order to obtain a heteromeric cocrystal, the interactions between the two components, must be stronger than the attractive forces that exist between the homomeric as-

Table 3 Geometric parameters for the hydrogen bonds in **1**^a

<i>D</i> - <i>H</i> ... <i>A</i>	$r(\text{H} \cdots \text{A})/\text{Å}$	$r(\text{D} \cdots \text{A})/\text{Å}$	$(\text{DH} \cdots \text{A})^\circ$
O(11A)-H ... O(42B)'	1.702(3)	2.676(3)	171.3(1)
O(3A)-H ... O(42B)''	2.027(3)	2.999(3)	170.2(1)
O(41A)-H ... O(12B)'''	1.836(4)	2.684(4)	173.8(1)
O(11B)-H ... O(42A)''''	1.764(4)	2.641(4)	166.6(1)
O(2B)-H ... O(12A)'''''	2.038(3)	2.856(3)	173.2(1)
O(3B)-H ... O(2B)''''''	1.923(3)	2.815(3)	164.8(1)
O(41B)-H ... O(12A)'''''''	1.670(3)	2.644(3)	176.1(1)

^aSymmetry elements: (') $x - 1, y, z + 1$; (')' $x, y - 1, z + 1$; (''') $x + 1, y - 1, z$; (''''') $x - 1, y + 1, z$; (''''''') $x, y + 1, z - 1$; (''''''''') $x - 1, y, z$; (''''''''''') $x + 1, y, z - 1$.

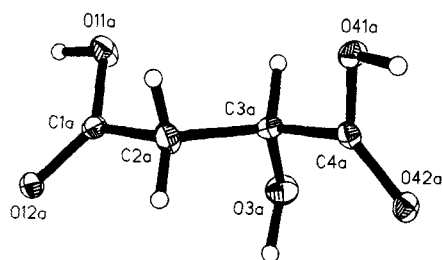
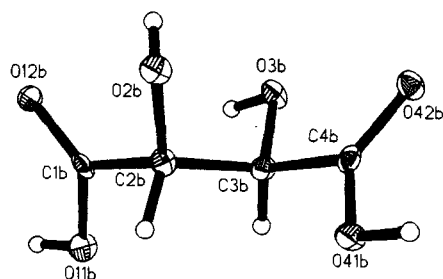


Figure 1 Geometry, labelling scheme and thermal ellipsoids (50%) for the cocystal *L*-malic acid *L*-tartaric acid (1/1) **1**.

semblies. Also, if the reaction is carried out in solution, the solubilities of the starting materials must be very similar. A possible key to the successful preparation of *L*-malic acid *L*-tartaric acid, is the collection of short, and nearly linear, head-to-head dimeric interactions (O-H...O hydrogen bonds) that dominate the crystal structure of **1**. Furthermore, the number of unique intermolecular hydrogen bonds is seven in **1**, six in malic acid and four in tartaric acid. An illustration of the thermodynamic balance between the acids and the cocystal, is provided by a series of lattice energy calculations. Using charge equilibrium charges¹² and the Universal force-field,¹³ as implemented in the Crystal Packer module within Cerius², the lattice energies for malic acid, tartaric acid and **1**, are *ca.* 80, 125 and 160 kJ mol⁻¹, respectively. The value for malic acid is based upon estimated hydrogen-atom positions, and may therefore be somewhat unreliable, but there are nevertheless some significant differ-

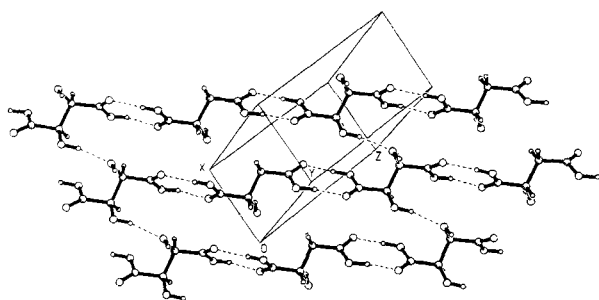


Figure 2 Face-on view of the hydrogen bonded layer in **1**, incorporating the dimeric, head-to-head, interactions between neighbouring malic acid and tartaric acid molecules, and the O...O crosslink between adjacent chains. (See color plate I.)

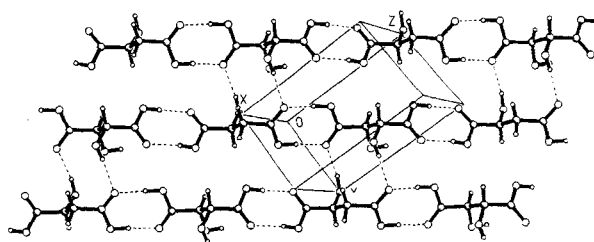


Figure 3 Edge-on view of the dominating structural planes in **1**, showing the two hydrogen-bonded interactions between adjacent layers. (See color plate II.)

ences between the three compounds, favouring the formation of **1**.

Several important lines of work can be identified as a result of the synthesis and structure determination of **1**. First of all, the physical properties of the cocystal *e.g.* optical and electrical, must be examined. Secondly, it may also be possible to incorporate both hydrogenmalate and hydrogentartarate anions within the same ionic framework, either with divalent, or monovalent cations.¹⁴ This also introduces the exciting possibility of combining several different stereochemical 'versions' of the two anions in order to induce subtle changes to the anionic scaffolding, a feature which is critical in crystal engineering.

EXPERIMENTAL SECTION

Data collection

C₈H₁₂O₁₁, *M_w* = 284.18, triclinic, *P*1, *Z* = 1, *a* = 4.835(1), *b* = 6.488(1), *c* = 9.227(1) Å, α = 73.83(1), β = 88.32(1), γ = 77.32°, *V* = 271.06(8) Å³, *Z* = 1, *F*(000) = 148, *D*_{calc} = 1.741 Mg m⁻³, *T* = 123(2) K, μ(Mo-Kα) = 0.169 mm⁻¹.

Data were collected using a Siemens P4 four-circle diffractometer with graphite monochromated Mo-Kα radiation. Crystal stability was monitored every 100 reflections and there were no significant variations (±1%). Cell parameters were obtained from 35 accurately centred reflections in the 2θ-range 10–28°. ω scans were employed for the data collection, and Lorentz and polarization corrections were applied. A total of 1238 reflections were measured for 2.3 < 2θ < 25.0° and -5 ≤ *h* ≤ 1, -7 ≤ *k* ≤ 7, -10 ≤ *l* ≤ 10, and 1181 unique reflections with |*F*²| > 3σ(*F*²) were used in the refinement where σ(*F*²) = {σ(*I*) + (0.04*I*)²}^{1/2}/*Lp*. The configuration for the cocystal was determined by the fact that enantiomerically pure *L*-malic acid and *L*-tartaric acid were used as starting materials.

Structure determination

The structure was solved by direct methods and the non-hydrogen atoms were refined with anisotropic ther-

mal parameters by full-matrix least-squares. Hydrogen atom positions were located from difference Fourier maps. A riding model with fixed thermal parameters ($U_{ij} = 1.2U_{eq}$) was used for subsequent refinement. The function minimized was $\sum[\omega(|F_0|^2 - |F_c|^2)]$ with reflection weights $\omega^{-1} = [\sigma^2|F_0|^2 + (g_1P)^2 + (g_2P)]$ where $P = [\max |F_0|^2 + 2|F_c|^2]/3$. Final parameters for observed data were $R = 0.0303$, $R_w^2 = 0.0855$ and $R = 0.0337$, $R_w^2 = 0.1344$ for all data. $S = 1.125$, 172 variables, $(\Delta\rho)_{\max, \min} = 0.299, -0.249 \text{ e } \text{Å}^{-3}$ on a final difference map. The XSCANS, SHELXTL PC and SHELXL-93 packages were used for data reduction and structure solution and refinement.

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