Brucine salts of L-α-hydroxy acids: brucinium hydrogen (S)-malate pentahydrate and anhydrous brucinium hydrogen (2R,3R)-tartrate at 130 K

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The structures of two brucinium (2,3-dimethoxy-10-oxostrychnidinium) salts of the α-hydroxy acids l-malic acid and l-tartaric acid, namely brucinium hydrogen (S)-malate pentahydrate, C 4 H 4 N 2 O 7 - C 4 H 7 O 4 2- - 7 H 2 O, (I), and anhydrous brucinium hydrogen (2R,3R)-tartrate, C 4 H 7 N 2 O 7 - C 4 H 7 O 4 2- - (II), have been determined at 130 K. Compound (I) has two brucinium cations, two hydrogen malate anions and ten water molecules of solvation in the asymmetric unit, and forms an extensively hydrogen-bonded three-dimensional framework structure. In compound (II), the brucinium cations form the common undulating brucinium sheet substructures, which accommodate parallel chains of head-to-tail hydrogen-bonded tartrate anion species in the interstitial cavities.

Comment

Although the crystal structures of the strychnine salts of both D-tartaric acid [strychninium hydrogen (2S,3S)-tartrate trihydrate] and L-tartaric acid [bis(strychninium) (2R,3R)-tartrate hexahydrate] have been reported by Gould et al. (1987), surprisingly no brucinium tartrate salts are known. Although brucine is well known as an agent for the resolution of chiral species from enantiomeric mixtures of many organic molecule types, including α-hydroxy acids (Wilén, 1972), it is not considered the usual one for the simple series analogues, which include glyceral, malic and tartaric acids. However, the reported resolution of L-glyceric acid from a racemic mixture of the acid and the structure determination of its brucinium salt by Białońska et al. (2005) prompted us to attempt similar resolutions with malic and tartaric acids. We subsequently

Figure 1

The molecular configuration and atom-numbering scheme for the two independent brucinium cations (A and B) in the asymmetric unit in (I). Non-H atoms are shown as 40% probability displacement ellipsoids.
obtained crystals of brucinium hydrogen 1-malate penta-
hydrate, (I), by simple refluxing of brucine with d,l-malic acid
in 50% ethanol–water. The resolution of d,l-tartaric acid was
not as successful under these conditions, so the reaction with
tartaric acid was completed in 50% 2-propanol–water. The
use of 2-propanol rather than ethanol was also to test the
observation of Sada et al. (1998) that this solvent promoted the
 crystallization of brucinium carboxylates, often with incor-
poration of 2-propanol molecules of solvation. However, with
our preparation, the well formed clusters of crystals obtained
were found to have no molecules of solvation, giving bruci-
nium hydrogen 1-tartrate, (II). The structures of both (I) and
(II) are reported here.

The structure determination of (I) confirmed the presence
of two independent brucinium cations (A and B) (Fig. 1), two
hydrogen 1-malate anions (C and D, having the expected S
configuration and being conformationally similar; Table 1) and
ten water molecules of solvation (Fig. 2) in the crystal-
lographic asymmetric unit. In (I), as well as in (II) (Fig. 3),
the atom-numbering scheme for the brucine cage follows the
original Robinson convention employed for styrchnine
(Holmes, 1952). In both (I) and (II), this gives the overall
Cahn–Ingold–Prelog absolute configuration for the proto-
nated brucinium species as C7(S), C8(S), C12(S), C13(R),
C14(R), C16(S) and N19(S). In the hydrogen malate anions in
(I), the carboxylic acid group adjacent to the α-hydroxy group is
preferentially deprotonated on the basis of its decreased
pKa value compared with the C4 carboxylic acid group
(Tapscott, 1982). This is consistent with observations for other
dydrogen malates, e.g. ammonium hydrogen (S)-malate
(Verschel et al., 1978).

The isolation of the enantiomeric 1-malate salt of (I)
represents a facile resolution from d,l-malic acid using
brucine, which has not previously been considered among
recognized resolving agents for this acid. More commonly,
1-phenylethylamine or cinchonine have been the agents of
choice for the resolution of both d- and l-malic acid, while
both of these, as well as quinine, have been used for d-malic
acid resolution (McKenzie et al., 1923; Newman, 1981). The
structures of the three configurational isomers 1-phenylethylaminiun d-, l- and d,l-malate have been reported
(Turkington et al., 2004). In (I), the cations, anions and water
molecules form an extensively hydrogen-bonded three-
dimensional framework structure (Fig. 4 and Table 2). This
structure is in many respects [viz. space group (P1), unit-cell
dimensions and contents] similar to the structures of both

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**Figure 2**
The molecular configuration and atom-numbering scheme for the two
1-malate anions (C and D) and the ten water molecules of solvation in (I).
Non-H atoms are shown as 40% probability displacement ellipsoids.

**Figure 3**
The molecular configuration and atom-numbering scheme for the brucinium cation and the hydrogen 1-tartrate anion in (II). The intramolecular hydroxy–carboxyl O–H · · · O hydrogen bond in the tartrate anion is shown as a broken line. Non-H atoms are shown as 40% probability displacement ellipsoids.
brucinium 1-glycerate 4.75-hydrate (Bialońska et al., 2005) and brucinium citrate pentahydrate (Smith et al., 2005). In brucine compounds generally, the brucine species commonly form regular undulating parallel or antiparallel host sheet substructures built from partially overlapping head-to-tail molecular associations (Gould & Walkinshaw, 1984; Dijksma, Gould, Parsons, Taylor & Walkinshaw, 1998; Bialońska & Ciunik, 2004). However, in (I), there is no such directional substructuring, although, as with the 1-glycerate and citrate compounds, there is significant structuring within the guest cavity, including numerous cyclic and extended-chain water–water and water–anion hydrogen-bonding interactions. In addition, in (I), there are brucine $N^+ - H \cdots O$(malate) interactions (four-centred in A and three-centred in B) and malate $O - H \cdots O$(brucine) host–guest interactions.

The brucine molecules in (II) form the previously described parallel-mode substructures, which in (II) extend along the $a$ direction in the unit cell, with a dimeric repeat of ca 12.27 Å and a chain offset angle $\alpha$ (Smith et al., 2006) of ca 118° (Fig. 5). These values compare with 12.66 Å and 123°, respectively, in the similar parallel-mode brucinium d-glucuronate structure (Dijksma, Gould, Parsons & Walkinshaw, 1998). The inter-sheet cavities accommodate the hydrogen tartrate anion species, which form parallel chain structures through head-to-tail cyclic $K_2(9)$ hydrogen-bonding interactions (Table 4). These associations incorporate an intramolecular tartrate $O21T$(hydroxy)–$H \cdots O11T$(carboxyl) hydrogen bond (Table 4). The chains are linked peripherally to the brucinium cation substructure through $O$(hydroxy)–$H \cdots O$(carbonyl) and $N^+$(brucine)–$H \cdots O$(carboxyl) interactions, giving a three-dimensional cage structure. The tartrate chains in (II) are similar to the succinate chain substructure found in styrchnidinium hydrogen succinate (Maurin et al., 2006). In this analysis, the accepted $2R,3R$ absolute configuration is confirmed for the L-tartrate residue, which also adopts an extended conformation (Table 3).

**Experimental**

The two title compounds were synthesized by heating 1 mmol quantities of either $\alpha,\alpha$-malic acid for (I) or $\alpha$-tartaric acid for (II) and brucine tetrahydrate in 50 ml of either 50% ethanol–water for (I) or 50% 2-propanol–water for (II) for 10 min under reflux. Compound (I) was obtained as colourless plates (m.p. 493.5–495.8 K), while (II) was obtained as clusters of colourless prisms (m.p. 522.4–523.6 K), after partial room-temperature evaporation of the solvent.

**Compound (I)**

**Crystal data**

$C_{23}H_{27}N_2O_5$$^+$-C$_2$H$_6$O$_5$$^-$$^\cdot$5H$_2$O

$M_r = 618.63$

Triclinic, $\text{P}1$

$a = 9.2915$ (10) Å

$b = 9.4337$ (9) Å

$c = 16.9287$ (17) Å

$\alpha = 76.401$ (2°)

$\beta = 88.716$ (2°)

$\gamma = 82.104$ (2°)

$V = 1428.5$ (3) Å$^3$

$Z = 2$

$D_\text{c} = 1.383$ Mg m$^{-3}$

Mo $\text{K}_α$ radiation

$\mu = 0.12$ mm$^{-1}$

$T = 130$ (2) K

Plate, colourless

$0.40 \times 0.35 \times 0.05$ mm

**Data collection**

Bruker CCD area-detector

Diffraction

5034 independent reflections

4397 reflections with $I > 2\sigma(I)$

$\theta$ and $\omega$ scans

5714 measured reflections

$\theta_{\text{max}} = 25.0°$

**Refinement**

Refinement on $F^2$

$R(F^2) = 0.036$

$wR(F^2) = 0.072$

$S = 0.90$

5034 reflections

772 parameters

H-atom parameters constrained

$\Delta_{\text{max}} = 0.17$ e Å$^{-3}$

$\Delta_{\text{min}} = -0.18$ e Å$^{-3}$

**Table 1**

Selected torsion angles (°) for (I).

<table>
<thead>
<tr>
<th>O11C–C11C–C21C</th>
<th>1.1 (4)</th>
<th>O11D–C11D–C21D</th>
<th>1.1 (4)</th>
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<tr>
<td>O11C–C11C–C21C</td>
<td>1.1 (4)</td>
<td>O11D–C11D–C21D</td>
<td>1.1 (4)</td>
</tr>
<tr>
<td>O12C–C12C–C21C</td>
<td>125.0 (3)</td>
<td>O12D–C12D–C21D</td>
<td>157.3 (3)</td>
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<tr>
<td>O12C–C12C–C21C</td>
<td>179.3 (3)</td>
<td>O12D–C12D–C21D</td>
<td>175.7 (3)</td>
</tr>
<tr>
<td>O12C–C12C–C21C</td>
<td>56.8 (4)</td>
<td>O12D–C12D–C21D</td>
<td>54.2 (4)</td>
</tr>
<tr>
<td>C11C–C21C–C11C</td>
<td>-62.9 (6)</td>
<td>C11D–C21D–C11D</td>
<td>128.1 (3)</td>
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<tr>
<td>C11C–C21C–C11C</td>
<td>62.7 (4)</td>
<td>C11D–C21D–C11D</td>
<td>66.7 (4)</td>
</tr>
<tr>
<td>C21C–C11C–C21C</td>
<td>-169.1 (3)</td>
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<td>90.0 (5)</td>
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<tr>
<td>C21C–C11C–C21C</td>
<td>11.8 (5)</td>
<td>C21D–C11D–C21D</td>
<td>171.8 (3)</td>
</tr>
</tbody>
</table>


Smith et al. • C$_2$H$_8$N$_2$O$_5$$^+$-C$_2$H$_6$O$_5$$^-$$^\cdot$5H$_2$O and C$_2$H$_7$N$_2$O$_5$$^+$-C$_4$H$_8$O$_6$$^-$. o355

Figure 4

The packing of (I), viewed down the $a$ axial direction, showing hydrogen-bonding interactions as broken lines. Non-interactive H atoms have been omitted. For symmetry codes, see Table 2.

Figure 5

A perspective view of the packing of (II), viewed approximately down the $b$ axial direction. Non-interactive H atoms have been omitted. For symmetry codes, see Table 4.
Table 2

<table>
<thead>
<tr>
<th>D—H⋯⋅A</th>
<th>D—H</th>
<th>H⋯⋅A</th>
<th>D—A</th>
<th>D—H⋯⋅A</th>
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</thead>
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<td>N1—H1—O1—C1</td>
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<td>N1—H1—O1—C2</td>
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<td>2.36</td>
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<td>N1—H1—O2—C4</td>
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<td>2.59</td>
<td>3.097 (4)</td>
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<td>N1—H1—O1—C3</td>
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<td>2.759 (4)</td>
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<td>N1—H2—O1—C6</td>
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<td>2.51</td>
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<tr>
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<td>1.82</td>
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<tr>
<td>O4—C1—H1—C5</td>
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<td>1.73</td>
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<td>2.826 (4)</td>
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<td>1.91</td>
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<td>1.83</td>
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<td>1.95</td>
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<tr>
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<td>2.712 (5)</td>
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<td>1.76</td>
<td>2.659 (4)</td>
<td>179</td>
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<tr>
<td>O4—H1—O1—O13</td>
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<td>2.808 (4)</td>
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<td>2.799 (5)</td>
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<td>1.76</td>
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<td>O10—H1—O1—O12</td>
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<td>1.92</td>
<td>2.795 (5)</td>
<td>160</td>
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<tr>
<td>O10—H1—O1—O13</td>
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<td>1.94</td>
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<td>0.97</td>
<td>2.60</td>
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</tr>
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</table>

Symmetry codes: (i) x + 1/2, y, z + 1; (ii) x − 1/2, y, z; (iii) x, y − 1, z; (iv) x, y, z − 1; (v) x + 1, y, z; (vi) x, y + 1, z.

Table 3

| O11—C7—C17—O217 | −161.2 (2) |
| O11—C17—C7—C37 | 59.5 (2) |
| O127—C17—C7—O317 | 63.1 (2) |
| O127—C7—C17—O217 | 164.6 (2) |
| O11—C17—C7—C137 | −149.7 (17) |
| O11—C7—C37—O417 | 44.2 (2) |
| O11—C7—C17—C137 | −175.5 (18) |
| O11—C7—O317—O217 | −117.85 (18) |
| O11—C7—C17—O317 | 62.2 (2) |

H atoms potentially involved in hydrogen-bonding interactions were generally located by difference methods or, in the case of (I), where the water H atoms could not be located by difference methods, positioned in their probable interactive sites. For (II), both positional and isotropic displacement parameters for the interactive H atoms were refined. However, for (II), because of the low reflection/refined parameter ratio, the interactive H atoms were fixed in the final cycle of refinement. Other brucine and hydroxy H atoms in both (I) and (II) were included at calculated positions (aromatic C—H = 0.93 Å and aliphatic C—H = 0.96–1.00 Å) and treated as riding $U_{eq}(H) = 1.2U_{eq}(C)$. In both structures, Friedel pairs were averaged for the data used in the refinements. The absolute configuration determined for the parent strychnine (Peerdeman, 1956) was invalid.

For both compounds, data collection: SMART (Bruker, 2000); cell refinement: SMART; data reduction: SAINT (Bruker, 1999); program(s) used to solve structure: SHELXL97 (Sheldrick, 1997) in WinGX (Farrugia, 1999); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997) in WinGX; molecular graphics: PLATON (Spek, 2003); software used to prepare material for publication: PLATON.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: G23010). Services for accessing these data are described at the back of the journal.

References


Smith et al. C$_2$H$_5$Ni$_2$O$_6$$^+$C$_6$H$_5$O$_3$$^-$·5H$_2$O and C$_{21}$H$_{15}$Ni$_2$O$_8$$^+$C$_4$H$_3$O$_6$$^-$