

## (*R*)-Mandelic acid (*S*)-alanine hemihydrate

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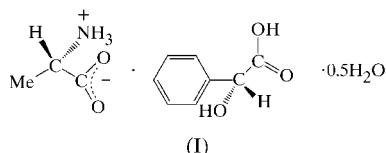
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Crystals of the title complex,  $C_3H_7NO_2 \cdot C_8H_8O_3 \cdot 0.5H_2O$ , were obtained from an aqueous solution containing racemic mandelic acid and (*S*)-alanine. The unit cell includes two independent molecular complexes and one water molecule. The structure formed by (*R*)-mandelic acid and (*S*)-alanine in a 1:1 molar ratio shows the successful optical separation of racemic mandelic acid. Strong hydrogen bonding, with a rather short O...O separation of 2.494 (3) Å, is observed between the carboxyl and carboxylate groups. A structural comparison suggests that the strong hydrogen bonding affects the neighbouring covalent bond.

### Comment

Optical resolution of racemic mandelic acid has been performed using chiral separating reagents, such as (*S*)-2-benzylaminobutanol (Kozma *et al.*, 2000) and (1*R*,3*S*)-camphoramic acid (Hu *et al.*, 2001). Recently, we separated racemic mandelic acid using (*S*)-alanine as the separating reagent. The crystal structure of the title complex, (I), shows this successful optical resolution.



The structure of (I) is shown in Fig. 1. The structure has two independent (*R*)-mandelic acid molecules, two independent (*S*)-alanine molecules and one water molecule in the unit cell.

The (*R*)-mandelic acid molecules have almost identical structures. The C—O(hydroxy) bond is *syn* to the C=O bond of the carboxyl group, with an O(H)—C—C=O torsion angle of 14.3 (3)° in the C1-mandelic acid molecule and an angle of

8.5 (3)° in the C12-mandelic acid molecule. This is in agreement with data for (*R*)-mandelic acid reported previously by Wei & Ward (1977).

An intramolecular hydrogen bond (O3—H3...O2) between the hydroxy and carboxyl groups is observed in the C1-mandelic acid molecule but not in the C12-mandelic acid molecule, the hydroxy group (O8—H14) in the C12-mandelic acid forming an intermolecular hydrogen bond with a carboxyl group from a neighbouring mandelic acid molecule, as shown in Fig. 1. This is the most distinct structural difference between the two mandelic acid molecules in (I).

Both (*S*)-alanine molecules display the normal inner-salt structure (Destro *et al.*, 1988). The difference of 0.017 (4) Å in the C—O bond distances observed in the C20-alanine molecule agrees well with the difference of 0.016 (2) Å determined by neutron diffraction (Lehmann *et al.*, 1972), but is significantly smaller than the difference of 0.040 (4) Å between C—O bond distances in the C9-alanine molecule in (I). This may result from the strong hydrogen bonding, discussed below.

An extensive hydrogen-bond network exists in the crystal structure of (I), with all O and N atoms involved in the network. A strong hydrogen bond with a rather short O1...O5 separation of 2.494 (3) Å is observed between the carboxyl group of the C1-mandelic acid molecule and the carboxylate group of the C9-alanine molecule, which is comparable with the value of 2.501 (2) Å found between mandelic acid and mandelate (Larsen & Lopez de Diego, 1993).

Several structures of compounds containing mandelic acid, mandelate or alanine have been reported to date, all with the carboxylate group involved in the hydrogen bonding (Larsen & Lopez de Diego, 1993; Lopez de Diego, 1995; Okamura *et al.*, 1997). A structural comparison reveals that the shorter the

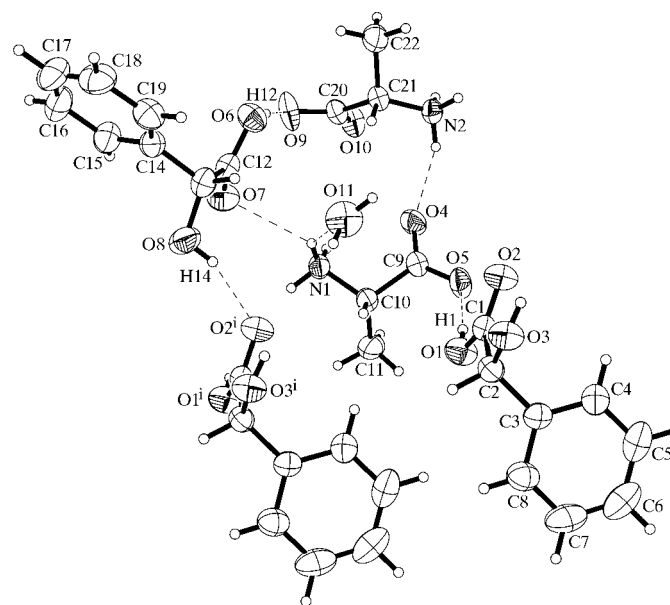


Figure 1

The structure of (I), drawn with 50% probability displacement ellipsoids. The dashed lines indicate the intermolecular hydrogen bonds [symmetry code: (i) 1 + x, y, z].

donor–acceptor separation in the hydrogen bond, the larger the difference between the C–O bond distances in the carboxylate group. For example, a short hydrogen-bond O···O separation of 2.501 (2) Å corresponds to a large difference of 0.040 (2) Å between the C–O bond distances in the carboxylate (Larsen & Lopez de Diego, 1993), whereas a long (normal) hydrogen-bond N···O separation of 2.813 (1) Å corresponds to a small difference of 0.016 (2) Å between the C–O bond distances in the carboxylate (Lehmann *et al.*, 1972). This conclusion also agrees well with the present work; the large difference of 0.040 (4) Å between the O5–C9 and O4–C9 bonds corresponds to the short O1···O5 separation of 2.494 (3) Å, and the small difference of 0.017 (4) Å between the O9–C20 and O10–C20 bonds corresponds to the long O6···O9 separation of 2.554 (3) Å. These facts may point to the effect of a strong hydrogen bond on the neighbouring covalent bond (Larsen & Lopez de Diego, 1993).

Several bifurcated hydrogen bonds are observed in the structure of (I). The O3–H3 hydroxy group, in addition to being the acceptor linking to an amine group from the adjacent alanine molecule, acts as a bifurcated hydrogen-bond donor, intramolecularly to the C1=O2 group and intermolecularly to the C20–O10 carboxyl group from an adjacent alanine molecule. The other hydroxy group, O8–H14, is involved in a similar hydrogen-bonding network. In addition to being the donor linking to the C1–O2 carboxyl group from a neighbouring mandelic acid molecule, the O8–H14 group also acts as a bifurcated hydrogen-bond acceptor, intermolecularly to both the adjacent N2-amine group and the solvate water molecule. The water molecule also acts as both acceptor and donor, with both H atoms involved in the hydrogen bonding. It is notable that, of the carboxyl groups involved in the stronger hydrogen bonds, O1–H1 and O6–H12 serve only as donors.

## Experimental

Racemic mandelic acid (1.52 g, 10 mmol) and (*S*)-alanine (0.89 g, 10 mmol) were dissolved in turn in hot water (10 ml) with continuous stirring. The solution was kept at room temperature and powder crystals were obtained from the solution after 2 d. These crystals were separated from the solution and dried *in vacuo* at 333 K. The C, H and N contents were analyzed using an Eager 200 elemental analysis instrument. Analysis calculated for C<sub>22</sub>H<sub>32</sub>N<sub>2</sub>O<sub>11</sub>: C 52.75, H 6.44, N 5.59%; found: C 52.80, H 6.40, N 5.60%. The specific optical rotation [ $\alpha$ ]<sub>D</sub> of –78.8° (H<sub>2</sub>O, *c* = 0.19) was determined using a Wzz-1s instrument for the powder crystal sample. Recrystallization was performed from an aqueous solution at room temperature and well-shaped single crystals of complex (I) were obtained after one week. This crystal was used in the X-ray diffraction experiment. In order to investigate whether the optical separation procedure was successful, a small amount of (I) was dissolved in water and the pH of the solution was adjusted to 2 with dilute HCl; the solution was then kept in a refrigerator. Colourless crystals of a different shape were obtained. The specific optical rotation [ $\alpha$ ]<sub>D</sub> of –153.9° (H<sub>2</sub>O, *c* = 0.35) agrees well with that of (*R*)-mandelic acid (Swinney *et al.*, 1999), showing that the complex crystals do not include (*S*)-mandelic acid.

## Crystal data

C<sub>3</sub>H<sub>7</sub>NO<sub>2</sub>·C<sub>8</sub>H<sub>8</sub>O<sub>3</sub>·0.5H<sub>2</sub>O  
*M<sub>r</sub>* = 250.25  
 Triclinic, *P*1  
*a* = 6.0193 (11) Å  
*b* = 8.2285 (10) Å  
*c* = 12.5811 (11) Å  
 $\alpha$  = 82.545 (9)°  
 $\beta$  = 86.000 (14)°  
 $\gamma$  = 89.752 (13)°  
*V* = 616.36 (15) Å<sup>3</sup>

*Z* = 2  
*D<sub>x</sub>* = 1.348 Mg m<sup>–3</sup>  
 Mo *K*α radiation  
 Cell parameters from 20 reflections  
 $\theta$  = 4.9–9.8°  
 $\mu$  = 0.11 mm<sup>–1</sup>  
*T* = 298 (2) K  
 Prism, colourless  
 0.60 × 0.55 × 0.30 mm

## Data collection

Rigaku AFC-7S diffractometer  
 $\omega/2\theta$  scans  
 2617 measured reflections  
 2436 independent reflections  
 2011 reflections with *I* > 2σ(*I*)  
*R*<sub>int</sub> = 0.016  
 $\theta_{\max}$  = 26°

*h* = 0 → 7  
*k* = –10 → 10  
*l* = –15 → 15  
 3 standard reflections  
 every 150 reflections  
 intensity decay: 0.3%

## Refinement

Refinement on *F*<sup>2</sup>  
*R*[*F*<sup>2</sup> > 2σ(*F*<sup>2</sup>)] = 0.030  
*wR*(*F*<sup>2</sup>) = 0.084  
*S* = 1.04  
 2436 reflections  
 324 parameters  
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0474P)^2 + 0.0307P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\max} = 0.010$   
 $\Delta\rho_{\max} = 0.14 \text{ e } \text{Å}^{-3}$   
 $\Delta\rho_{\min} = -0.15 \text{ e } \text{Å}^{-3}$

**Table 1**

Selected geometric parameters (Å, °).

O1–C1	1.296 (3)	O6–C12	1.309 (3)
O2–C1	1.223 (3)	O7–C12	1.210 (3)
O4–C9	1.224 (3)	O9–C20	1.252 (3)
O5–C9	1.264 (3)	O10–C20	1.235 (3)
O2–C1–O1	124.8 (3)	O7–C12–O6	124.5 (3)
O4–C9–O5	125.5 (2)	O10–C20–O9	126.1 (2)

**Table 2**

Hydrogen-bonding geometry (Å, °).

<i>D</i> –H··· <i>A</i>	<i>D</i> –H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> –H··· <i>A</i>
O1–H1···O5	0.82	1.68	2.494 (3)	174
O11–H1W···O10 <sup>i</sup>	0.93	2.03	2.924 (3)	160
O11–H2W···O7 <sup>ii</sup>	0.86	2.47	3.263 (3)	154
O11–H2W···O8 <sup>iii</sup>	0.86	2.36	3.045 (4)	137
O3–H3···O2	0.82	2.20	2.656 (3)	115
O3–H3···O10 <sup>iii</sup>	0.82	2.22	2.916 (3)	142
N1–H9A···O3 <sup>iv</sup>	0.89	2.05	2.879 (3)	155
N1–H9C···O5 <sup>v</sup>	0.89	1.99	2.861 (3)	168
N1–H9B···O7	0.89	2.44	3.024 (3)	124
N1–H9B···O11	0.89	2.23	2.959 (3)	139
O6–H12···O9	0.82	1.74	2.554 (3)	175
O8–H14···O2 <sup>v</sup>	0.82	2.08	2.856 (3)	158
N2–H20A···O8 <sup>vi</sup>	0.89	2.08	2.899 (3)	152
N2–H20B···O4	0.89	1.98	2.811 (3)	156
N2–H20C···O9 <sup>iii</sup>	0.89	1.96	2.824 (3)	163

Symmetry codes: (i) *x*, 1 + *y*, *z*; (ii) *x* – 1, *y*, *z*; (iii) *x* – 1, 1 + *y*, *z*; (iv) 1 + *x*, *y* – 1, *z*; (v) 1 + *x*, *y*, *z*; (vi) *x* – 1, *y* – 1, *z*.

The H atoms were placed in calculated positions, with C–H = 0.93–0.98 Å, O–H = 0.82 Å and N–H = 0.89 Å, guided by difference Fourier maps. The H atoms were included in the final cycles of the refinement as riding, with *U*<sub>iso</sub>(H) = 1.2*U*<sub>eq</sub> of the carrier atoms, except for the H atoms of the water molecules, which had fixed

positional parameters and  $U_{\text{iso}}(\text{H}) = 0.08 \text{ \AA}^2$ . A torsional parameter was refined for each  $\text{CH}_3$ ,  $\text{NH}_3$  and  $\text{OH}$  group. The absolute configuration was assigned based on that of the starting reagent, (*S*)-alanine, and could not be determined directly from the X-ray data. Friedel pairs were averaged.

Data collection: *MSC/AFD Diffractometer Control Software* (Molecular Structure Corporation, 1992); cell refinement: *MSC/AFD Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1985); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* (Siemens, 1994); software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1385). Services for accessing these data are described at the back of the journal.

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