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*Acta Cryst.* (1995). **C51**, 935–937

### (*R,S*)-1-Phenylethylammonium (*R,S*)-Mandelate

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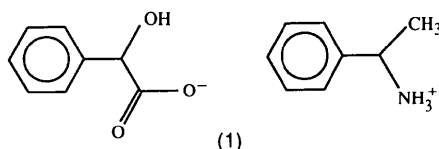
(Received 19 October 1994; accepted 10 November 1994)

## Abstract

The title compound,  $C_8H_{12}N^+ \cdot C_8H_7O_3^-$ , contains equal amounts of (*R*)- and (*S*)-1-phenylethylammonium ions and of (*R*)- and (*S*)-mandelate ions ( $\alpha$ -hydroxybenzeneacetate). Hydrogen bonds connect cations with anions of the same chirality, including ions related by the symmetry of the  $2_1$  axis. This hydrogen-bond pattern and the conformation of the ions are identical to those found in (*S*)-1-phenylethylammonium (*S*)-mandelate.

## Comment

The crystal structures of five different compounds made from mixtures of 1-phenylethylamine and mandelic acid have been reported previously (Brianso, Leclercq & Jacques, 1979; Larsen & Lopez de Diego, 1993*a,b*; Lopez de Diego, 1994*a,b*, 1995). These compounds differ in the chirality of the ions and in the base-to-acid ratio. The title compound (1) is thus the sixth salt in the series, and it contains both enantiomers of the 1-phenylethylammonium ion and both enantiomers of the mandelate ion.



The cation and the anion in the chosen asymmetric unit have (*R*)-configuration. The atom-labelling scheme and the conformation of the ions is shown in Fig. 1. The mandelate ion contains two planar groups, the phenyl ring and the carboxylate group; consequently, the conformation of the ion is described by two torsion angles, O1—C1—C2—O3 and O3—C2—C3—C4, and the conformation of the 1-phenylethylammonium ion is determined by the torsion angle N—C10—C11—C12. These torsion angles differ by less than  $1.4^\circ$  from the equivalent angles in (*S*)-1-phenylethylammonium (*S*)-mandelate if these are inverted to correspond to the (*R,R*)-configuration (Larsen & Lopez de Diego, 1993*a*), thus, the conformation of the ions is the same in these two salts.

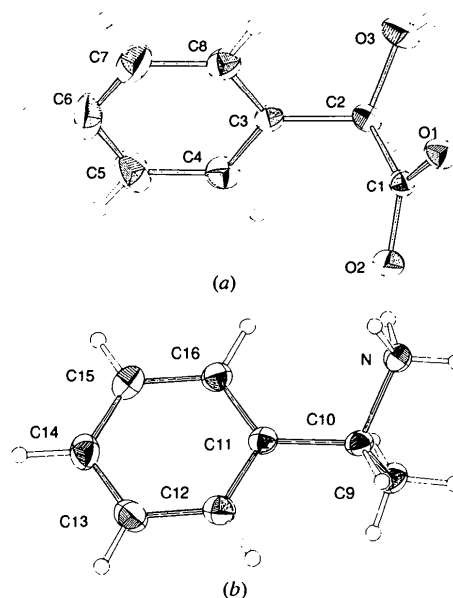


Fig. 1. ORTEPII (Johnson, 1976) drawings of (a) the (*R*)-mandelate and (b) the (*R*)-1-phenylethylammonium ions, illustrating the atomic numbering scheme. The displacement ellipsoids enclose 50% probability and the H atoms are drawn as spheres with a fixed radius.

This structure contains both enantiomers of the cation and anion, so it could be expected that hydrogen bonds could be found between homochiral, as well as between heterochiral, ions. Therefore, it is remarkable that hydrogen bonds are formed only between ions of identical chirality. Hydrogen bonds from the ammonium group of the cation to the carboxylate group of two mandelate ions, related by translation symmetry, form chains parallel to the *c* axis. The ions in neighbouring chains are related by the symmetry of the  $2_1$  axis. The third H atom of the ammonium group, HN3, is a donor in a hydrogen bond to a carboxylate group in a neighbouring chain at one side, and the hydroxy group is involved in a hydrogen bond to a carboxylate

group at the other side, extending the hydrogen-bond pattern into layers of homochiral ions parallel to the crystallographic  $bc$  plane. Fig. 2 shows the packing with hydrogen bonds shown as thin lines. Exactly the same hydrogen-bond pattern is found in (*S*)-1-phenylethylammonium (*S*)-mandelate. The only difference between the two structures is that the layers encountered along the  $a$  axis in the title compound are of alternating chirality.

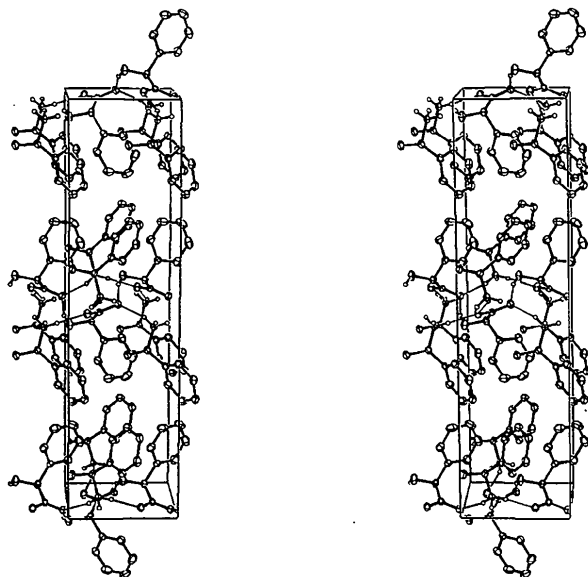
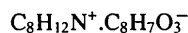


Fig. 2. Stereodrawing of the packing in (*R,S*)-1-phenylethylammonium (*R,S*)-mandelate seen in the direction of the crystallographic  $b$  axis, with vertical  $a$  axis and horizontal  $c$  axis.

## Experimental

The crystals were prepared by mixing equimolar amounts of racemic 1-phenylethylamine and racemic mandelic acid in aqueous solution and allowing the solvent to evaporate slowly.

### Crystal data



$M_r = 273.32$

Orthorhombic

$Pca2_1$

$a = 25.601(3) \text{ \AA}$

$b = 8.3508(14) \text{ \AA}$

$c = 6.8213(10) \text{ \AA}$

$V = 1458.3(4) \text{ \AA}^3$

$Z = 4$

$D_x = 1.245 \text{ Mg m}^{-3}$

Cu  $K\alpha$  radiation

$\lambda = 1.54180 \text{ \AA}$

Cell parameters from 20 reflections

$\theta = 40.183\text{--}42.874^\circ$

$\mu = 0.696 \text{ mm}^{-1}$

$T = 122(2) \text{ K}$

Prismatic

$0.30 \times 0.25 \times 0.05 \text{ mm}$

Colourless

### Data collection

CAD-4 diffractometer

$\omega$ - $2\theta$  scans

Absorption correction:

none

5669 measured reflections

$R_{\text{int}} = 0.0284$

$\theta_{\text{max}} = 74.94^\circ$

$h = 0 \rightarrow 32$

$k = 0 \rightarrow 10$

$l = 0 \rightarrow 8$

1640 independent reflections

1574 observed reflections

$[I > 2\sigma(I)]$

### Refinement

Refinement on  $F^2$

$R(F) = 0.0288$

$wR(F^2) = 0.0749$

$S = 1.058$

1640 reflections

239 parameters

Only coordinates of H atoms refined

$w = 1/[\sigma^2(F_o^2) + (0.0535P)^2 + 0.0825P]$

where  $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\text{max}} < 0.001$

5 standard reflections

frequency: 167 min

intensity decay: none

$\Delta\rho_{\text{max}} = 0.26 \text{ e \AA}^{-3}$

$\Delta\rho_{\text{min}} = -0.18 \text{ e \AA}^{-3}$

Extinction correction:

SHELXL93 (Sheldrick, 1995)

Extinction coefficient:

0.0060 (7)

Atomic scattering factors

from *International Tables for Crystallography* (1992),

Vol. C, Tables 4.2.6.8 and

6.1.1.4)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters ( $\text{\AA}^2$ )

$$U_{\text{eq}} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^* \cdot \mathbf{a}_i \cdot \mathbf{a}_j$$

	$x$	$y$	$z$	$U_{\text{eq}}$
O1	0.48699 (5)	0.83502 (15)	0.1752 (2)	0.0233 (3)
O2	0.50270 (5)	0.71434 (15)	0.4614 (2)	0.0234 (3)
C1	0.48343 (6)	0.7191 (2)	0.2910 (2)	0.0184 (3)
C2	0.45369 (6)	0.5683 (2)	0.2264 (2)	0.0200 (3)
O3	0.44327 (6)	0.5737 (2)	0.0223 (2)	0.0321 (3)
C3	0.40394 (6)	0.5506 (2)	0.3442 (3)	0.0191 (3)
C4	0.40266 (7)	0.4580 (2)	0.5140 (3)	0.0272 (4)
C5	0.35675 (9)	0.4394 (2)	0.6194 (4)	0.0385 (5)
C6	0.31154 (8)	0.5154 (3)	0.5573 (4)	0.0398 (5)
C7	0.31257 (7)	0.6092 (3)	0.3905 (4)	0.0372 (5)
C8	0.35843 (7)	0.6275 (2)	0.2837 (3)	0.0270 (4)
C9	0.39572 (7)	0.9848 (2)	0.5302 (3)	0.0248 (4)
C10	0.40110 (6)	0.8915 (2)	0.7217 (3)	0.0205 (3)
N	0.45772 (6)	0.8860 (2)	0.7789 (2)	0.0209 (3)
C11	0.36723 (6)	0.9649 (2)	0.8796 (3)	0.0206 (3)
C12	0.31720 (7)	0.9021 (2)	0.9081 (3)	0.0253 (4)
C13	0.28247 (7)	0.9756 (2)	1.0356 (3)	0.0305 (4)
C14	0.29694 (7)	1.1124 (2)	1.1370 (3)	0.0296 (4)
C15	0.34704 (8)	1.1743 (2)	1.1112 (3)	0.0293 (4)
C16	0.38186 (7)	1.1009 (2)	0.9833 (3)	0.0255 (4)

Table 2. Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ )

O1—C1	1.252 (2)	C2—C3	1.513 (2)
O2—C1	1.264 (2)	C9—C10	1.527 (2)
C1—C2	1.537 (2)	C10—N	1.502 (2)
C2—O3	1.418 (2)	C10—C11	1.512 (2)
O1—C1—O2	125.2 (2)	C3—C2—C1	110.17 (13)
O1—C1—C2	119.27 (14)	N—C10—C11	112.37 (14)
O2—C1—C2	115.56 (14)	N—C10—C9	108.94 (13)
O3—C2—C3	111.47 (14)	C11—C10—C9	110.53 (14)
O3—C2—C1	110.38 (14)		
O1—C1—C2—O3	11.8 (2)	N—C10—C11—C12	-143.7 (2)
O3—C2—C3—C4	143.5 (2)		

Table 3. Hydrogen-bonding geometry ( $\text{\AA}$ ,  $^\circ$ )

$D\cdots H\cdots A$	$H\cdots A$	$D\cdots A$	$D\cdots H\cdots A$
N—HN1 $\cdots$ O2	1.93 (3)	2.841 (2)	162 (2)
N—HN2 $\cdots$ O1 <sup>i</sup>	1.96 (3)	2.838 (2)	166 (2)
N—HN3 $\cdots$ O1 <sup>ii</sup>	1.93 (3)	2.816 (2)	152 (3)
O3—HO3 $\cdots$ O2 <sup>iii</sup>	1.82 (3)	2.806 (2)	164 (3)

Symmetry codes: (i)  $x, y, 1+z$ ; (ii)  $1-x, 2-y, \frac{1}{2}+z$ ; (iii)  $1-x, 1-y, z-\frac{1}{2}$ .

The Flack parameter (Flack, 1983) was 0.05 (20). Refinement of the inverted structure gave the same value and refinement

as a racemic twin did not improve the result, so the absolute structure could not be determined.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *DREADD* (Blessing, 1987). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1995). Molecular graphics: *ORTEPII* (Johnson, 1976). Software used to prepare material for publication: *SHELXL93*, local programs.

I am grateful to Mr Flemming Hansen for help with the experimental crystallographic work and Dr Sine Larsen for valuable discussions. The support from The Carlsberg Foundation is gratefully acknowledged.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1135). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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*Acta Cryst.* (1995). **C51**, 937–939

## 8-Acid Derivative of the Antitumour Agent Mitozolomide

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(Received 22 September 1994; accepted 31 October 1994)

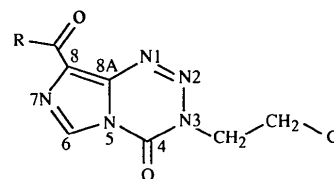
### Abstract

The crystal structure of 3-(2-chloroethyl)-3,4-dihydro-4-oxoimidazo[5,1-*d*][1,2,3,5]tetrazine-8-carboxylic acid, C<sub>7</sub>H<sub>6</sub>ClN<sub>5</sub>O<sub>3</sub>, a derivative of the novel bicyclic

antitumour agent mitozolomide, 3-(2-chloroethyl)-3,4-dihydro-4-oxoimidazo[5,1-*d*][1,2,3,5]tetrazine-8-carboxamide, has been determined at 293 K. The expected dimer, hydrogen bonded *via* the two carboxyl groups, does not occur. In preference, the two molecules in the asymmetric unit utilize hydrogen bonding between the carboxyl group of one and the N atom and CH in the imidazo ring of the other. These two then further interact *via* the same scheme with their centrosymmetrically related pair to produce a fully hydrogen-bonded planar tetramer.

### Comment

Although in itself not a particularly active antitumour agent, the title compound (1) proved to be an important intermediate in the preparation of a range of active 8-carbamoyl derivatives of mitozolomide (2) (Horspool *et al.*, 1990). Previous attempts at preparing these directly from (2) had resulted in nucleophilic attack at O4 and the resultant destruction of the molecule. Preparation of the 8-acid and then the acid chloride had allowed nucleophilic reactions under much milder conditions without affecting the ring system.



- (1) R = OH, 8-acid derivative  
 (2) R = NH<sub>2</sub>, mitozolomide

As with mitozolomide (Lowe, Schwalbe & Stevens, 1985), the 8-acid derivative contains two molecules in the asymmetric unit.

Both chloroethyl side chains at N3 and N3P, as with the two independent molecules in (2), adopt a *gauche* conformation with the N3–C31–C32–Cl1 torsion angles being 64.9 (2) and 73.9 (3)°, respectively, for the unprimed and primed molecules. The carboxyl groups are almost coplanar with the ring system as shown by the torsion angle C8A–C8–C81–O82 and its primed equivalent being 177.5 (2) and –174.0 (2)°, respectively.

However, by far the most interesting feature is the overall hydrogen-bonding scheme. Whilst it was tempting to hypothesize a hydrogen-bonded dimer *via* the two carboxyl groups, this does not occur. Instead, the two molecules in the asymmetric unit form a hydrogen-bonded pair utilizing the carboxyl group of one and N7P and the electropositive C6P H atom of the other. This pair of molecules then further hydrogen bond to a centrosymmetrically related pair *via* the same arrangement (Table 3) to produce a fully hydrogen-bonded planar tetramer. In order to check the logic behind this hydrogen-bonding scheme, which utilizes