Isolation of Different Enantiomers caused by Variation in the Stoichiometric Ratio of Racemate and Resolving Agent. The Crystal Structure of (*R*)-1-Phenylethylammonium (*S*)-Mandelate·Dimandelic Acid

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From an aqueous solution of racemic 1-phenylethylamine and (*S*)-mandelic acid in the molar ratio 1:3, the less soluble compound isolated is (*R*)-1-phenylethylammonium (*S*)-mandelate cocrystallized with two molecules of mandelic acid. This compound, $C_8H_{12}N^+·C_8H_7O_3^-·(C_8H_8O_3)_2$, has been characterized by X-ray diffraction at −163 °C measured with Cu-Kα radiation. It crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 9.5497(5)$, $b = 9.8186(9)$, $c = 31.001(3)$ Å, $V = 2906.8(7)$ Å^3, $Z = 4$, refinement using 5177 observed reflections gives $R = 0.037$. An extensive system of hydrogen bonds stabilizes the structure. Comparisons are made to the product formed by the reaction of equimolar amounts of racemic 1-phenylethylamine and (*S*)-mandelic acid in water, where (*S*)-1-phenylethylammonium (*S*)-mandelate precipitates as the less soluble salt. The solubility in water of the 1:3 compound has been determined and the observation that different enantiomers of 1-phenylethylamine can be precipitated with (*S*)-mandelic acid depending on the ratio between the base and the acid is rationalized from the solubilities in water.

The resolution of a racemate into its enantiomers is often achieved through diastereomeric salt formation. The racemate is reacted with a suitable optically active compound and if the difference in the solubility between the two diastereomeric compounds formed is sufficiently large, a separation of the enantiomers can be achieved. For the separation of racemic acids or bases a suitable chiral base or acid is normally added in a stoichiometric quantity. The resolution may be influenced by different molar ratios between the racemate and the resolving agent but very few investigations[1] have been performed on this aspect.

Though it has been reported in the literature that the diastereomeric mandelates of 1-phenylethylamine form a solid solution[2,3] several patents exist[4] that describe the resolution of 1-phenylethylamine with mandelic acid. In accordance with the patents we observe that when the amine is treated with (*S*)-mandelic acid, (*S*)-1-phenylethylammonium (*S*)-mandelate [(*S*-PEA)·(*S*-MA)] is obtained as the less soluble salt.[5] This salt precipitates either in an orthorhombic or in a monoclinic modification depending on the temperature.[5] The crystal structure of the orthorhombic form obtained at 25 °C was determined earlier by Brianso, Leclercq and Jacques.[6] In a recent paper we have reported the crystal structure of the monoclinic modification precipitated at 5 °C and discussed the relationship between the two polymorphs.[5] As it has proved to be very difficult to get crystals suitable for a diffraction study of the more soluble (*R*)-1-phenylethylammonium (*S*)-mandelate [(*R*-PEA)·(*S*-MA)], the crystal structure of this salt has not yet been established. In our attempts to make suitable crystals of (*R*)-1-phenylethylammonium (*S*)-mandelate we unexpectedly obtained a compound that contains the base and the acid in the ratio 1:3 [(*R*-PEA)·3(*S*-MA)]. To our knowledge no other diastereomeric salt with cocrystallization of the resolving agent has been described previously, so this prompted further investigations of the (*R*-PEA)·3(*S*-MA) compound. In this paper we describe its crystal structure and the relation to the compounds that are formed when equimolar amounts of racemic 1-phenylethylamine and (*S*)-mandelic acid are mixed. The observation that different enantiomers of 1-phenylethylamine can be precipitated depending on the ratio between the base and the resolving agent [(*S*)-mandelic acid] is discussed.

Experimental

(R)-1-*Phenylethylammonium* (S)-*Mandelate·Dimandelic Acid.*—*Preparation of the crystal used in determination of structure by X-ray diffraction.* (*S*)-Mandelic acid (1.1915 g) was dissolved in water and an equimolar amount (1.0 cm^3) of (*R*)-1-phenylethylamine was added dropwise while stirring the solution. After cooling the solution was left to evaporate slowly at 5 °C. No crystals appeared and after six months a yellow sticky mass remained. One year later colourless platelike crystals had been formed that were suitable for a X-ray diffraction study. M.p. = 106.7 °C, determined by DSC.

Preparation with (R)-1-*phenylethylamine and* (S)-*mandelic acid in the ratio* 1:3. (*S*)-Mandelic acid (3.5870 g) was dissolved in water and (*R*)-phenylethylamine (1.0 cm^3) was added as above, giving a solution containing the base and the acid in the ratio 1:3. It was allowed to evaporate slowly at 5 °C and large thin colourless plates could be isolated (Found: C, 66.3; H, 6.15; N, 2.45. Calcd. for $C_{32}H_{35}NO_9$ C, 66.55; H, 6.1; N, 2.45%). M.p. = 106.8 °C, determined by DSC. $[\alpha]_D = 113.4$ (*c* 0.5, H_2O). Weissenberg photographs confirmed that the crystals obtained were identical to the one used for the structure determination.

Resolution of racemic 1-*phenylethylamine with mandelic acid in the base:acid ratio* 1:3. An aqueous solution containing racemic 1-phenylethylamine (1.0 cm^3) and (*S*)-mandelic acid (3.589 g) gave by slow evaporation a less soluble salt which crystallized as colourless needles elongated in the direction of the *a*-axis. Despite the different crystal shape Weissenberg photographs confirmed that the compound was identical to the crystals prepared previously. M.p. = 104 °C, determined on a Koffler bench. $[\alpha]_D = 113.2$ (*c* 0.5, H_2O).

A Perkin-Elmer DSC-7 differential scanning calorimeter operated at a heating rate of 2 °C min^{-1} was used for the determination of melting points.

Determination of Solubility.—The concentration at 22 °C of the saturated solutions of (*R*)-1-phenylethylammonium (*S*)-mandelate·dimandelic acid were determined from both optical rotation and UV–VIS absorption measurements.

Standard solutions were made in the concentration range 0.2–1.0 g/100 cm^3 solution. A Perkin-Elmer polarimeter Model

Table 1 Crystal data

Formula	$C_{32}H_{35}NO_9$
Formula weight (g mol^{-1})	577.63
Temperature	−163.0(5) °C
Space group	$P2_12_12_1$
Crystal size (mm)	0.03 × 0.3 × 0.6
a (Å)	9.5497(5)
b (Å)	9.8186(9)
c (Å)	31.001(3)
V (Å^3)	2906.8(7)
Z	4
D_x (g cm^{-3})	1.249
Number of contributing reflections	5177
Number of variables	484
R	0.037
R_w	0.057

Table 2 Bond lengths (Å)

Mandelic acid moieties	Acid A	Acid B	Anion C
O(1)–C(1)	1.208(2)	1.226(2)	1.238(2)
O(2)–C(1)	1.332(2)	1.306(2)	1.278(2)
C(1)–C(2)	1.525(2)	1.525(2)	1.533(2)
C(2)–O(3)	1.435(2)	1.418(2)	1.421(2)
C(2)–C(3)	1.513(2)	1.518(2)	1.526(2)
C(3)–C(4)	1.391(3)	1.400(2)	1.395(3)
C(3)–C(8)	1.398(3)	1.393(2)	1.397(2)
C(4)–C(5)	1.393(3)	1.389(3)	1.385(3)
C(5)–C(6)	1.389(3)	1.384(3)	1.396(3)
C(6)–C(7)	1.387(3)	1.389(3)	1.382(3)
C(7)–C(8)	1.385(3)	1.385(3)	1.389(3)
1-Phenylethylammonium ion			
N–C(10)	1.516(2)		
C(9)–C(10)	1.520(3)		
C(10)–C(11)	1.519(2)		
C(11)–C(12)	1.390(3)		
C(11)–C(16)	1.404(2)		
C(12)–C(13)	1.390(3)		
C(13)–C(14)	1.384(3)		
C(14)–C(15)	1.392(3)		
C(15)–C(16)	1.386(3)		

141 was used to measure the optical rotations at λ = 589 nm. 1.0 cm^3 of a solution saturated at 22 °C was diluted to 10.0 cm^3. From its optical rotation, the solubility was calculated to be 6.34 g/100 cm^3 solution.

The absorbance measurements and calculations were performed using an HP 8452A Diode Array Spectrophotometer coupled to HP 89531A UV–VIS Operating Software. The absorbances of the standard solutions were measured at 272 nm. A second-order fit of the points gave an error of less than 0.25%. From the absorbance of a solution saturated at 22 °C and diluted 1 : 10, the solubility was calculated to be 6.34 g/100 cm^3 solution. 100 cm^3 saturated solution of (*R*-PEA)·3(*S*-MA) weighs 100.9 g which gives the solubility 6.28 g/100 g solution, and 6.70 g/100 g H_2O.

X-Ray Crystallography.—The crystal used for the diffraction measurements was from the initial preparation and had dimensions 0.03 × 0.3 × 0.6 mm^3. The data collection was performed with an Enraf-Nonius CAD-4 diffractometer with graphite-monochromatized Cu-Kα radiation (λ = 1.5418 Å) and equipped with an Enraf-Nonius gas flow low temperature device. The crystal was cooled to 110 K during the experiment. The temperature monitored with a thermocouple in the exhaust pipe was constant within 0.5 K. The intensities were measured using an ω–2θ scan. Unit cell dimensions were determined from a least squares refinement of 18 reflections with $33° < \theta < 42°$. The orientation of the crystal was checked after every 300 reflections. The remeasurement of the reflections 020, 008 and 211 every 10 000 s showed no significant decrease or variation in their intensities. 6796 Reflections were measured in the range $0 < h < 11, 0 < k < 12, -38 < l < 38$, the maximum $\sin\theta/\lambda$ was 0.626 Å^{-1}. Data reduction included corrections for Lorentz polarization and background effects as no correction for absorption or decay was necessary. The symmetry equivalent reflections were averaged according to the crystal class, $R_{\text{int}} = 0.023$. Of the 5978 unique reflections 5177 were considered observed with $|F^2| > 2\sigma(|F^2|)$. The structure was solved by direct methods with the program SHELXS-86[7] and refined using the full-matrix least-squares method minimizing $\Sigma w(|F_o| - |F_c|)^2$, $w^{-1} = \sigma^2_{cs}(F) + 0.0006F^2$. After anisotropic displacement parameters were introduced in the refinement, a $\Delta\rho$-map showed the positions of all H atoms. The positional parameters for the H atoms were refined with the isotropic temperature factors fixed at 2.0 Å^2. The final residuals were $R = 0.037$, and $R_w = 0.057$ for 484 parameters and 5177 reflections, $S = \sqrt{\Sigma w \Delta F^2/(n - m)} = 1.710$ and $(\Delta/\sigma)_{\text{max}} = 0.01$. The final difference Fourier had $(\Delta\rho)_{\text{max}} = 0.456$ e Å^{-3} and $(\Delta\rho)_{\text{min}} = -0.578$ e Å^{-3}. The crystal data are listed in Table 1. Fractional coordinates (including H-atoms), anisotropic displacement parameters and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.*

All calculations except the structure determination were performed using the Enraf-Nonius SDP program system.[8] Scattering-factor values for all atoms were taken from *International Tables for X-ray Crystallography*.[9]

Results and Discussion

Description of the Crystal Structure.—The crystal structure determination has revealed that the compound formed after more than 18 months from a mixture of (*R*)-1-phenylethylamine and (*S*)-mandelic acid is the expected diastereomeric salt cocrystallized with two molecules of (*S*)-mandelic acid. Fig. 1 shows the four entities as they are found in the asymmetric unit. In the atomic numbering of the mandelic acid moieties, O(2) designates the oxygen atom of the carboxylate group that is anti to the hydroxy oxygen atom O(3). Likewise C(4) in the phenyl groups are anti relative to O(3). The two mandelic acid molecules are labelled A and B respectively and the mandelate ion C. The molecular geometry is described in Tables 2 and 3. In both mandelic acid molecules the hydrogen atom of the carboxylic acid is bonded to O(2). The difference in the protonation of the mandelic acid moieties is reflected in the C–O bond lengths of the CO_2 groups. The two uncharged acid molecules have C(1)–O(2) bond lengths that are markedly longer than the C(1)–O(2) bonds in the mandelate ion. In a carboxylate group with idealized geometry the two C–O bond lengths should be of equal length. The carboxylate group of the mandelate ion (C) has markedly different C(1)–O bonds, Δ(C–O) = 0.04 Å. This difference seems to be caused by the formation of a very short hydrogen bond between the carboxylate group and the carboxylic acid group of the mandelic acid molecule labelled B (*vide infra*), which in turn has a shorter C(1)–O(2) bond than observed in molecule A. Apart from these differences in the dimensions of the CO_2 groups, the mandelic acid moieties have very similar bond lengths and angles. However Fig. 1 and the torsion angles given in Table 3 illustrate that the three mandelic acid fragments differ in their

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* For details of the deposition scheme see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 2*, 1993, issue 1.

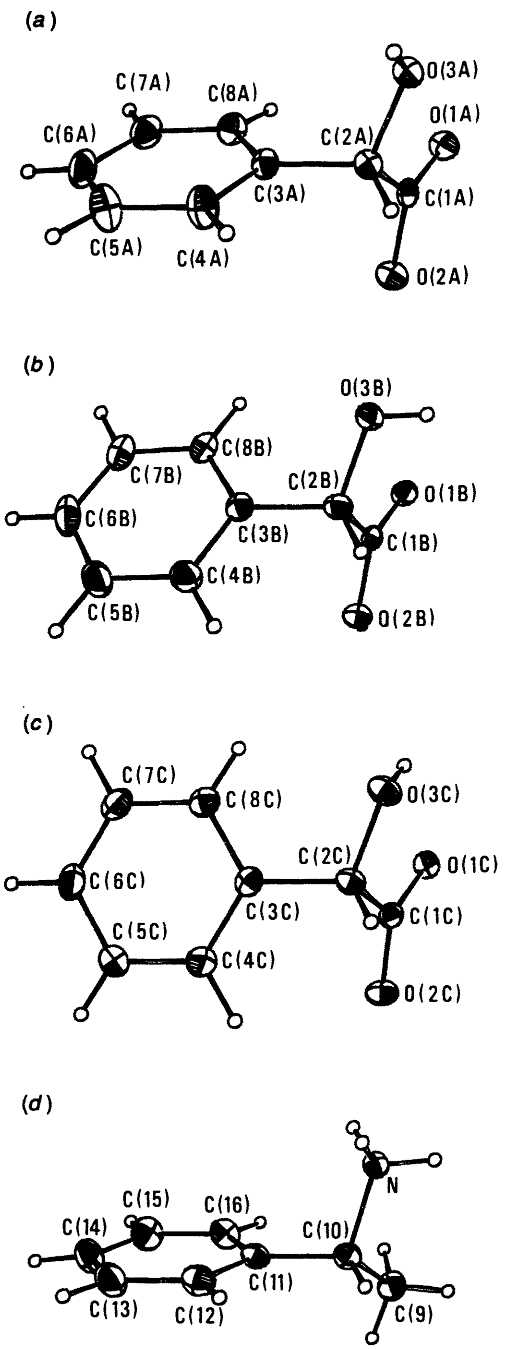

Fig. 1 ORTEP drawings illustrating the atomic numbering scheme of the mandelic acid molecules labelled A and B, the mandelate anion labelled C, and the 1-phenylethylammonium cation. The thermal ellipsoids enclose 50% probability, and the H atoms are drawn as spheres with a fixed radius.

conformation. The relative orientation of the carboxylate and the hydroxy group is very similar in all three molecules as described by the torsion angle O(1)–C(1)–C(2)–O(3) that is found in the range −11.7° to −14.2°. In contrast to this the three mandelic acid fragments differ with respect to the orientation of the phenyl group. The torsion angle C(1)–C(2)–C(3)–C(4) takes very different values in the three molecules. Both the relatively narrow interval found for the O(1)–C(1)–C(2)–O(3) torsion angle and the large variation in the C(1)–C(2)–C(3)–C(4) torsion angle are in accordance with the observations made in an investigation of the structural features of mandelate salts.[5]

Table 3 Bond angles and selected torsion angles (°)

Mandelic acid moieties	Acid A	Acid B	Anion C
O(1)–C(1)–O(2)	124.7(2)	124.1(2)	124.7(2)
O(1)–C(1)–C(2)	123.7(2)	123.5(2)	118.2(2)
O(2)–C(1)–C(2)	111.7(1)	112.4(1)	117.1(1)
C(1)–C(2)–O(3)	105.9(1)	111.1(1)	109.5(1)
C(1)–C(2)–C(3)	108.9(1)	106.0(1)	110.4(1)
O(3)–C(2)–C(3)	113.7(1)	110.1(1)	111.4(1)
C(2)–C(3)–C(4)	119.9(2)	119.8(2)	120.7(2)
C(2)–C(3)–C(8)	120.9(2)	120.7(2)	120.5(2)
C(4)–C(3)–C(8)	119.1(2)	119.4(2)	118.8(2)
C(3)–C(4)–C(5)	120.1(2)	120.0(2)	120.7(2)
C(4)–C(5)–C(6)	120.4(2)	120.3(2)	120.2(2)
C(5)–C(6)–C(7)	119.8(2)	119.8(2)	119.3(2)
C(6)–C(7)–C(8)	119.9(2)	120.4(2)	120.7(2)
C(3)–C(8)–C(7)	120.7(2)	120.1(2)	120.2(2)
O(1)–C(1)–C(2)–O(3)	−13.0(3)	−11.7(3)	−14.2(3)
O(1)–C(1)–C(2)–C(3)	109.6(2)	107.8(2)	108.8(2)
C(1)–C(2)–C(3)–C(4)	232.7(2)	103.0(2)	73.0(3)
O(3)–C(2)–C(3)–C(4)	−109.5(2)	−136.8(2)	−165.2(2)
1-Phenylethylammonium ion			
N–C(10)–C(9)	108.8(1)		
N–C(10)–C(11)	108.4(1)		
C(9)–C(10)–C(11)	114.7(2)		
C(10)–C(11)–C(12)	119.9(2)		
C(10)–C(11)–C(16)	121.5(2)		
C(12)–C(11)–C(16)	118.6(2)		
C(11)–C(12)–C(13)	121.1(2)		
C(12)–C(13)–C(14)	119.8(2)		
C(13)–C(14)–C(15)	120.1(2)		
C(14)–C(15)–C(16)	120.1(2)		
C(11)–C(16)–C(15)	120.4(2)		
N–C(10)–C(11)–C(12)	−98.2(2)		
C(9)–C(10)–C(11)–C(12)	140.1(2)		

The torsion angle N–C(10)–C(11)–C(12) describes the conformation *e.g.* relative orientation of the phenyl group of the (*R*)-1-phenylethylammonium ion. The molecular geometry compares well with results from other structure determinations of compounds containing this ion. A recent survey[10] showed that its conformation shows little variation, the torsion angle typically takes a value around −120°, corresponding to a minimum in the energy. In the present structure this torsion angle is significantly different from this normal value. This variation is probably caused by the intermolecular interactions in the crystal.

The packing in the crystal is strongly influenced by hydrogen bonding. Table 4 provides information about the hydrogen bond geometry in the structure. All possible donor atoms are involved in hydrogen bonding. The cation donates protons to two mandelate ions, a carboxylate and a hydroxy group respectively, and the mandelic acid labelled A. A very short hydrogen bond links the carboxylic acid group of mandelic acid labelled B and the mandelate ion, C. The hydroxy group of the mandelate ion donates a proton to the hydroxy group in mandelic acid B related by translational symmetry along the *a*-axis. The interaction between mandelic acid B and the mandelate ion C gives rise to infinite chains. These chains are linked by the mandelic acid molecules labelled A as shown on the stereo packing diagram in Fig. 2. This leads to a two dimensional network of hydrogen bonds parallel to the *a*–*b* plane. As illustrated in the schematic drawing of the network in Fig. 3, it is completed by hydrogen bonds from the ammonium group to the mandelic acid A and the mandelate ion C. There are interactions between the hydrogen bonded two dimensional network and an equivalent network generated by the twofold screw axis parallel to the *b*-axis. Hydrogen bonds between the ammonium ion and the carboxylate group of the mandelate ion, and between the hydroxy groups of mandelic acid molecules, connect the hydrogen bonded networks. The hydrogen bonds that connect all the hydrophilic groups lead to an arrangement where the phenyl groups are pointing out almost perpendicular to the hydrophilic hydrogen bonded network that is parallel to the *a–b* plane. The weak interactions between the phenyl groups in the direction of the *c*-axis explain the crystals form as plates with (001) as the plate face.

Optical Resolution of 1-*Phenylethylamine with* (S)-*Mandelic Acid*.—The unexpected formation of the compound described above gives rise to a number of questions that we will attempt to answer in the following. First of all, why did we obtain a compound that contains the acid and the base in a stoichiometric ratio that is very different from the one in the initial reaction mixture?

The formation of this compound can be rationalized as follows. The vapour pressure of the amine is significantly higher than that of mandelic acid, 1-phenylethylamine being a liquid (b.p. 187 °C) and mandelic acid a solid (m.p. 133 °C). After evaporation of the solvent a sticky mass remained in which an equilibrium between the salt and the free base and acid was established. Over a very long period the system was open to the atmosphere and some of the free amine could slowly evaporate providing an excess of free mandelic acid. With a sufficient excess of mandelic acid crystals of the apparently very stable 1 : 3 compound would grow, and this will shift the equilibrium leading to a continuous evaporation of the amine and crystallization of the compound.

The next question to emerge is why is (*S*-PEA)·(*S*-MA) obtained as the less soluble salt when the resolution is performed with equimolar amounts of racemic PEA and *S*-MA, while the (*R*-PEA)·3(*S*-MA) precipitates when the racemic base and *S*-MA is mixed in the ratio 1 : 3. In order to understand this behaviour we have made some calculations based on the solubilities of the salts. We have assumed ideal behaviour of the solutions though we are aware that the errors introduced are not negligible. In the calculations molalities are used with the standard state defined as 1 molal solution. We have determined the solubility of the 1 : 3 compound at 22 °C. The solubilities of the two other diastereomeric salts have been reported at 10 °C and 30 °C respectively. Two independent estimations are made of the solubilities in water at the two temperatures for the less soluble diastereomeric salt (*S*-PEA)·(*S*-MA).[3] Both sets of measurements show that the solubilities increase with temperature, but the actual values are different, 3.5 and 4.2 g/100 g H_2O at 10 °C and 6.4 and 4.9 g/100 g H_2O respectively at 30 °C. For each temperature the solubilities are estimated as an average and the van't Hoff equation used to determine the solubility at 22 °C. For the more soluble (*R*-PEA)·(*S*-MA) salt only one set of experimental data is given at 10 °C and 30 °C. They are significantly larger than those of the equivalent less soluble salt, and this may explain why it is very difficult to get crystals of this compound. The solubility in water at 22 °C was estimated by the van't Hoff equation as described above for (*S*-PEA)·(*S*-MA). The solubilities in water at 22 °C for the three mandelate salts are given in Table 5. As shown in Table 5 the solubility measured in g/100 g H_2O is higher for the (*R*-PEA)·3(*S*-MA) than for (*S*-PEA)·(*S*-MA), but, expressed in molal concentrations, their relative solubilities are reversed. The associated solubility products calculated from the solubilities are $L_{SS} = 3.2 \times 10^{-2}$ mol^2 kg^{-2} and $L_{R:3S} = 7.2 \times 10^{-4}$ mol^4 kg^{-4}. When racemic 1-phenylethylamine and (*S*)-mandelic acid are mixed in the ratio 1 : 1, (*S*-PEA)·(*S*-MA) is obtained as the less soluble salt. If instead the racemic base and the acid are mixed in the ratio 1 : 3, (*R*-PEA)·3(*S*-MA) is obtained as the less soluble salt. Assuming ideal behaviour of the solution made from equimolar racemic base and (*S*)-acid, (*S*-PEA)·(*S*-MA) will precipitate when the molal concentration of the (*S*)-1-phenylethylammonium ion exceeds 0.12 mol kg^{-1}. Under these conditions the concentration of the free mandelic acid is very small so the solubility product of the (*R*-PEA)·3(*S*-MA) is not exceeded. In a solution containing the racemic base and the (*S*)-mandelic acid in the ratio 1 : 3, (*R*-PEA)·3(*S*-MA) will precipitate when the molal concentration of (*R*)-1-phenylethylammonium ion is 0.069 mol kg^{-1}. In this solution the product of the (*S*)-PEA$^+$ and (*S*)-MA$^-$ concentrations does not exceed the solubility product of the (*S*-PEA)·(*S*-MA).

Table 4 Hydrogen-bond geometry (Å, °)

D–H ··· A	D–A	H–A	∠DHA
N–H(N1)–O(1C)[a]	2.833(2)	1.92(2)	165(8)
N–H(N2)–O(3C)[b]	2.798(2)	1.89(3)	170(2)
N–H(N3)–O(3A)[c]	2.856(2)	1.88(3)	177(2)
O(2A)–H(O2A)–O(1B)[d]	2.681(2)	1.84(3)	172(2)
O(3A)–H(O3A)–O(2C)	2.614(2)	1.66(2)	178(2)
O(2B)–H(O2B)–O(2C)[d]	2.501(2)	1.59(3)	170(2)
O(3B)–H(O3B)–O(3A)	2.886(2)	2.05(2)	175(2)
O(3C)–H(O3C)–O(3B)[e]	2.859(2)	2.08(3)	156(2)

[a] $(x, -1 + y, z)$. [b] $(-x, -1\tfrac{1}{2} + y, 1\tfrac{1}{2} - z)$. [c] $(-x, -\tfrac{1}{2} + y, 1\tfrac{1}{2} - z)$. [d] $(1 - x, -\tfrac{1}{2} + y, 1\tfrac{1}{2} - z)$. [e] $(-x, \tfrac{1}{2} + y, 1\tfrac{1}{2} - z)$.

The precipitation of the two salts should be equally likely at a certain ratio between the racemic base and the optically active (*S*)-mandelic acid. From the solubilities we have estimated this ratio to be *ca.* 1.6. An acid/base ratio below this number will give (*S*-PEA)·(*S*-MA) as the first precipitate and above this ratio (*R*-PEA)·3(*S*-MA) would be obtained.

Conclusions

(*R*)-1-phenylethylamine and (*S*)-mandelic acid form a very stable compound that contains the base and the acid in the molar ratio 1 : 3. The stability seems to be due to a very extended system of hydrogen bonds between the molecules in the crystal. The existence of this compound makes it possible to isolate the two enantiomers of 1-phenylethylamine in a two stage process. Calculations based on the solubilities in water show that when racemic 1-phenylethylamine and (*S*)-mandelic acid are mixed in at molar ratio which is smaller than 1.6 (*S*-PEA)·(*S*-MA) is obtained, at higher molar ratios (*R*-PEA)·3(*S*-MA) precipitates. It follows that a very efficient resolution of 1-phenylethylamine with (*S*)-mandelic acid can be achieved, by firstly mixing the base and the acid in equimolar amounts and isolating (*S*-PEA)·(*S*-MA), thereafter adding more (*S*-MA) to the mother liquor to make the acid/base ratio 3 : 1 which will make the other enantiomer precipitate as (*R*-PEA)·3(*S*-MA).

Table 5 Solubilities at 22 °C

	(*R*-PEA)·3(*S*-MA)	(*S*-PEA)·(*S*-MA)	(*R*-PEA)·(*S*-MA)
Formula	$C_{32}O_9NH_{35}$	$C_{16}O_3NH_{19}$	$C_{16}O_3NH_{19}$
Formula weight (g mol^{-1})	577.63	273.33	273.33
D_x (g cm^{-3})	1.249	1.245	1.252
Solubility (g/100 g H_2O)	6.70	4.8[a]	22[a]
Solubility (molal conc.)	0.116	0.18	0.81

[a] Calculated from values given by M. Leclercq and J. Jacques, *Bull. Soc. Chim. Fr.*, 1975, 2052.

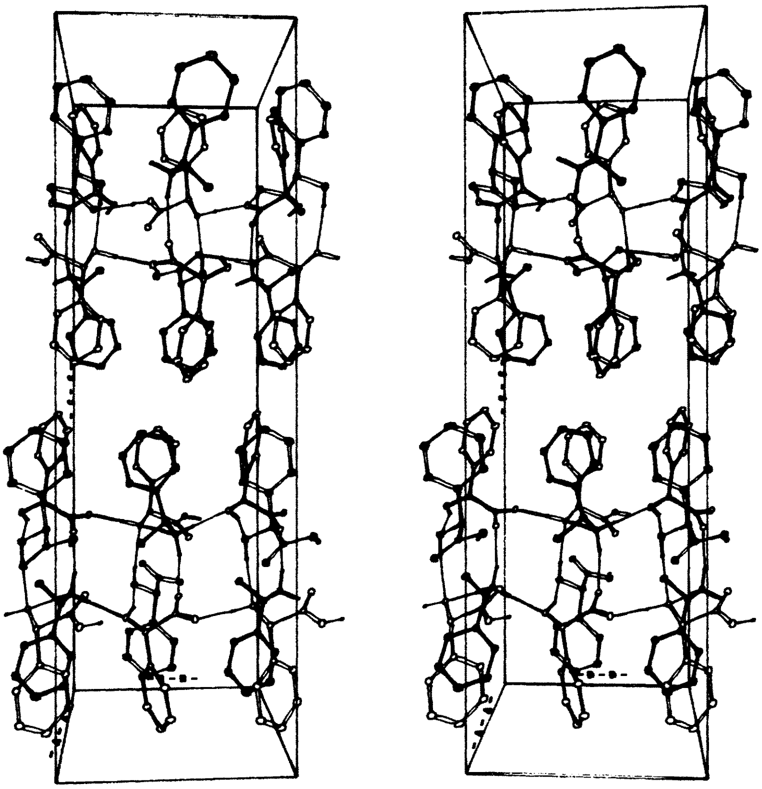

Fig. 2 Stereo drawing of the packing in the compound seen in the direction of the *a*-axis. The molecules are identified by A: open bonds, white atoms; B: open bonds, black atoms; C: full bonds, white atoms; cation: full bonds, black atoms. The hydrogen bonds are indicated by the thin lines.

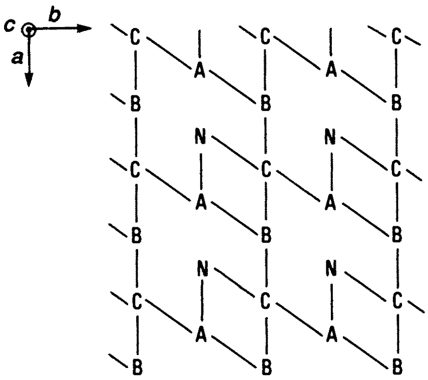

Fig. 3 Schematic illustration of a hydrogen bonded layer. The ammonium cation is symbolized by N, A & B are the mandelic acid molecules, and C is the mandelate ion.

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