

## The Optical Resolution of 3-(2'-Hydroxy-2'-phenylethyl)-2-thiazolidinimine, and the Crystal Structure of the (2*R*,3*R*)-*O*,*O*'-Dibenzoyl Hydrogen Tartrate Salt of the (*S*)-(+) -Enantiomer

Katalin Marthi,<sup>a</sup> Sine Larsen,<sup>\*a</sup> Mária Ács,<sup>†,b</sup> József Bálint,<sup>b</sup> and Elemér Fogassy<sup>b</sup>

<sup>a</sup>Centre for Crystallographic Studies, Department of Chemistry, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark and <sup>b</sup>Department of Organic Chemical Technology, Technical University of Budapest, PO Box 91, H-1521 Budapest, Hungary

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The optical resolution has been investigated for 3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidinimine with (2*R*,3*R*)-*O*,*O*'-dibenzoyltartaric acid. The most effective separation of the enantiomers is attained if the resolution is performed in methanol with the reactants in a 1:1 ratio. The crystal structure at 122 K of the precipitating salt (C<sub>11</sub>H<sub>15</sub>N<sub>2</sub>OS<sup>+</sup> · C<sub>18</sub>H<sub>13</sub>O<sub>8</sub><sup>-</sup> · CH<sub>3</sub>OH) has been determined by X-ray diffraction methods. Crystals are monoclinic, space group *P*2<sub>1</sub>, with *a* = 7.5831(9), *b* = 12.5698(14), *c* = 15.835(2) Å, β = 101.980(9)°, *V* = 1476.5(3) Å<sup>3</sup>, *Z* = 2, *D*<sub>x</sub> = 1.378 g cm<sup>-3</sup>, μ = 15.00 cm<sup>-1</sup>. The crystal structure refined to *R* = 0.0255 for 6046 contributing reflections, established that the (+)<sub>D</sub> rotation of the cation corresponds to the *S*-enantiomer. The strongest intermolecular interactions are the short hydrogen bonds between the carboxylic acid and the carboxylate groups of anions related by translational symmetry along the *a*-axis. Methanol also plays a significant role in the hydrogen-bonding system. The packing mode in the present structure is compared to that of the mono-, dibenzoyl- and di-*p*-toluoyl hydrogen tartrates found in the Cambridge Structural Database.

One of the most effective anthelmintic agents is 6-phenyl-2,3,5,6-tetrahydroimidazo[2,1*b*]thiazol. It is prescribed as Tetramisole (the racemate) or Levamisole (the *S*-enantiomer). The latter is the biologically active enantiomer, which is obtained by resolution of the racemate.

In the different synthetic routes used in the preparation of 6-phenyl-2,3,5,6-tetrahydroimidazo[2,1*b*]thiazol, 3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidinimine (T-alcohol) is an important reaction intermediate.<sup>1–4</sup> We are performing an investigation of the possible stereochemical changes during one of the preparative routes for Levamisole. The purpose is to determine at which step it is most efficient to perform the optical resolution. As part of this study an optical resolution was performed for T-alcohol with (2*R*,3*R*)-*O*,*O*'-dibenzoyltartaric acid (DBTA) as the resolving agent. Here we report the results of the resolution process supported by the crystal structure determination

of the less soluble diastereomeric salt describing the absolute configuration of the cation.

In the literature there are contradictory statements with respect to the relation between the absolute configuration and the optical rotation of the cation. In the abstract of a Japanese patent the absolute configuration of (–)-T-alcohol is reported to be *S*.<sup>3</sup> However, in a letter paper the *S* absolute configuration is assigned to the (+) rotation of the T-alcohol.<sup>4</sup> This stereochemical contradiction is also clarified by the structure determination. The crystal structure analysis revealed that the less soluble diastereomeric salt is a methanol adduct. The role of the solvent for stabilizing the crystal packing is also described.

The analogous mono-, dibenzoyl- and di-*p*-toluoyltartaric acids are not as widely used resolving agents as the unsubstituted tartaric acid. When tartaric acid is used as the resolving agent, short hydrogen bonds link the hydrogen tartrate ions into infinite chains<sup>5</sup> in the diastereomeric salts. We have examined if similar packing modes exist for the mono-, dibenzoyl- and di-*p*-toluoyl hydrogen tartrate salts.

\* To whom correspondence should be addressed.

† Deceased.

## Experimental

### Preparations

**Racemic 3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidinimine.** Racemic 3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidinimium chloride (T-alcohol·HCl) was prepared according to the method described in Ref. 1 for the optically active salts. A detailed account of the preparations will be published elsewhere.<sup>6</sup> 18.0 g (69.6 mmol) T-alcohol·HCl was dissolved in 180 ml of water. The solution was cooled to 10°C and stirred for 1 min after addition of 10 ml of conc. NH<sub>3</sub> solution. The precipitate was removed by filtration and washed twice with 20 ml portions of 1:10 diluted conc. NH<sub>3</sub> solution. Racemic T-alcohol was isolated as a white powder and dried under infrared light. Yield: 13.1 g (58.9 mmol, 84.6%).

**Resolution.** Resolution experiments were attempted in methanol with the resolving agent added in 1, 0.75 and 0.5 molar equivalents following the general recipe described below. The starting quantities, yields and melting points are given in Table 1. Racemic T-alcohol was dissolved in hot methanol, and after the solution had been cooled to room temperature on an ice bath, (2R,3R)-O,O'-dibenzoyltartaric acid (DBTA) monohydrate dissolved in methanol was added. Crystallization was initiated by seeding with crystals from a previous batch. The mixture was stirred on the ice bath for 30 min, filtered and washed twice with 5 ml portions of methanol. The material was dried to give the precipitate A.

The mother liquor was concentrated *in vacuo*. Crystallization was initiated by seeding with crystals of the more soluble salt. After 1 h a solid mass was obtained (precipitate B) which was dried and powdered.

Optically active T-alcohol was obtained from the diastereomeric salts by the following method. A quantity of precipitate A or B (Table 1) was suspended in the mixture

of 20 ml of water and 20 ml of CH<sub>2</sub>Cl<sub>2</sub>. 12 ml of 2 M NaOH solution were added. The mixture was stirred, and after 10 min two phases were observed. These were separated, and the aqueous phase was extracted three times with 10 ml portions of methylene chloride. The combined organic phases were dried with Na<sub>2</sub>SO<sub>4</sub>. The solvent was evaporated to dryness to obtain a white powder of the T-alcohol. We found that the T-alcohol decomposes in methanol solutions (and fairly slowly in chloroform also), so special care has to be taken when measuring the optical rotation of the base. The optical rotation changes sign after 20 h. Thus (optically) pure T-alcohol has to be prepared by transforming it to its hydrochloride, recrystallizing the salt from methanol and regaining the base by precipitating it with conc. NH<sub>3</sub> solution.

**Preparation of optically active 3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidinimium chloride.** 1.70 g (7.65 mmol) of the optically active T-alcohol was dissolved in 20 ml methylene chloride. Isopropanol saturated with hydrogen chloride was added until wet universal indicator paper showed ca. pH 1. After evaporation of the solvent, T-alcohol·HCl was obtained in a quantitative yield.

**Thermogravimetric analysis.** The thermogravimetric measurements (TGA) were performed with a PL-TGA-1000 thermogravimetric balance calibrated with Ni. A heating rate of 10 K min<sup>-1</sup> was used between 303 and 473 K with nitrogen gas flowing over the sample. Sampling was made every 1.25 s. The mass of the samples varied between 2.6 and 4.6 mg measured with a precision of 0.001 mg.

The samples used in the TGA analysis were prepared from optically pure bases. The enantiomers of T-alcohol and DBTA monohydrate were dissolved in a 1:1 molar ratio in methanol or ethanol. The diastereomeric salts were obtained after evaporation of the solvent.

Table 1.

Ratio	T-alcohol			DBTA·H <sub>2</sub> O			Precipitate A			Precipitate B		
	mg	mmol	cm <sup>3</sup>	mg	mmol	cm <sup>3</sup>	Yield/g	[α] <sub>D</sub> <sup>a</sup>	M.p./°C	Yield/g	[α] <sub>D</sub> <sup>a</sup>	M.p./°C
1:1	4.45	20.02	27	7.55	20.06	15	5.82	-46.8	162-166	5.79	-100.6	152-158
1:0.75	4.45	20.02	27	5.65	15.01	11	5.14	-44.4	162-168	5.13	-83.0	45-58
1:0.5	4.45	20.02	27									
Precipitate	T-alcohol						T-alcohol·HCl					
	Yield			[α] <sub>D</sub> <sup>b</sup>			Yield			[α] <sub>D</sub> <sup>b</sup>		
	g	mmol	%	[α] <sub>D</sub> <sup>b</sup>	[α] <sub>D</sub> <sup>c</sup>	M.p./°C	g	mmol	%	[α] <sub>D</sub> <sup>b</sup>	[α] <sub>D</sub> <sup>d</sup>	M.p./°C
1:1 A	2.15	9.67	97	+25.1	+121.8	130-133	1.99	7.69	100.5	+64.2	+46.4	184-197
1:1 B	2.14	9.63	96	-24.7	-117.5	126-131	1.99	7.69	100.5	-62.6	-45.3	183-193
1:0.75 A	1.89	8.50	85	+26.4	+128.2	129-134	1.99	7.69	100.5	+67.2	+49.1	185-195
1:0.75 B	2.41	10.84	108	-20.5	-99.1	120-127	1.97	7.61	99.5	-52.3	-37.4	185-197

<sup>a</sup> c=0.5 methanol, <sup>b</sup> c=1, methanol, <sup>c</sup> c=1, chloroform, <sup>d</sup> c=2, water. Melting points were determined in capillary tubes with a Gallenkamp capillary-melting-point apparatus.

*Spectroscopic measurements.* Optical rotations were measured at room temperature at 589 nm ( $N_{\text{D}}$ ) with a Perkin Elmer 241 polarimeter.

$^1\text{H}$  NMR spectra were recorded on a 400 MHz Bruker spectrometer in  $\text{C}_6\text{D}_6$ . (*R*)-(–)-2,2,2-trifluoro-1-(9-anthryl)ethanol was used as chiral shift reagent in a 1:5 mass ratio for the determination of the optical purity. The T-alcohol used for purity determination was prepared as follows. 1 g of T-alcohol·HCl  $\{[\alpha]_{\text{D}} = +72.9$  ( $c = 1$ , methanol),  $[\alpha]_{\text{D}} = +52.6$  ( $c = 2$ , water) $\}$  was dissolved in 10 ml water and 0.7 ml of conc.  $\text{NH}_3$  solution was added. The precipitated T-alcohol (0.8 g) had an optical rotation of  $[\alpha]_{\text{D}} = +30.5(4)$  ( $c = 1$ , methanol).

*X-Ray powder diffraction patterns.* A Guinier–Hägg camera was used to record the diagram of the less soluble T-alcohol·DBTA salt. Graphite-monochromated  $\text{CuK}\alpha$  radiation was used, and Si was employed as an internal standard. The program LAZY-PULVERIX<sup>7</sup> was used to compute the powder diffraction diagram from the results obtained from the single-crystal X-ray diffraction study.

*Structure determination for (S)-3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidiniminium (2R,3R)-O,O'-dibenzoyl hydrogen tartrate.* Crystals suitable for the single-crystal diffraction study were obtained by recrystallization of precipitate A from methanol.

The data collection was performed with a CAD4 diffractometer.  $\text{CuK}\alpha$  ( $\lambda = 1.54184 \text{ \AA}$ ) radiation obtained from a graphite monochromator was used. The crystal was cooled with an Enraf-Nonius gas-flow low-temperature device. The temperature, 122.0(5) K, was monitored with a thermocouple placed a few centimetres above the crystal in the exhaust pipe. It remained constant within 1 K during the experiment. The different experimental conditions with a summary of the information of the results from data reduction and structure refinement are presented in Table 2. An analysis of reflection profiles provided the basis for the selection of  $\omega-2\theta$  scan mode and scan interval for the data collection. The intensities of three standard reflections were measured after every  $10^4$  s. They showed a decay of up to 8.6%. The orientation of the crystal was checked after every 300 reflections. In the data reduction performed with the DREADD programs,<sup>8</sup> corrections were made for the degradation, Lorentz, polarization, background and absorption effects. Reflections related by the symmetry of the crystal class were averaged. The structure was solved by direct methods using SHELXS-86<sup>9</sup> and refined by full matrix least-squares with SHELXL-93<sup>10</sup> minimizing  $\Sigma w(F_o^2 - F_c^2)^2$ . Scattering factors were taken from Ref. 11 and used as contained in the program. After anisotropic displacement parameters were introduced for the non-hydrogen atoms, the difference Fourier map showed the positions for all the hydrogen atoms. The positional parameters of the hydrogen atoms bonded to N or O atoms were included in the refinement; the isotropic displacement parameters for these hydrogen atoms were made

Table 2. Crystal data and summary of the data collection and structure refinement results.

Formula	$\text{C}_{11}\text{H}_{15}\text{N}_2\text{O}_8^+ \cdot \text{C}_{18}\text{H}_{13}\text{O}_8^- \cdot \text{CH}_4\text{O}$
Formula weight	612.64
Radiation	$\text{CuK}\alpha$ ( $\lambda = 1.54184 \text{ \AA}$ )
Temperature/K	122.0(5)
Space group	$P2_1$
$a/\text{\AA}$	7.5831(9)
$b/\text{\AA}$	12.5698(14)
$c/\text{\AA}$	15.835(2)
$\beta/^\circ$	101.980(9)
$V/\text{\AA}^3$	1476.5(3)
$Z$	2
$F(000)$	644
Crystal size/mm	$0.05 \times 0.32 \times 0.40$
$D_x/\text{g cm}^{-3}$	1.378
$\mu(\text{CuK}\alpha)/\text{mm}^{-1}$	1.50
Reflection used in determination of cell parameters	20
$\theta$ range/ $^\circ$	33.86–38.53
Scan type	$\omega-2\theta$
$(\sin \theta/\lambda^{-1})_{\text{max}}/\text{\AA}^{-1}$	0.626
Standard reflections	(2 1 –2) (1 1 –3) (0 2 1)
Max. variation of intensity control reflections (%)	8.6
$\theta$ -Range for data collection/ $^\circ$	2.85–74.88
Range of $h$	–9 to 9
Range of $k$	–15 to 15
Range of $l$	–19 to 19
$R_{\text{int}}$	0.0188
Transmission factor range	0.610–0.928
No. of measured reflections, including standard reflections	10288
No. of independent reflections	6084
No. of observed reflections [ $I > 2\sigma(I)$ ]	6046
$w^{-1}$ ( $P = (F_o^2 + 2F_c^2)/3$ )	$\sigma^2(F_o^2) + (0.0455P)^2 + 0.3143P$
No. of variables	404
$R$ for $F > 4\sigma(F)$	0.0255
$wR_2$ for all $F^2$ data	0.0710
$S$ for all $F^2$ data	1.038
Max. shift/e.s.d.	0.003
Max. and min. $\Delta\rho/e \text{ \AA}^{-3}$	0.182, –0.262

equal to  $U_{\text{eq}}$  of the parent N and O atom multiplied by 1.2 and 1.5, respectively. The hydrogen atoms bonded to C atoms were refined as 'riding' on the C atom to which they are bonded, with restraints on their position and isotropic displacement parameters.

Polar axis restraints were applied according to the method of Flack and Schwarzenbach,<sup>12</sup> and the absolute structure of the crystal was chosen to match the known configuration of (2*R*,3*R*)-*O,O'*-dibenzoyltartaric acid. The refinement resulted in an absolute structure parameter<sup>13</sup> of 0.011(10), thus establishing the absolute configuration of the cation as *S*. Anisotropic displacement parameters, parameters for the hydrogen atoms and lists

of the observed and calculated structure factors can be obtained from the authors (S.L.).

## Results and discussion

**The resolution process.** 3-(2'-Hydroxy-2'-phenylethyl)-2-thiazolidinium chloride (T-alcohol·HCl) is the intermediate in the selected synthesis. The optical resolution of the free base (T-alcohol) in methanol was attempted with (2R,3R)-O,O'-dibenzoyltartaric acid (DBTA) monohydrate in different molar ratios. No precipitation was obtained when 0.5 equiv. of resolving agent was used, whereas a very efficient resolution was obtained both by 1 and 0.75 equiv. DBTA. The efficiency achieved in the latter two resolutions is very high as described by the *S*-parameter (defined as the product of the yield and the optical purity of the base<sup>14</sup>). The resolution process using 1 equiv. resolving agent has the higher efficiency (*S* = 0.80), since the yield is almost quantitative (97%). The resolution performed with 0.75 equiv. resolving agent has a slightly lower efficiency (0.74), but a base with higher optical purity is obtained, 87% compared to 82% from the resolution with 1 equiv. resolving agent. Preliminary resolution experiments in ethanol<sup>15</sup> gave yields and optical purities that are lower than in those performed in methanol, illustrating that the resolution process is strongly affected by the solvent. Thermogravimetric analysis (TGA) results have shown that the less soluble diastereomeric salts obtained from either methanol or ethanol are solvated.

The less soluble salt obtained from methanol loses the solvent at 124–147°C, a very high temperature compared to the normal boiling point of methanol. This shows that the solvent is strongly involved in the crystal packing. From the crystal structure determination we found one molecule of methanol per cation–anion pair. TGA experiments showed that after two weeks this ratio falls to 0.5; after a few months it drops even further, especially in powdered material, whereas the crystalline state seems to keep the methanol longer.

The more soluble salt (obtained from precipitate B) also contains methanol. This salt loses solvent in the weighing process, so the total loss cannot be accurately measured; it contains 30–40% of methanol, decreasing with time. The methanol is not only on the surface (it would have disappeared in samples left alone for two weeks). This indicates that methanol cannot be as strongly bound in the crystal as in the less soluble salt.

The less soluble salt obtained from ethanol behaves similarly to that from methanol, except that the loss of ethanol occurs at a considerably lower temperature (106–121°C relative to 124–147°C), which is surprising, since methanol has a higher partial pressure. In accordance with the lower partial pressure for ethanol the loss when kept at room temperature is 15% in two weeks.

The more soluble salt obtained from ethanol starts to lose ethanol immediately after its precipitation; it dissolves/melts at 118–132°C and decomposes at 155°C.

These features of the salts obtained from ethanol explain why the resolution is more efficient in methanol.

The powder diffraction pattern calculated from the single-crystal data was identical to that measured for the less soluble T-alcohol·DBTA. This assured that the investigated crystal represents the major component of the less soluble diastereomeric salt, and thus the *S* absolute configuration can be associated with the positive rotation of the base (*c* = 1, methanol). The optical rotations listed in Table 1 show that precipitate A has (*S*)-(+)-T-alcohol·DBTA as its major component.

The optical purity of T-alcohol was determined by <sup>1</sup>H NMR spectroscopy. A comparison of the spectra revealed that the signal at 4.66 ppm present in the spectrum of the racemic base was absent in the spectrum of the optically active base; conversely the signal at 4.72 ppm is present in the spectra of both the racemic and enantiomeric base. The enantiomeric excess was estimated in the optically active base to be higher than 0.97, as addition of 3% of racemic T-alcohol made the signal at 4.66 ppm appear.

**Description of the crystal structure.** The crystal contains discrete (*S*)-3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidinium cations, (2R,3R)-O,O'-dibenzoyl hydrogen tartrate anions and methanol molecules linked by an extensive system of hydrogen bonds.

**The (*S*)-3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidinium ion.** The molecular geometry of this cation is illustrated by Fig. 1 and by the bond lengths and angles listed in Table 4. The thiazolidine ring is slightly puckered, with the nitrogen atom in an almost planar configuration. The S–C1 distance is shorter than the other S–C4 bond [1.781(14) compared to 1.815(2) Å], in accordance with the sp<sup>2</sup> character of C1, but it should be noted that this difference is smaller than those observed in related structures.<sup>17,18</sup> The similarity of the C1–N15 and C1–N2 bond lengths and the planar environment of C1 is consistent with the partial double-bond character of the C1–N2

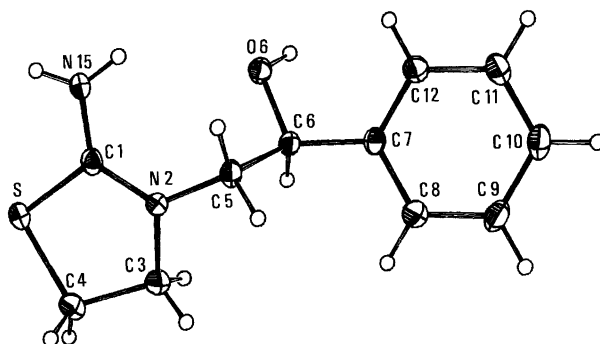


Fig. 1. ORTEP<sup>16</sup> drawing showing the molecular geometry of the 3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidinium cation. The thermal ellipsoids are scaled to include 50% probability. The hydrogen atoms are drawn as spheres with a fixed radius.

Table 3. Atomic coordinates and equivalent isotropic displacement parameters in ( $\text{\AA}^2$ ).

	x	y	z	$U_{\text{eq}}^a$
Cation				
S	0.18754(4)	0.13945(3)	0.03005(2)	0.02106(7)
O6	-0.44217(3)	0.12179(8)	-0.11263(6)	0.0206(2)
N15	-0.0307(2)	0.14211(11)	-0.12431(8)	0.0211(2)
N2	-0.0942(2)	0.02258(9)	-0.02089(7)	0.0188(2)
C1	0.0019(2)	0.09871(10)	-0.04822(9)	0.0175(2)
C3	-0.0441(2)	-0.00078(3)	0.07143(9)	0.0252(3)
C4	0.1517(2)	0.03155(3)	0.10082(9)	0.0271(3)
C5	-0.2550(2)	-0.02736(11)	-0.07255(9)	0.0187(2)
C6	-0.4304(2)	0.02747(10)	-0.06226(8)	0.0166(2)
C7	-0.5894(2)	-0.04741(11)	-0.08853(8)	0.0170(2)
C8	-0.6046(2)	-0.13408(12)	-0.03523(9)	0.0222(3)
C9	-0.7502(2)	-0.20331(12)	-0.05546(10)	0.0259(3)
C10	-0.8821(2)	-0.18626(12)	-0.12944(10)	0.0272(3)
C11	-0.8683(2)	-0.10084(12)	-0.18250(10)	0.0250(3)
C12	-0.7218(2)	-0.03123(11)	-0.16259(9)	0.0206(3)
Anion				
O2A	-0.64192(12)	-0.73439(8)	-0.35800(6)	0.0192(2)
O3A	-0.57416(12)	-0.53966(7)	-0.27631(6)	0.0165(2)
O11A	-0.20798(13)	-0.66822(8)	-0.23186(6)	0.0205(2)
O12A	-0.30315(4)	-0.68695(9)	-0.37550(6)	0.0265(2)
O21A	-0.5752(2)	-0.90790(9)	-0.36246(8)	0.0356(3)
O31A	-0.57165(13)	-0.44430(8)	-0.15617(6)	0.0219(2)
O41A	-0.74899(13)	-0.73870(8)	-0.15361(7)	0.0236(2)
O42A	-0.89102(12)	-0.61426(8)	-0.24493(6)	0.0210(2)
C1A	-0.3271(2)	-0.69027(10)	-0.30330(9)	0.0170(2)
C2A	-0.5072(2)	-0.72197(10)	-0.28031(8)	0.0158(2)
C3A	-0.5719(2)	-0.63550(10)	-0.22726(8)	0.0153(2)
C4A	-0.7555(2)	-0.66460(11)	-0.20761(8)	0.0162(2)
C21A	-0.6601(2)	-0.83101(11)	-0.39444(9)	0.0214(3)
C22A	-0.7890(2)	-0.83254(13)	-0.47850(10)	0.0258(3)
C23A	-0.8125(2)	-0.9276(2)	-0.52449(12)	0.0397(4)
C24A	-0.9178(3)	-0.9297(2)	-0.60720(14)	0.0521(6)
C25A	-0.9993(2)	-0.8372(2)	-0.64352(12)	0.0527(6)
C26A	-0.9823(3)	-0.7438(2)	-0.59712(12)	0.0465(5)
C27A	-0.8771(2)	-0.7402(2)	-0.51395(11)	0.0331(3)
C31A	-0.5673(2)	-0.44803(11)	-0.23205(8)	0.0167(2)
C32A	-0.5477(2)	-0.35479(11)	-0.28685(8)	0.0196(2)
C33A	-0.5128(2)	-0.25588(12)	-0.24736(10)	0.0275(3)
C34A	-0.4947(3)	-0.16767(13)	-0.29705(12)	0.0373(4)
C35A	-0.5151(3)	-0.17716(13)	-0.38575(12)	0.0355(4)
C36A	-0.5541(2)	-0.27529(14)	-0.42527(11)	0.0315(3)
C37A	-0.5676(2)	-0.36478(13)	-0.37603(9)	0.0248(3)
Solvent				
O1M	-0.2150(2)	0.06658(10)	-0.28846(7)	0.0336(2)
C1M	-0.1085(3)	0.0775(2)	-0.35243(13)	0.0497(5)

<sup>a</sup>  $U_{\text{eq}}$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

bond. O6 of the hydroxy group is almost in the plane of the phenyl ring.

These results agree well with those obtained in an investigation<sup>17</sup> of the similar ion where C6 is chloro-substituted. The chloro-substituted cation was investigated as a *p*-toluenesulfonate salt and the crystal contained the cation as two different conformers in different populations. The T-alcohol cation adopts a conformation that is similar to one of the conformers found for the corresponding chloro-substituted cation.

*The (2R,3R)-O,O'-dibenzoyl hydrogen tartrate ion.* The bond lengths and angles of the anion listed in Table 5 as well as the drawing shown in Fig. 2 illustrate its molecular geometry. The tartaric acid moiety of the anion has molecular dimensions and a conformation that are very similar to those observed in unsubstituted hydrogen tartrates. The two carboxy groups have distinctly different geometries, showing that O11A–C1A–O12A is the carboxylic acid and O41A–C4A–O42A the carboxylate group. The atoms O2A and O3A are almost in the planes

Table 4. Bond distance (in Å), bond and selected torsion angles (in °) in the (S)-(+)-3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidininium cation.

S–C1	1.781(14)	C5–C6	1.536(2)
S–C4	1.815(2)	C6–C7	1.518(2)
O6–C6	1.421(2)	C7–C12	1.391(2)
N15–C1	1.299(2)	C7–C8	1.397(2)
N2–C1	1.329(2)	C8–C9	1.390(2)
N2–C3	1.462(2)	C9–C10	1.390(2)
N2–C5	1.461(2)	C10–C11	1.381(2)
C3–C4	1.516(2)	C11–C12	1.398(2)
C1–S–C4	90.97(7)	O6–C6–C7	114.17(10)
C1–N2–C3	115.09(11)	C7–C6–C5	110.41(11)
C1–N2–C5	125.37(11)	C6–C7–C12	122.24(12)
C3–N2–C5	119.15(11)	C8–C7–C12	119.19(12)
N15–C1–N2	126.27(13)	C6–C7–C8	118.56(12)
N15–C1–S	120.32(11)	C7–C8–C9	120.66(13)
N2–C1–S	113.31(10)	C8–C9–C10	119.74(13)
N2–C3–C4	106.74(11)	C9–C10–C11	120.03(13)
C3–C4–S	105.86(10)	C10–C11–C12	120.45(14)
N2–C5–C6	112.82(11)	C7–C12–C11	119.94(13)
O6–C6–C5	105.64(10)		
C8–C7–C6–C5	70.8(2)	C4–S–C1–N2	8.39(11)
C7–C6–C5–N2	–159.17(11)	S–C1–N2–C3	8.9(2)
C6–C5–N2–C1	–92.5(2)	N2–C5–C6–O6	76.92(13)
C1–N2–C3–C4	–25.4(2)	C8–C7–C6–O6	–170.36(12)
N2–C3–C4–S	29.1(2)	C12–C7–C6–O6	8.2(2)
C3–C4–S–C1	–21.66(11)		

defined by the carboxylic acid and the carboxylate groups, respectively. The dihedral angle between these two virtually planar halves of the anion is 53.83(5)°. Apart from the difference between the two carboxy groups the two halves of the anion have virtually identical geometry. The carbon chain C1A–C2A–C3A–C4A is found in an anti-periplanar conformation.

*Crystal packing.* The packing in the crystal shown in Fig. 3 is influenced by interactions between phenyl groups as well as several hydrogen-bond interactions ranging from strong to weak. The cation contains three potential donor atoms, two from the iminium group and one from the hydroxy group, and two potential acceptor atoms O6 and S. Conversely the anion has only one possible hydrogen-bond donor and eight possible acceptor atoms. In addition, the methanol solvent with a O1M–C1M distance of 1.427(2) Å may donate one proton and has one proton acceptor. The resulting hydrogen bonding scheme is listed in Table 6.

As shown in Fig. 3 hydrogen-bonded buckled sheets are separated by two hydrophobic sections: one with interacting phenyl rings and one consisting of phenyl rings and thiazolidininium rings. In the hydrogen-bonded section short hydrogen bonds of 2.547 Å (O11A···O42A) between the carboxylic acid and the carboxylate groups connect the anions into infinite chains along the *a*-axis. The iminium group of the cation donates protons to the O41A and methanol, which in turn donates its proton to O21, making the methanol molecule form a link between the cation and the anion. The hydroxy group of the cation

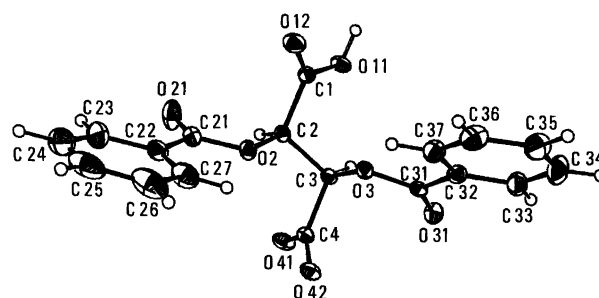


Fig. 2. ORTEP<sup>16</sup> drawing showing the molecular geometry of the (2R,3R)-O,O'-dibenzoyl hydrogen tartrate anion. The numbers refer to the labels in Tables 3 and 4 with the letter A omitted. The thermal ellipsoids are scaled to include 50% probability. The hydrogen atoms are drawn as spheres with a fixed radius.

is a hydrogen-bond donor to O41A. Thus the oxygen atom O41A of the carboxylate group links two cations related by translational symmetry along the *a*-axis. This results in a packing where the cations and the anions are each interacting directly to two oppositely charged ions. The two ions that are interacting through the hydroxy-carboxylate hydrogen bond are also linked by the hydrogen bonds involving the methanol molecule.

*Comparison of substituted hydrogen tartrate structures.* The very short 2.547(1) Å donor-acceptor hydrogen bonds between O11A and O42A are similar to those observed in the structures of hydrogen tartrates<sup>5</sup> linking the anions head-to-tail into infinite chains.

We have investigated if this is also a common struc-

Table 5. Bond distances (in Å), bond and selected torsion angles (in °) in the (2*R*,3*R*)-*O*-*O'*-dibenzoyl hydrogen tartrate anion.

O2A–C21A	1.339(2)	O3A–C31A	1.344(2)
O2A–C2A	1.435(2)	O3A–C3A	1.432(2)
O11A–C1A	1.322(2)	O41A–C4A	1.258(2)
O12A–C1A	1.195(2)	O42A–C4A	1.246(2)
O21A–C21A	1.212(2)	O31A–C31A	1.210(2)
C1A–C2A	1.537(2)	C3A–C4A	1.533(2)
C2A–C3A	1.516(2)		
C21A–C22A	1.479(2)	C31A–C32A	1.484(2)
C22A–C23A	1.392(2)	C32A–C33A	1.392(2)
C22A–C27A	1.398(2)	C32A–C37A	1.394(2)
C23A–C24A	1.385(3)	C33A–C34A	1.383(2)
C24A–C25A	1.385(4)	C34A–C35A	1.386(3)
C25A–C26A	1.376(4)	C35A–C36A	1.387(3)
C26A–C27A	1.392(2)	C36A–C37A	1.385(2)
C21A–O2A–C2A	117.33(10)	C31A–O3A–C3A	116.32(9)
O11A–C1A–O12A	126.78(12)	O41A–C4A–O42A	127.60(12)
O12A–C1A–C2A	123.68(12)	O41A–C4A–C3A	113.91(11)
O11A–C1A–C2A	109.54(11)	O42A–C4A–C3A	118.49(11)
O2A–C2A–C1A	109.54(10)	O3A–C3A–C4A	113.70(10)
O2A–C2A–C3A	107.35(10)	O3A–C3A–C2A	105.75(10)
C1A–C2A–C3A	110.55(10)	C2A–C3A–C4A	110.70(10)
O21A–C21A–O2A	123.02(12)	O31A–C31A–O3A	123.04(12)
O21A–C21A–C22A	124.05(13)	O31A–C31A–C32A	125.23(12)
O2A–C21A–C22A	112.90(12)	O3A–C31A–C32A	111.69(11)
C23A–C22A–C27A	120.3(2)	C33A–C32A–C37A	120.39(14)
C21A–C22A–C23A	118.1(2)	C31A–C32A–C33A	118.38(12)
C21A–C22A–C27A	121.47(14)	C31A–C32A–C37A	121.21(13)
C22A–C23A–C24A	119.8(2)	C32A–C33A–C34A	119.50(14)
C23A–C24A–C25A	119.8(2)	C33A–C34A–C35A	120.3(2)
C24A–C25A–C26A	120.7(2)	C34A–C35A–C36A	120.2(2)
C25A–C26A–C27A	120.4(2)	C35A–C36A–C37A	120.2(2)
C22A–C27A–C26A	119.0(2)	C32A–C37A–C36A	119.5(2)
O11A–C1A–C2A–O2A	173.62(10)	O41A–C4A–C3A–O3A	–169.47(11)
O12A–C1A–C2A–O2A	–6.4(2)	O42A–C4A–C3A–O3A	10.2(2)
C1A–C2A–C3A–C4A	117.49(10)		
C2A–O2A–C21A–O21A	3.9(2)	C3A–O3A–C31A–O31A	–5.1(2)
O2A–C21A–C22A–C23A	176.96(14)	O3A–C31A–C32A–C33A	–170.92(12)
O2A–C21A–C22A–C27A	0.9(2)	O3A–C31A–C32A–C37A	10.5(2)

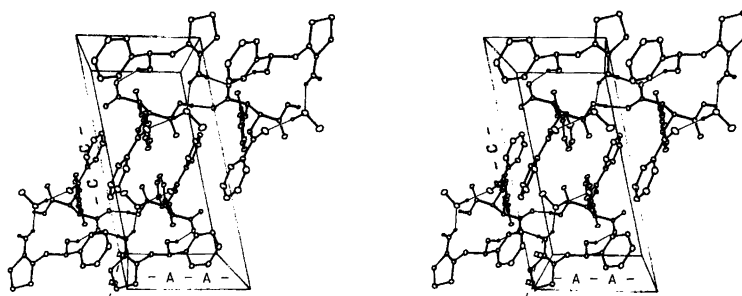


Fig. 3. Stereo pairs<sup>16</sup> illustrating the packing of 3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidiniminium-(2*R*,3*R*)-*O*,*O'*-dibenzoyl hydrogen tartrate methanol adduct viewed along the *b*-axis. The hydrogen bonds are shown as thin lines. The hydrogen atoms not involved in the hydrogen-bonding system are omitted for clarity.

tural motif for the substituted hydrogen tartrates. A search was made in the Cambridge Structural Database<sup>19</sup> (update April 1994) for structures with *R*-values less than 0.07 that contain a tartaric acid fragment with one of the hydroxy groups converted into a benzoyl ester, and this resulted in 13 hits. These structures were classified ac-

cording to the deprotonation of the carboxy groups. As the coordinates for hydrogen atoms were unavailable for some of the structures, symmetry and chemical knowledge, e.g. possible protonation of the counter-ion and differences in the carboxy group C–O distances, were used to make this classification.

Table 6. Hydrogen bonds for (S)-3-(2'-hydroxy-2'-phenylethyl)-2-thiazolidiniminium (2R,3R)-O-O'-dibenzoyl hydrogen tartrate methanol adduct.

D—H···A	D···A/Å	D—H···A/°	H···A/Å
N15—H1N···O1M	2.846(2)	147(2)	2.07(2)
N15—H2N···O41A <sup>a</sup>	2.727(2)	168(2)	1.93(2)
O6—HO···O41A <sup>b</sup>	2.878(1)	155(2)	2.07(2)
O11A—H11A···O42A <sup>c</sup>	2.547(1)	172(2)	1.72(2)
O1M—H1M···O21A <sup>b</sup>	2.759(2)	178(2)	1.78(3)

<sup>a</sup> x+1, y+1, z. <sup>b</sup> x, y+1, z. <sup>c</sup> x+1, y, z.

For two of the compounds no deprotonation of the tartaric acid has occurred, and another three are dicarboxylates. The remaining eight can be classified as *O*-substituted hydrogen tartrates; their reference codes are listed in Table 7. Of these three are di-*p*-toluoyl hydrogen tartrates (SUBWAN, VARBEV and YADBUA), GAZSOP is a monobenzoyl substituted hydrogen tartrate, and the remaining four are dibenzoyl hydrogen tartrates.

In all these salts short intermolecular O—H···O hydrogen bonds between the carboxylate and the carboxylic acid groups are observed. In seven of these a head-to-tail arrangement is found identical to that observed in the present structure and in the structures of hydrogen tartrates, connecting the anions to form infinite chains, parallel to a translational period of the crystal lattice. As discussed later, DUHZUB differs from the common pattern. Apart from VARBEV and YADBUA they crystallize either in space group  $P2_1$  or  $P2_12_12_1$ .

YADBUA is unique because it contains two molecules of substituted hydrogen tartrate in the asymmetric unit. They form two independent chains parallel to the *a*-axis, each chain containing only one of the conformers. The substituted hydrogen tartrates connected by head-to-tail hydrogen bonds are related by translational symmetry giving rise to chains parallel to one of the crystallographic axes with a length in the range 7.05–7.83 Å, as described by Fogassy *et al.*<sup>5</sup> for the similar arrangements in unsubstituted hydrogen tartrates.

Table 7. Substituted hydrogen tartrates extracted from the Cambridge Structural Database (CSD).

Refcode <sup>a</sup>	Space group	Translational period/Å	O···O /Å	C1—C2—C3—C4/°
DUHZUB <sup>B</sup>	$P2_1$	Intramolecular	2.428	−80
FEZPAB <sup>B</sup>	$P2_12_12_1$	$a=7.478(2)$	2.429	−172
GAZSOP <sup>mB</sup>	$P2_12_12_1$	$a=7.803(2)$	2.526	−173
KIBPIU <sup>B</sup>	$P2_1$	$a=7.547(2)$	2.562	−172
SICWEG <sup>B</sup>	$P2_12_12_1$	$a=7.490(1)$	2.425	−178
SUBWAN <sup>T</sup>	$P2_12_12_1$	$b=7.635(2)$	2.523	−170
VARBEV <sup>T</sup>	$P1$	$a=7.628(1)$	2.472	−166
YADBUA <sup>T</sup>	$P1$	$a=7.675(2)$	2.482	−160
			2.447	−171

<sup>a</sup> T, di-*p*-toluoyl; B, dibenzoyl; mB; monobenzoyl.

DUHZUB is the salt that does not fit into this common pattern. The positive ion is a chiral ruthenium complex carrying one formal positive charge and no potential hydrogen-bond donors. In the compound the dibenzoyl hydrogen tartrate ion makes a very short intramolecular hydrogen bond. As a consequence the hydrogen tartrate ion is not found in the usual extended conformation, but in a syn-clinal conformation, as the torsion angle of the tartaric fragment (C1—C2—C2—C4) reflects.

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