Crystal structure of (1R,2R)-trans-1,2-cyclohexanedicarhoxylic acid-(R)- 1-phenylethylamine salt

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Crystal Structure of (1*R*, 2*R*)-*trans* -1,2-Cyclohexanedicarboxylic Acid-(*R*)-1-Phenylethylamine Salt

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Although recent advances in asymmetric synthesis and biotechnology are noteworthy, they do not completely satisfy the increasing demand for optically pure compounds. Traditional optical resolutions and physicochemical separations are still employed as useful procedures for the preparation of optically pure compounds in industry.[1] We have studied the optical resolution of *trans*-1,2-cyclohexanedicarboxylic acid (CHDC) through diastereomer crystallization using (*R*)-1-phenylethylamine ((*R*)-PEA) as a resolving agent. In order to perform the optical resolution rationally and with a high probability of success, an improved understanding of the correlation between the crystal structure and the physicochemical properties is indispensable.

Racemic CHDC was dissolved in ethanol at 70 °C and subsequently an equimolar of (*R*)-PEA was added. The solution was allowed to stand undisturbed at 30 °C for 30 h. The precipitated crystals of (*R*, *R*)-CHDC · (*R*)-PEA **1** were filtered off and dried in vacuo. The diastereomeric salt was recrystallized from ethanol twice (mp 172-174 °C). By acidifying the salt with hydrochloric acid, optically pure (*R*,*R*)-CHDC was obtained. (59 % yield, 99.5 % e.e., mp 183-185℃)

A colorless prism crystal of **1** with dimensions 0.6×0.3×0.2 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC-5R diffractometer with a graphite monochromated Cu Kα radiation (λ= 1.54178 Å). The detailed measurement conditions and crystal data are listed in Table 1. The intensity data were collected at 23°C using the ω-2θ scan technique to a maximum 2θ value of 120.1°. A total of 1426 reflections were collected. The intensities of three representative reflections which were measured after every 150 reflections remained constant throughout data collection, indicating crystal and electronic stability. No decay correction was applied. The linear absorption coefficient for Cu Kα is 6.8 cm^{-1}. Azimuthal scans of several reflections indicated no need for absorption correction. The data were corrected for Lorentz and

polarization effects.

The structure was solved by direct methods.[2] The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located from a difference Fourier map and included in the final cycle of the full-matrix least squares refinement. The atomic scattering factors and anomalous dispersion terms were taken from the International Tables for X-ray Crystallography, Vol. IV.[3] All calculations were performed using the program TEXSAN crystallographic software package.[4] Positional parameters for non-hydrogen atoms are listed in Table 2. The molecular structure is shown in Fig. 2, together with the atomic labeling scheme. Bond distances and selected bond angles are listed in Table 3.

In the crystal structure the (*R*, *R*)-CHDC molecule is protonated on one of the two carboxylate groups. This is demonstrated by the C-O bond length of the structure. The C8-O4 bond (1.311(3) Å) is significantly longer than the C8-O3 bond (1. 209(3) Å) in the carboxylic acid group. On the other hand, the C-O bonds have similar bond lengths in the carboxylate group (C7-O1, 1.231(3) Å; C7-O2, 1.273(3) Å). The (*R*, *R*)-CHDC molecules are linked by intermolecular hydrogen bondings between the carboxylic acid and the carboxylate groups (O2···O4' 2.561(3) Å, O2···H'-O4' 177.0(4) °, a prime denotes atoms in the neighboring molecules). This hydrogen bonding network forms a pleated sheet structure along the a axis. The ammonium groups of the (*R*)-PEA molecules are situated between the rows of the (*R*, *R*)-CHDC moieties and connect the pleated sheets through the intermolecular hydrogen bondings (N1···O1' 2.700(3) Å, N1-H···O1' 162.0(3) °; N1···O2' 2.833(3) Å, N1-H···O2' 164.0(3) °; N1···O3' 2.821(3) Å, N1-H ···O3' 136.0(3) °).

References

1. R. A. Sheldon, "*Chirotechnology: Industrial Synthesis of Optically Active Compounds*", Chap. 6, pp.173 -204, Marcel Dekker, Inc., New York, 1993.

2. C. J. Gilmore, *J. Appl. Cryst.*, **17**, 42 (1984).

3. "*International Tables for X-ray Crystallography*", vol. IV, The Kynoch Press, Birmingham, England, 1974.

4. "*TEXAN*", TEXRAY Structure Analysis Package, Molecular Structure Corporation, The Woodlands, TX, USA 1985.

Table 1 Crystal and experimental data

Formula: $C_{16}H_{23}NO_4$

Formula weight: 293.36

Crystal system: orthorhombic

Space group: $P2_12_12_1$ Z=4

a= 9.9880(9)Å

b= 26.034(2)Å

c= 6.0826(4)Å

V= 1581.7(2)Å^3

$Dcalc$= 1.232 g/cm^3

R=0.041, R_w=0.052

Goodness-of-fit = 3.01

$\Delta\rho_{max}$(eÅ^{-3}) / $\Delta\rho_{min}$(eÅ^{-3}) = 0.17/-0.28

No. of reflections used= 1360 ($I>1.20\sigma(I)$)

No. of parameters = 282

Measurement: Rigaku AFC-5R

Program system: TEXSAN

Structure determination: direct method

Refinement: full-matrix least-squares

Table 2 Fractional coordinates and thermal parameters for non-hydrogen atoms

Atom	x	y	z	B_{eq}/Å^2
O1	0.8166(2)	0.16392(9)	1.3442(3)	5.1(1)
O2	0.8255(2)	0.20735(7)	1.0323(3)	4.01(8)
O3	0.4884(2)	0.19424(7)	1.1399(3)	4.6(1)
O4	0.4647(2)	0.22043(8)	0.7959(3)	4.1(1)
N1	0.9778(2)	0.2105(1)	0.6397(5)	3.3(1)
C1	0.6992(2)	0.12927(8)	1.0415(4)	2.7(1)
C2	0.6099(2)	0.15021(9)	0.8589(4)	2.7(1)
C3	0.5304(3)	0.1071(1)	0.7466(6)	4.1(1)
C4	0.6220(4)	0.0649(1)	0.6634(6)	4.3(1)
C5	0.7090(3)	0.0437(1)	0.8483(6)	4.1(1)
C6	0.7884(3)	0.0856(1)	0.9575(5)	3.5(1)
C7	0.7856(2)	0.1699(1)	1.1501(4)	3.0(1)
C8	0.5166(3)	0.19058(8)	0.9473(4)	3.0(1)
C9	1.1204(3)	0.1352(1)	0.7031(5)	3.7(1)
C10	1.1678(4)	0.1174(2)	0.9037(6)	5.7(2)
C11	1.1698(5)	0.0649(2)	0.947(1)	7.7(3)
C12	1.1274(6)	0.0309(2)	0.790(1)	8.2(3)
C13	1.0829(4)	0.0474(1)	0.589(1)	6.9(2)
C14	1.0771(3)	0.1002(1)	0.5470(7)	4.9(1)
C15	1.1182(3)	0.1923(1)	0.6583(5)	3.7(1)
C16	1.1941(4)	0.2074(1)	0.4540(8)	5.1(2)

Beq=(4/3)$\Sigma_i\Sigma_j\beta_{ij}a_i^*a_j^*(a_i\ a_j)$

Table 3 Bond distances(Å) and selected bond angles(°)

Atom	Atom	Distance	Atom	Atom	Distance
O1	C7	1.231(3)	C4	C5	1.524(5)
O2	C7	1.273(3)	C5	C6	1.503(4)
O3	C8	1.209(3)	C9	C10	1.388(5)
O4	C8	1.311(3)	C9	C14	1.386(5)
N1	C15	1.485(4)	C9	C15	1.511(4)
C1	C2	1.525(3)	C10	C11	1.392(7)
C1	C6	1.533(3)	C11	C12	1.366(8)
C1	C7	1.518(3)	C12	C13	1.374(8)
C2	C3	1.535(4)	C13	C14	1.397(5)
C2	C8	1.504(3)	C15	C16	1.508(5)
C3	C4	1.517(4)			

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
O1	C7	O2	124.0(2)	C4	C5	C6	111.4(2)
O1	C7	C1	118.1(2)	C6	C1	C7	109.4(2)
O2	C7	C1	117.8(2)	C9	C10	C11	119.8(5)
O3	C8	O4	122.8(3)	C9	C14	C13	120.6(4)
O3	C8	C2	123.1(2)	C9	C15	N1	110.0(2)
O4	C8	C2	114.1(2)	C9	C15	C16	113.5(3)
C1	C2	C3	111.4(2)	C10	C11	C12	120.1(5)
C1	C2	C8	110.6(2)	C10	C9	C14	119.3(3)
C1	C6	C5	112.2(2)	C10	C9	C15	119.4(3)
C2	C1	C6	111.3(2)	C11	C12	C13	121.2(4)
C2	C1	C7	113.6(2)	C12	C13	C14	118.9(5)
C2	C3	C4	111.5(2)	C14	C9	C15	121.3(3)
C3	C4	C5	111.1(3)	C16	C15	N1	109.1(3)
C3	C2	C8	110.4(2)				

Estimated standard deviations in the least significant figure are given in parentheses.

Figure Captions

Fig. 1 Chemical structure of **1**.

Fig. 2 Molecular structure with the numbering of the atoms.
Thermal ellipsoids of the non-hydrogen atoms are scaled to enclose 50 % probability.
The spheres of the hydrogen atoms are drawn in an arbitrary scale.

Fig. 3 Molecular packing viewed along the *c* -axis.

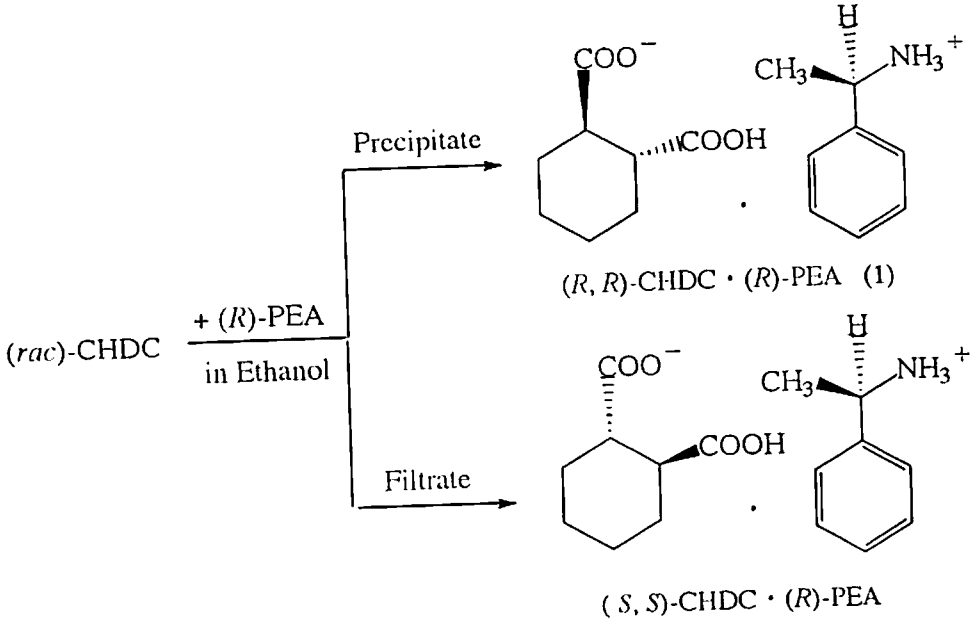
(rac)-CHDC
+ (R)-PEA
in Ethanol
Precipitate
Filtrate
COO⁻
COOH
CH3
NH3+
H
(R, R)-CHDC · (R)-PEA (1)
(S, S)-CHDC · (R)-PEA

Fig. 1

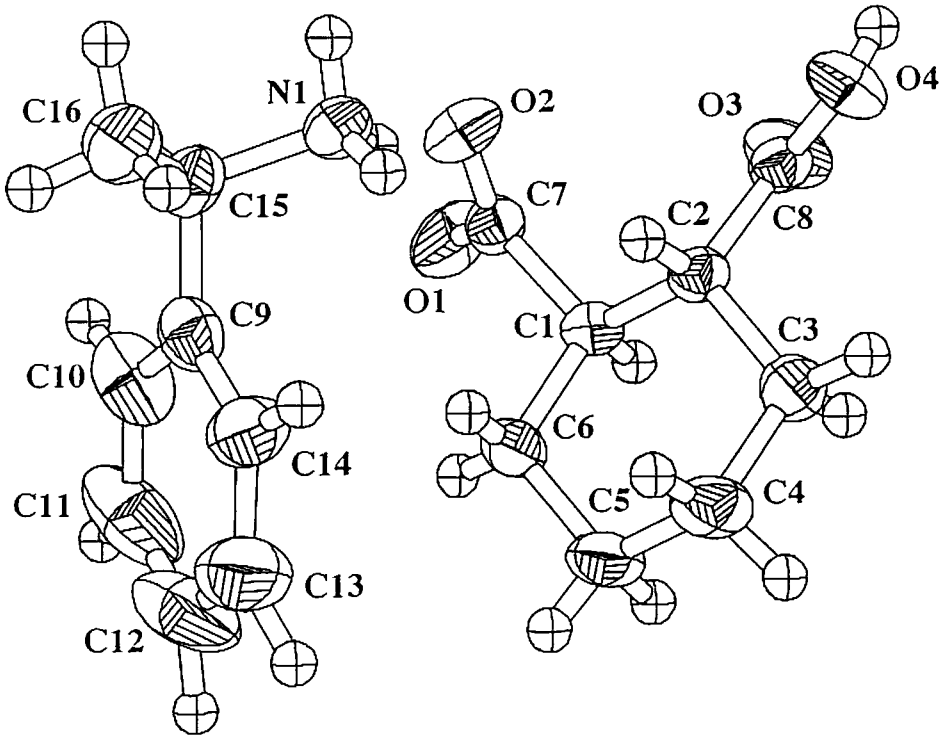

Fig. 2

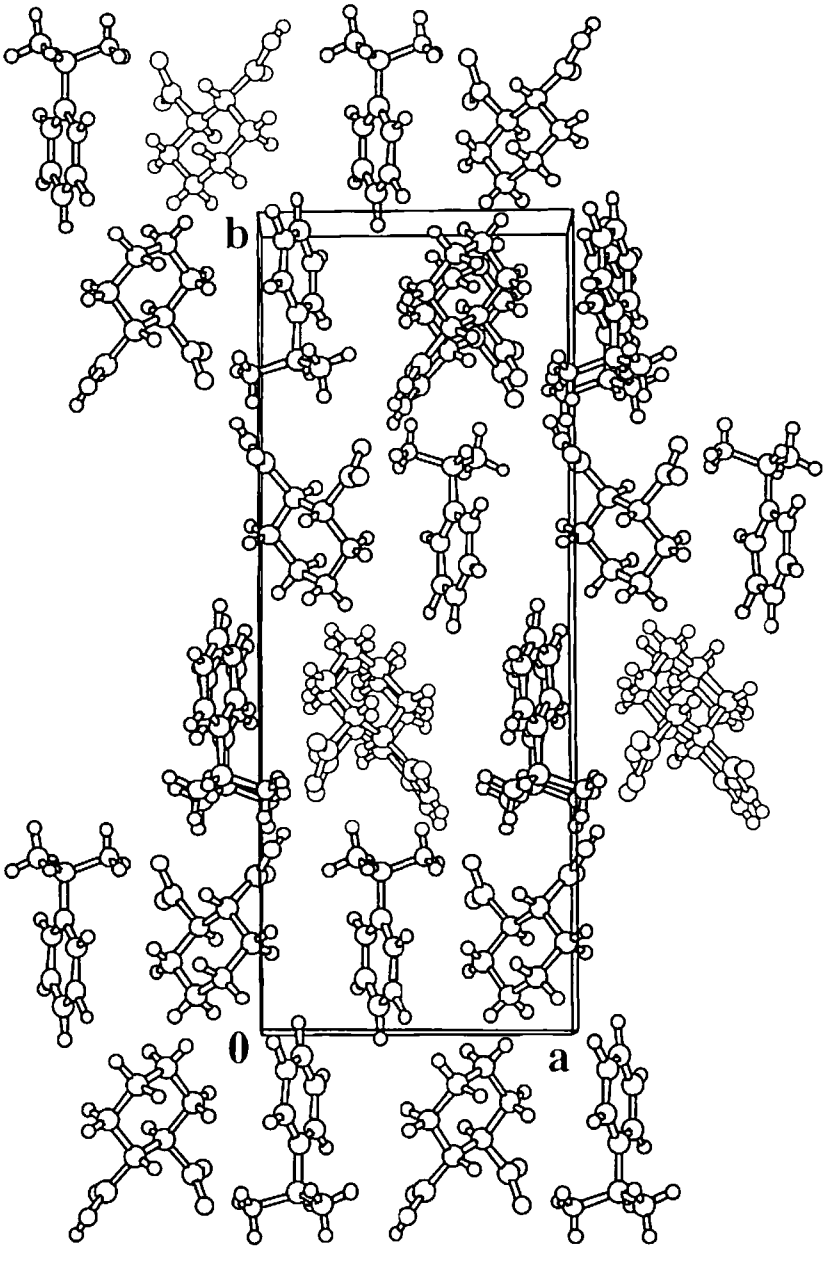

Fig. 3