Crystal Structure of a Salt Complex between (*R*)-2-Benzylsuccinic Acid and (*R*)-1-Phenylethylamine

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Optically pure 2-benzylsuccinic acid is obtained by optical resolution of the racemates with the chiral host 1-phenylethylamine. The structure of the salt complex between (*S*)-2-benzylsuccinic acid and (*R*)-1-phenylethylamine was first elucidated by X-ray analysis, indicating that the hydrogen bonds are formed between the acetate anions and the protonated amino group. The intermolecular hydrogen bond links the salt complex into a quasi-two-dimensional net-like structure.

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The optical resolution of racemates by diastereoisomeric salt formation is a common way to prepare optical isomers.¹ 2-Benzylsuccinic acid is a very important component that is widely used, especially in preparing pharmaceutical active ingredients, such as Mitiglinide, which is useful in the treatment of non-insulin dependent diabetes.² In this paper, we report on the crystal structure of a salt complex between (*R*)-2-benzylsuccinic acid and (*R*)-1-phenylethylamine (shown in Fig. 1).

Racemic 2-benzylsuccinic acid and (*R*)-1-phenylethylamine in a molar ratio of 2:1 were dissolved in hot ethanol. The solution was allowed to stand at room temperature, and the salt complex of (*R*)-2-benzylsuccinic acid was formed. The salts were collected by filtration and recrystallized from ethanol four times to give rod-like colorless crystals (45% yield, mp 122 – 123°C).

A colorless crystal with dimensions of 0.26 mm × 0.20 mm × 0.14 mm was mounted on a BRUKER SMART 1000 CCD diffractometer equipped with a graphite monochromator. Determinations of unit-cell parameters and data collections were performed with Mo K_{α} radiation ($\lambda = 0.71073$ Å). All data were corrected by using the SADABS method.³ The structure was solved by direct methods with the SHELXL-97 program.⁴ The final refinement was performed by least-squares methods with anisotropic thermal parameters for non-hydrogen atoms on F^2 . C(11), O(3) and O(4) show disorder with occupancy factors for C(11)*, O(3)* and O(4)* of 0.15, respectively. Hydrogen atoms were added theoretically, riding on the concerned atoms

and being refined with fixed thermal factors. Full crystallographic details were deposited with the Cambridge Crystallographic Data Center and allocated the deposition number CCDC-241568. The crystal data are summarized in Table 1. Positional parameters and atomic coordinates are given in Table 2. Selected bond distances and angles are listed in Table 3.

An ORTEP drawing of the complex composed of (*R*)-2-benzylsuccinic acid and (*R*)-1-phenylethylamine with atomic labeling is shown in Fig. 2. The analyzed structure data showed that the complex is produced by the formation of hydrogen bonds. 2-Benzylsuccinic acid is deprotonated, and the C=O bond lengths of the carboxyl group are homogenized, being 1.244(7) Å (C9–O1) and 1.266(7) Å (C9–O2). They are shorter than the C–O bond of the hydroxyl groups (C11–O3, 1.337(7) Å). The amino group of 1-phenylethylamine is protonated, and the

Fig. 1 Chemical structure of the title complex.

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Table 1 Crystallographic data and structure refinement summary for inclusion salt complex

Formula: C ₁₉ H ₂₃ NO ₄
Formula weight = 329.38
Crystal system: monoclinic
Space group: $P2_1$ $Z = 2$
$a = 6.088(5)$ Å
$b = 8.697(7)$ Å
$c = 17.624(14)$ Å
$\beta = 97.873(13)^\circ$
$V = 924.3(13)$ Å ³
$D_x = 1.184$ Mg/m ³
No. of reflections used = 4393
$2\theta_{\max} = 50.02^\circ$ with Mo K_{α}
$R = 0.0989$
$(\Delta\sigma)_{\max} = 0.001$
$(\Delta\rho)_{\max} = 0.608$ eÅ ⁻³
$(\Delta\rho)_{\min} = -0.363$ eÅ ⁻³
Measurement: BRUKER SMART 1000 CCD
Program system: SAINT
Structure determination: direct methods (SHELXS-97)
Refinement: full matrix least-squares (SHELXL-97)

Table 2 Atomic coordinates (10^4) and equivalent isotropic displacement parameters

Atom	x	y	z	U(eq)
N(1)	8755(8)	9128(6)	729(3)	39(1)
C(1)	1974(16)	2411(12)	4006(5)	78(3)
C(2)	1800(20)	3442(17)	4629(5)	102(4)
C(3)	3470(40)	4432(17)	4880(7)	130(6)
C(4)	5210(30)	4533(15)	4514(7)	115(5)
C(5)	5531(19)	3614(11)	3907(5)	82(3)
C(6)	3896(12)	2497(9)	3644(3)	55(2)
C(7)	4218(12)	1470(8)	2971(4)	54(2)
C(8)	3686(9)	2270(7)	2190(3)	38(1)
C(9)	4403(9)	1176(6)	1576(3)	38(1)
O(1)	2977(7)	218(6)	1276(3)	59(1)
O(2)	6346(6)	1234(5)	1433(3)	52(1)
C(10)	1226(9)	2689(7)	2028(3)	40(1)
C(11)	706(11)	3416(8)	1247(4)	25(1)
O(3)	-1377(7)	3322(6)	893(3)	39(1)
O(4)	2084(7)	4073(6)	922(3)	37(1)
C(11)*	-590(40)	3340(50)	1412(16)	45(9)
O(3)*	-2580(60)	2930(70)	1060(30)	97(14)
O(4)*	760(60)	3470(50)	920(20)	61(10)
C(12)	7526(15)	7806(11)	2325(5)	68(2)
C(13)	8111(18)	7727(13)	3108(5)	85(3)
C(14)	10210(20)	7156(12)	3414(5)	86(3)
C(15)	11683(16)	6811(10)	2925(5)	75(2)
C(16)	11137(13)	6905(8)	2152(4)	59(2)
C(17)	8976(10)	7410(7)	1831(4)	44(1)
C(18)	8435(9)	7509(7)	969(4)	44(2)
C(19)	6059(11)	6992(9)	638(4)	55(2)

*The disordered atoms.

Table 3 Selected bond lengths ($\text{\AA}$) and angles ($^\circ$)

N(1)-C(18)	1.491(8)	C(6)-C(7)	1.518(10)
C(6)-C(7)	1.518(10)	C(10)-C(11)	1.508(7)
C(7)-C(8)	1.536(9)	C(11)-O(4)	1.220(9)
C(8)-C(10)	1.530(8)	C(11)-O(3)	1.337(7)
C(8)-C(9)	1.548(8)	C(17)-C(18)	1.512(9)
C(9)-O(2)	1.244(7)	C(18)-C(19)	1.550(8)
C(9)-O(1)	1.266(7)		
C(1)-C(6)-C(7)	121.7(7)	C(11)-C(10)-C(8)	110.4(5)
C(5)-C(6)-C(7)	119.8(7)	O(3)-C(11)-C(10)	117.9(6)
C(6)-C(7)-C(8)	113.5(6)	O(4)-C(11)-O(3)	110(4)
C(10)-C(8)-C(7)	110.9(5)	O(4)-C(11)-C(10)	123.5(5)
C(10)-C(8)-C(9)	112.2(5)	O(4)-C(11)-O(3)	118.6(5)
C(7)-C(8)-C(9)	107.6(5)	C(16)-C(17)-C(18)	118.5(6)
O(2)-C(9)-O(1)	124.0(5)	N(1)-C(18)-C(17)	108.7(5)
O(2)-C(9)-C(8)	118.9(5)	N(1)-C(18)-C(19)	108.6(5)
O(1)-C(9)-C(8)	117.0(5)	C(17)-C(18)-C(19)	115.2(5)

N-H group participates in N-H $\cdots$ O hydrogen bonds involving the O atom of the carboxyl anion. The N $\cdots$ O separation is 2.785 $\text{\AA}$ with the H $\cdots$ O separation being 1.896 $\text{\AA}$; the bond angle is 176.36 $^\circ$, falling into the normal range of the N $\cdots$ O separation for hydrogen bonding. In the crystal packing, a quasi-two-dimensional netlike structure was formed by the salt molecules through N-H $\cdots$ O hydrogen bonds in which O atoms of the carboxyl group link the N atoms of amino groups in the adjacent molecule, as shown in Fig. 3. The N $\cdots$ O separations of

Fig. 2 ORTEP drawing, representing heavy atoms as 50% probability ellipsoids. The dash line shows intermolecular hydrogen bond.

Fig. 3 Packing diagram of the title salt complex showing the hydrogen bonding.

the N-H $\cdots$ O hydrogen bond were in the range of 2.747 – 3.010 $\text{\AA}$ and the H $\cdots$ O separations were in the range of 1.878 – 2.185 $\text{\AA}$. The bond angles were in the range of 153.85 – 176.36 $^\circ$.

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