

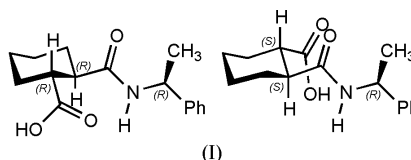
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Key indicators

Single-crystal X-ray study
 $T = 173\text{ K}$
Mean $\sigma(\text{C}-\text{C}) = 0.003\text{ \AA}$
 R factor = 0.040
 wR factor = 0.103
Data-to-parameter ratio = 10.1For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.A 1:1 diastereoisomeric complex of *trans*-2-[[*(R)*-(+)-1-phenylethylamino]carbonyl]-cyclohexanecarboxylic acidA novel cyclohexanecarboxylic acid derivative, $\text{C}_{16}\text{H}_{21}\text{NO}_3$, having a chiral amide group, was synthesized and its crystal structure has been determined. The crystal structure contains two diastereoisomers, namely (*1R,2R*)- and (*1S,2S*)-*trans*-2-[[*(R)*-(+)-1-phenylethylamino]carbonyl]cyclohexanecarboxylic acid.Received 3 September 2003
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Comment

On deprotonation, a carboxylic acid having a neighboring amide group can form an intramolecular $\text{N}-\text{H}\cdots\text{O}$ hydrogen bond between the carboxylate O atom and the neighboring amide NH group. The neighboring amide NH group lowers the $\text{p}K_{\text{A}}$ value of the carboxylic acid and the hydrogen bond prevents protonation of the carboxylate anion (Onoda *et al.*, 2001, 2002). These effects have been discussed mainly with respect to acylaminobenzoic acid derivatives.

In the present study, we synthesized an aliphatic carboxylic acid derivative, namely *trans*-2-[[*(R)*-(+)-1-phenylethylamino]carbonyl]cyclohexanecarboxylic acid, (I), from *trans*-1,2-cyclohexanedicarboxylic anhydride and determined its crystal structure to be a 1:1 complex of the (*1R,2R*)- and (*1S,2S*)-diastereoisomers (Fig. 1*a*). The ^1H NMR spectrum in [d_6]DMSO also shows that (I) contains two diastereoisomers. With the exception of amino acids, such a diastereoisomeric complex is rare in reported organic crystal structures; however, a diastereoisomeric Ru complex has been reported (Brunner *et al.*, 2003).

Fig. 1(*b*) shows the unit cell contents of (I). The $\text{N1B}\cdots\text{O1A}$ distance of 2.861 (2) Å suggests the presence, between the diastereoisomers, of an $\text{N}-\text{H}\cdots\text{O}$ hydrogen bond, *viz.* $\text{N1B}-\text{H1NB}\cdots\text{O1A}$. The other amide group is also involved in an $\text{N}-\text{H}\cdots\text{O}$ hydrogen bond, $\text{N1A}\cdots\text{O1B}^{\text{iii}}$ having a distance of 2.932 (2) Å (Table 2). Additionally, two carboxylic acid groups form a dimeric unit *via* $\text{O}-\text{H}\cdots\text{O}=\text{C}$ hydrogen bonds (Fig. 2). Because of the formation of these hydrogen bonds, the carboxylic acid group at the 1-position of cyclohexane and the amide group at the 2-position are oriented equatorially.

Experimental

trans-Cyclohexanedicarboxylic anhydride (1.0 g, 6.5 mmol) in tetrahydrofuran (10 ml) was added to (*R*)-(+)-1-phenylethylamine (1.0 ml,

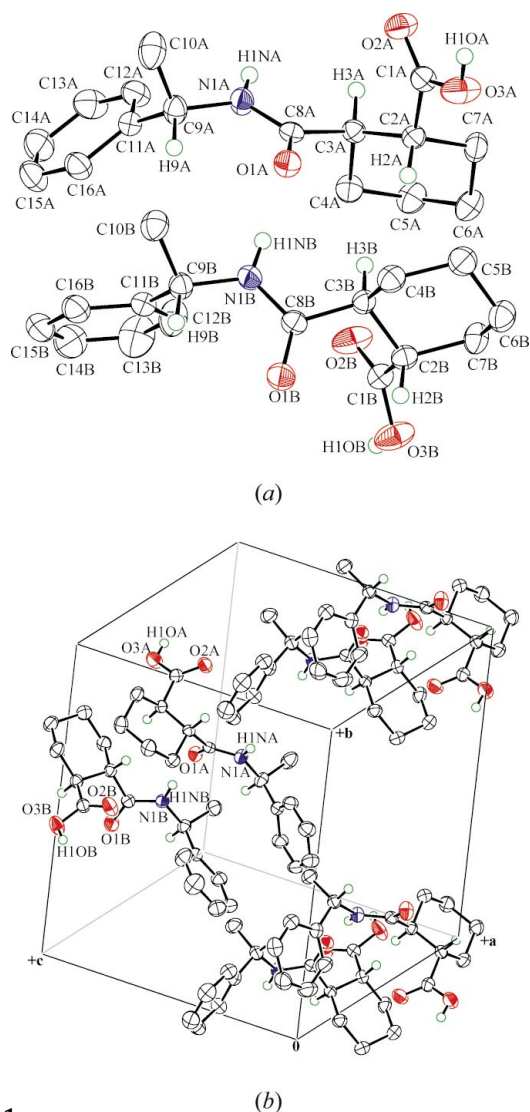


Figure 1
The structure of the title carboxylic acid, (I), showing (a) the diastereoisomeric pair and (b) the unit-cell contents.

8.3 mmol) in an ice-water bath and the solution was stirred at room temperature. After 12 h, 3.5% HCl aqueous solution was added and the mixture was concentrated to remove tetrahydrofuran. The residue was extracted with ethyl acetate and the organic layer was washed with distilled water. The organic layer was then dried over MgSO_4 and concentrated to give a white powder. The product was recrystallized from ethyl acetate to give crystals suitable for X-ray analysis. ^1H NMR ($[d_6]\text{DMSO}$ at 303 K): δ 1.15–1.28 (4H, br), 1.30 (3H, d), 2.42 (1H, t), 2.52 (1H, t), 4.85 (1H, m), 7.18 (1H, t), 7.28 (4H, m), 8.15 (1H, d), 11.88 (1H, br); analysis calculated for $\text{C}_{16}\text{H}_{21}\text{NO}_3$: C 69.79, H 7.69, N 5.09%; found: C 69.53, H 7.71, N 4.98%.

Crystal data

$\text{C}_{16}\text{H}_{21}\text{NO}_3$
 $M_r = 275.34$
 Monoclinic, $P2_1$
 $a = 9.6306$ (6) Å
 $b = 15.3825$ (8) Å
 $c = 10.8903$ (6) Å
 $\beta = 107.456$ (2)°
 $V = 1539.02$ (15) Å³
 $Z = 4$

$D_x = 1.188$ Mg m⁻³
 Mo $K\alpha$ radiation
 Cell parameters from 13296 reflections
 $\theta = 2.4$ – 27.5°
 $\mu = 0.08$ mm⁻¹
 $T = 173$ K
 Block, colorless
 0.20 × 0.20 × 0.20 mm

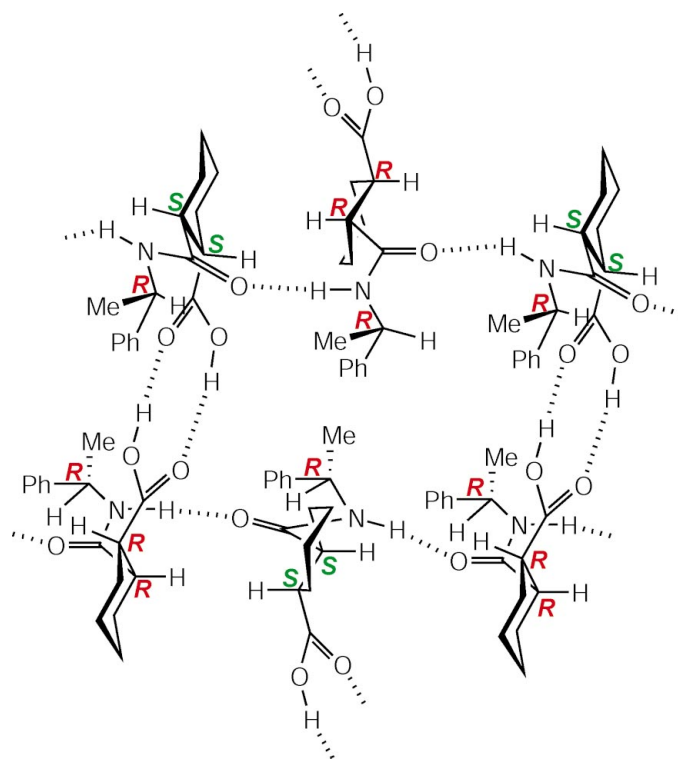


Figure 2
A schematic packing diagram of (I).

Data collection

Rigaku R-Axis RAPID imaging-plate diffractometer	3161 reflections with $I > 2\sigma(I)$
ω scans	$R_{\text{int}} = 0.026$
Absorption correction: none	$\theta_{\text{max}} = 27.5^\circ$
6718 measured reflections	$h = -12 \rightarrow 12$
3662 independent reflections	$k = -19 \rightarrow 19$
	$l = -14 \rightarrow 14$

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.040$	$w = 1/[\sigma^2(F_o^2) + (0.0647P)^2]$
$wR(F^2) = 0.103$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.06$	$(\Delta/\sigma)_{\text{max}} = 0.001$
3662 reflections	$\Delta\rho_{\text{max}} = 0.18$ e Å ⁻³
363 parameters	$\Delta\rho_{\text{min}} = -0.21$ e Å ⁻³

Table 1

Selected geometric parameters (Å, °).

O1A—C8A	1.239 (2)	O3B—C1B	1.318 (3)
O1B—C8B	1.235 (3)	N1A—C8A	1.334 (3)
O2A—C1A	1.217 (3)	N1A—C9A	1.469 (2)
O2B—C1B	1.211 (3)	N1B—C8B	1.339 (3)
O3A—C1A	1.315 (3)	N1B—C9B	1.462 (3)
C8A—N1A—C9A	122.86 (17)	O3B—C1B—C2B	113.91 (19)
C8B—N1B—C9B	123.81 (18)	O1A—C8A—N1A	123.32 (18)
O2A—C1A—O3A	123.1 (2)	N1A—C8A—C3A	115.50 (17)
O2A—C1A—C2A	123.7 (2)	O1B—C8B—N1B	123.21 (19)
O3A—C1A—C2A	113.15 (19)	N1B—C8B—C3B	115.62 (17)
O2B—C1B—O3B	122.7 (2)	N1A—C9A—C10A	111.0 (2)
O2B—C1B—C2B	123.4 (2)	N1B—C9B—C10B	108.83 (18)
C1A—C2A—C3A—C8A	−67.7 (2)	C1B—C2B—C3B—C8B	63.5 (2)

Table 2
Hydrogen-bonding geometry (Å, °).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
$O3A-H1OA \cdots O2B^i$	0.84	1.84	2.661 (3)	166
$O3B-H1OB \cdots O2A^{ii}$	0.84	1.87	2.688 (3)	166
$N1A-H1NA \cdots O1B^{iii}$	0.88	2.06	2.932 (2)	170
$N1B-H1NB \cdots O1A$	0.88	1.99	2.861 (2)	170

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

H atoms attached to C atoms were positioned geometrically and were treated as riding on their parent atoms, with aromatic C–H distances of 0.95 Å, and methyl, methylene and methine C–H distances of 0.98, 0.99 and 1.00 Å, respectively. H atoms attached to O and N atoms were also treated as riding on their parent atoms, with carboxylic acid O–H distances of 0.84 Å and amide N–H distances of 0.88 Å. Rotating-group refinement was used for the methyl and carboxylic acid groups. $U_{iso}(H)$ values were set to $1.2U_{eq}$ of the carrier atoms. In the absence of significant anomalous dispersion effects, Friedel pairs were averaged and the absolute configuration cannot be determined from the crystallographic experiment.

Data collection: *PROCESS-AUTO* (Rigaku Corporation, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *TEXSAN* (Molecular Structure Corporation, 2000); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine

structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *TEXSAN* and *MERCURY* (Bruno *et al.*, 2002); software used to prepare material for publication: *TEXSAN* and *MERCURY*.

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