ORGANIC COMPOUNDS

(S)-(−)-3-(4-Phenyl-1-piperazinyl)-1,2-propanediol N,N'-Dioxide

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Abstract

The piperazine ring of the title molecule, $C_{13}H_{20}N_2O_4$, assumes a chair conformation with the two N→O groups oriented *trans*-axially to each other. The O atoms of each molecule of the crystal are involved in an infinite three-dimensional O—H···O hydrogen-bond network, which is mainly responsible for the packing.

Comment

As part of our investigations into the relationship between molecular conformation and biological activity, levodropropizine [(S)-(−)-3-(4-phenyl-1-piperazinyl)-1,2-propanediol], a cough suppressant, and many of its derivatives have been considered (Calatozzolo, Celentano, Clerici, Giammarusti & Stradi, 1993). We report here on the solid-state conformation of (S)-(−)-3-(4-phenyl-1-piperazinyl)-1,2-propanediol N,N'-dioxide (I) (which is a potential metabolite of levodropropizine), as obtained from an accurate X-ray structure determination. The most relevant structural feature of the molecule is the *trans* conformation of the two N→O groups with respect to the piperazine ring.
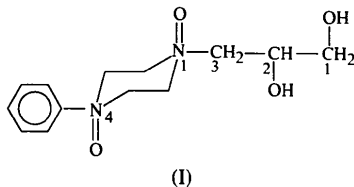
$$\text{(I)}$$

Fig. 1 shows a perspective view of the title molecule with the atom-numbering scheme. The chair-type piperazine ring is characterized by the coplanarity of

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atoms C(7), C(8), C(9) and C(10) [within 0.002 (2) Å], with atoms N(1) and N(2) symmetrically displaced on opposite sides of this plane by −0.706 (2) and 0.705 (2) Å, respectively. As a consequence, the two N—O bonds are oriented axially in a *trans* configuration with bond distances O(1)—N(1) 1.392 (3) and O(2)—N(2) 1.383 (3) Å, which are in good agreement with the values of 1.395 (1) Å found in N,N'-bis(p-chlorophenyl)piperazine N,N'-dioxide tetrahydrate, 1.397 (2) Å in N,N'-di(p-tolyl)piperazine N,N'-dioxide tetrahydrate, 1.402 (2) Å in N,N'-di(o-tolyl)piperazine N,N'-dioxide tetrahydrate and 1.387 (2) Å in N,N'-diphenylpiperazine N,N'-dioxide octahydrate (Kwok & Mak, 1988).
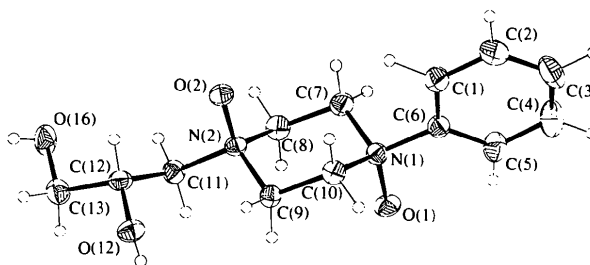

Fig. 1. *ORTEP* (Johnson, 1965) drawing of the title compound illustrating the stereochemistry and the atom-labelling scheme (displacement ellipsoids are drawn at the 40% probability level). H atoms are drawn as spheres of fixed radii.

The phenyl ring attached to atom N(1) is quasi-perpendicular to the C(7), C(8), C(9), C(10) plane, the dihedral angle being 79.36 (7)°, and is nearly coplanar with the N(1)—O(1) bond as indicated by the O(1)—N(1)—C(6)—C(1) torsion angle of −172.0 (3)°.

The 1,2-propanediol chain bonded to atom N(2) assumes an almost fully extended conformation with torsion angles C(8)—N(2)—C(11)—C(12) and N(2)—C(11)—C(12)—C(13) of −168.3 (2) and 166.6 (2)°, respectively.

The crystal structure is characterized by strong hydrogen-bonding interactions between the two hydroxyl groups of each molecule and the N-oxides of adjacent molecules giving rise to a three-dimensional network as shown in Fig. 2 [O(12)—H(12) 0.77 (3), O(12)···O(1^i) 2.653 (3), H(12)···O(1^i) 1.89 (3) Å and O(12)—H(12)···O(1^i) 170 (3)°; O(16)—H(16) 0.78 (4), O(16)···O(2^{ii}) 2.597 (3), H(16)···O(2^{ii}) 1.83 (4) Å and O(16)—H(16)···O(2^{ii}) 174 (4)°; symmetry codes: (i) $x - \frac{1}{2}, -y + \frac{1}{2}, -z + 2$; (ii) $-x, y - \frac{1}{2}, -z + \frac{3}{2}$].

The involvement of the O atoms of the N→O groups in hydrogen-bond interactions, generally with
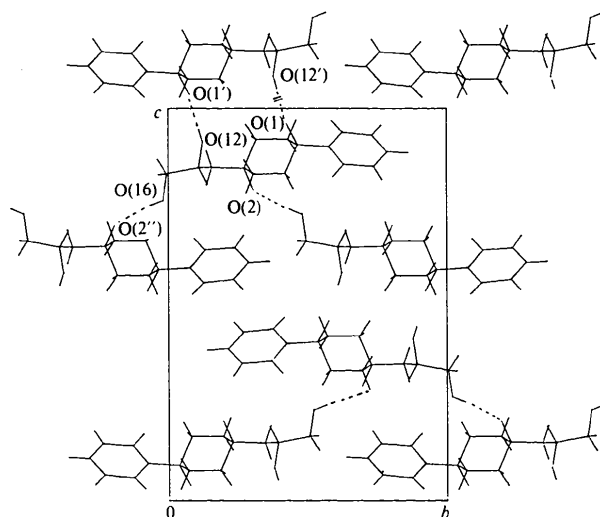
Fig. 2. Packing diagram (dotted lines indicate hydrogen-bond interactions).

water molecules present in the crystal structure, is rather common for the N,N'-piperazine N,N'-dioxide derivatives (Kwok & Mak, 1988, 1989), with formation of layer- or network-type structures depending on the number of water molecules. In the present structure, their role is played by the hydroxylic groups with the network type of packing just described.

Experimental

Crystal data

$C_{13}H_{20}N_2O_4$
$M_r = 268.3$
Orthorhombic
$P2_12_12_1$
$a = 5.518\,(1)$ Å
$b = 13.059\,(5)$ Å
$c = 18.246\,(4)$ Å
$V = 1314.6\,(7)$ Å^3
$Z = 4$
$D_x = 1.36$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 25 reflections
$\theta = 10-15°$
$\mu = 0.094$ mm^{-1}
$T = 298$ K
Irregular prism
$0.23 \times 0.10 \times 0.05$ mm
Colourless
Crystal source: from methanolic solution

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2916 measured reflections
2135 independent reflections
1585 observed reflections
$[I > 2.5\sigma(I)]$

$R_{int} = 0.014$
$\theta_{max} = 25°$
$h = -6 \rightarrow 6$
$k = -1 \rightarrow 15$
$l = -1 \rightarrow 21$
3 standard reflections
frequency: 60 min
intensity decay: none

Refinement

Refinement on F
$R = 0.030$
$wR = 0.033$
$S = 0.59$
1585 reflections
252 parameters
$w = 1/[\sigma^2(F_o) + 0.004976(F_o)^2]$

$(\Delta/\sigma)_{max} = 0.01$
$\Delta\rho_{max} = 0.23$ e Å^{-3}
$\Delta\rho_{min} = -0.21$ e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
O(1)	0.5354 (3)	0.4239 (1)	0.9623 (1)	0.0298 (6)
O(2)	0.0264 (3)	0.3047 (1)	0.7947 (1)	0.0286 (5)
O(12)	−0.2050 (4)	0.1220 (2)	0.9161 (1)	0.0320 (6)
O(16)	0.0695 (4)	−0.0207 (2)	0.7668 (1)	0.0410 (7)
N(1)	0.3832 (3)	0.4630 (2)	0.9083 (1)	0.0228 (6)
N(2)	0.1793 (3)	0.2709 (1)	0.8497 (1)	0.0213 (6)
C(1)	0.2415 (5)	0.6312 (2)	0.8598 (2)	0.0336 (9)
C(2)	0.2656 (6)	0.7367 (2)	0.8537 (2)	0.043 (1)
C(3)	0.4483 (6)	0.7866 (2)	0.8905 (2)	0.045 (1)
C(4)	0.6061 (6)	0.7317 (2)	0.9339 (2)	0.048 (1)
C(5)	0.5831 (5)	0.6268 (2)	0.9415 (2)	0.0361 (9)
C(6)	0.4004 (5)	0.5779 (2)	0.9037 (1)	0.0255 (7)
C(7)	0.4580 (5)	0.4188 (2)	0.8354 (1)	0.0278 (8)
C(8)	0.4368 (5)	0.3043 (2)	0.8350 (2)	0.0282 (8)
C(9)	0.1050 (5)	0.3151 (2)	0.9227 (1)	0.0222 (7)
C(10)	0.1253 (4)	0.4295 (2)	0.9227 (2)	0.0241 (7)
C(11)	0.1780 (5)	0.1553 (2)	0.8516 (2)	0.0260 (8)
C(12)	−0.0709 (5)	0.1069 (2)	0.8506 (1)	0.0241 (7)
C(13)	−0.0482 (6)	−0.0062 (2)	0.8345 (2)	0.034 (1)

Table 2. *Selected geometric parameters* (Å, °)

O(1)—N(1)	1.392 (3)	O(2)—N(2)	1.383 (3)
O(12)—C(12)	1.420 (3)	O(16)—C(13)	1.408 (4)
N(1)—C(6)	1.505 (3)	N(1)—C(7)	1.507 (3)
N(1)—C(10)	1.512 (3)	N(2)—C(8)	1.510 (3)
N(2)—C(9)	1.509 (3)	N(2)—C(11)	1.510 (3)
C(1)—C(2)	1.388 (4)	C(1)—C(6)	1.376 (4)
C(2)—C(3)	1.376 (5)	C(3)—C(4)	1.378 (5)
C(4)—C(5)	1.383 (4)	C(5)—C(6)	1.379 (4)
C(7)—C(8)	1.500 (4)	C(9)—C(10)	1.498 (4)
C(11)—C(12)	1.511 (4)	C(12)—C(13)	1.512 (4)
O(1)—N(1)—C(10)	109.8 (2)	O(1)—N(1)—C(7)	108.6 (2)
O(1)—N(1)—C(6)	111.5 (2)	C(7)—N(1)—C(10)	107.5 (2)
C(6)—N(1)—C(10)	110.9 (2)	C(6)—N(1)—C(7)	108.4 (2)
O(2)—N(2)—C(11)	109.4 (2)	O(2)—N(2)—C(9)	110.6 (2)
O(2)—N(2)—C(8)	110.7 (2)	C(9)—N(2)—C(11)	111.1 (2)
C(8)—N(2)—C(11)	107.3 (2)	C(8)—N(2)—C(9)	107.6 (2)
C(2)—C(1)—C(6)	119.2 (3)	C(1)—C(2)—C(3)	120.1 (3)
C(2)—C(3)—C(4)	119.8 (3)	C(3)—C(4)—C(5)	121.1 (3)
C(4)—C(5)—C(6)	118.4 (3)	C(1)—C(6)—C(5)	121.5 (3)
N(1)—C(6)—C(5)	118.7 (2)	N(1)—C(6)—C(1)	119.7 (2)
N(1)—C(7)—C(8)	111.4 (2)	N(2)—C(8)—C(7)	111.1 (2)
N(2)—C(9)—C(10)	111.2 (2)	N(1)—C(10)—C(9)	111.1 (2)
N(2)—C(11)—C(12)	115.0 (2)	O(12)—C(12)—C(11)	113.9 (2)
C(11)—C(12)—C(13)	109.6 (2)	O(12)—C(12)—C(13)	110.0 (2)
O(16)—C(13)—C(12)	109.8 (2)		

The structure was refined by full-matrix least squares with anisotropic displacement parameters for all non-H atoms. H atoms were located on a difference Fourier map and refined isotropically.

Program used to solve structure: *SHELX*86 (Sheldrick, 1985). Program used to refine structure: *SHELX*76 (Sheldrick, 1976).

$C_{13}H_{20}N_2O_4$

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1115). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Absolute Configuration of (S,S)-1,2-Dihydro-1,2-*trans*-acenaphthylene-dicarboxylic Acid

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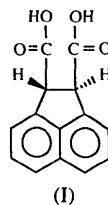
Abstract

The naphthalene ring system in the title compound, $C_{14}H_{10}O_4$, is essentially planar and the fused cyclopentane ring is in a slightly twisted conformation. The carboxylic acid groups associate *via* intermolecular hydrogen bonds [O···O 2.610 (4) and 2.655 (3) Å] forming chain structures that are held together by weak van der Waals interactions.

Comment

In the course of our studies on the direct asymmetric introduction of the tricarbonylchromium moiety on prochiral arenes, we required pure optically active η^6 ligands with C_2 symmetry. The title compound, (I), has two asymmetric centers and the absolute configuration was required for effective understanding of the mechanism of the ligand-transfer process. The X-ray structure determination was undertaken following the inability of ordinary spectral methods to furnish the essential structural information.

(I)

A view of the molecule is shown in Fig. 1 and the unit-cell packing is shown in Fig. 2. Both asymmetric centers in the molecule have the *S* configuration. The naphthalene ring system is essentially planar [maximum deviation of atoms C(1) to C(10) is $\pm$ 0.016 (8) Å]. The fused cyclopentane ring has a slightly twisted conformation with a torsion angle C(1)—C(11)—C(12)—C(9) of 9.52 (6)°. The potential molecular C_2 symmetry is not retained in the solid state. The carboxylic acid groups form intermolecular hydrogen bonds resulting in zigzag chains along the *b* axis; the O(1)···O(3)($\frac{3}{2} - x, y - \frac{1}{2}$, $2 - z$) and O(4)···O(2)($\frac{3}{2} - x, \frac{1}{2} + y, 2 - z$) distances are 2.610 (4) and 2.655 (3) Å, respectively.
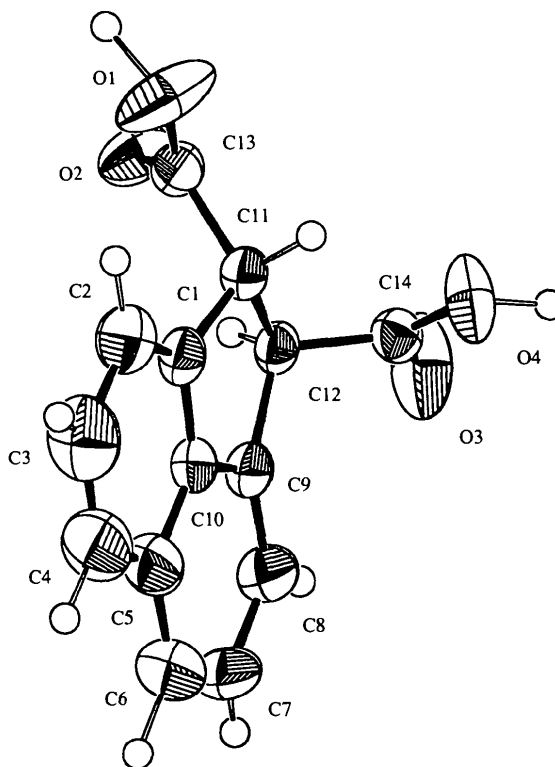

Fig. 1. Perspective drawing of the title compound with the crystallographic numbering scheme. Non-H atoms are shown with 50% probability ellipsoids.