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(+)-*cis*-3-Hydroxy-2-(4-methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine 1-oxide

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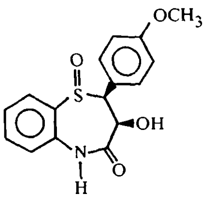
Abstract

The title compound, $C_{16}H_{15}NO_4S$, is a diltiazem drug intermediate. Diltiazem is an enantiomerically pure drug with calcium antagonist activity. The molecular packing is stabilized by hydrogen bonding. The amide and hydroxide groups form hydrogen bonds with neighbouring molecules. The seven-membered ring is in a twist-boat conformation. The methoxyphenyl group deviates slightly from planarity but the benzene ring is planar.

Comment

The title compound, (I), is a drug intermediate in the synthesis of diltiazem (Kojic-Prodic *et al.*, 1984). Diltiazem is useful for the treatment of cardiac and coronary diseases. In order to study the molecular geometry and the conformation of the molecule, an X-ray analysis has been carried out.



(I)

Fig. 1 shows the molecular structure of (I). Interatomic distances and angles in the 1,5-benzothiazepine ring reflect the usual seven-membered ring geometry and hybridization of atoms. The bond lengths S7—C2 [1.803 (4) Å] and C9—S7 [1.859 (4) Å] are unequal as one of them is affected by the conjugation of the adjacent π-electron system. Bond lengths involving Csp^3 atoms range from 1.512 (5) to 1.544 (6) Å. The carbon–oxygen bonds fall into three categories: a Csp^3—O single bond [C17—O16 1.416 (6) Å], two Csp^2—O single bonds [C13—O16 1.376 (5) and C18—O19 1.407 (5) Å] and a double C=O bond [C20—O21 1.218 (5) Å]. The carbon–nitrogen distances are unequal [C3—N22 1.419 (5) and N22—C20 1.359 (5) Å] as a result of different environments.

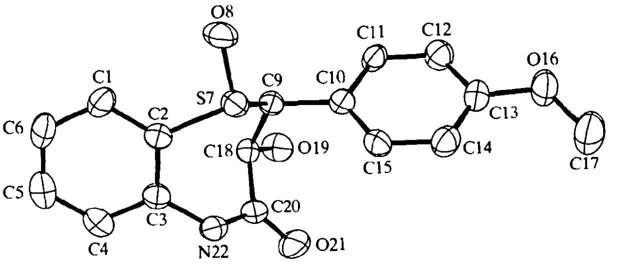


Fig. 1. The molecular structure of (I) showing 50% probability displacement ellipsoids. H atoms have been omitted for clarity.

The conformation of the benzothiazepine ring was determined by considering the least-squares plane passing through atoms S7, C9 and C18. Atoms C2 and C3 lie above, and atoms C20 and N22 lie below the plane. The values of the torsion angles of the seven-membered ring indicate a twist-boat conformation (Hendrickson, 1961) and are similar to those of diltiazem drug intermediates (Kumaradhas *et al.*, 1995, 1996; Kumaradhas & Nirmala, 1996, 1997). The torsion angle for the methoxy group/benzene ring is approximately 6°, indicating it to be slightly out of the plane of the benzene ring.

The methoxyphenyl and acetoxy groups at C9 and C18 are *gauche* oriented with respect to one another, as indicated by the torsion angle C10—C9—C18—O19 of −52.9 (5)°.

The molecular packing is stabilized by hydrogen bonding as shown in Fig. 2. The amide group forms a hydrogen bond with the sulfoxide O8^{i} atom (N—H···O) and the hydroxy group forms a hydrogen bond with the O16^{ii} atom (O—H···O) of the neighbouring molecule. The intermolecular distances are 2.852 (5) and

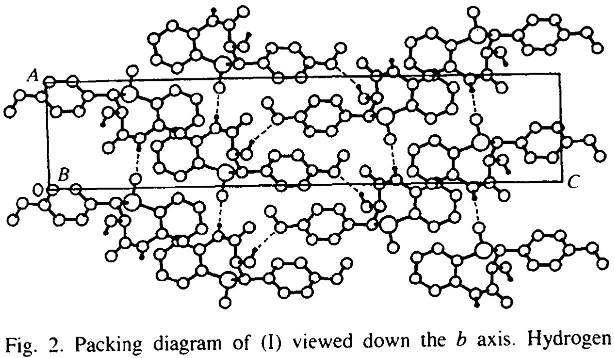


Fig. 2. Packing diagram of (I) viewed down the *b* axis. Hydrogen bonding is shown by dashed lines.

3.036 (5) Å and the angles are 169.9 (3) and 152.4 (2)°, respectively [symmetry codes: (i) $x - 1, y, z$; (ii) $x - \frac{1}{2}, -\frac{1}{2} - y, 2 - z$]. On the whole, the crystal packing is stabilized by hydrogen bonding between polar groups and van der Waals interactions between nonpolar groups.

Experimental

The synthesis of the compound will be published elsewhere. The compound was recrystallized from acetone at room temperature.

Crystal data

$C_{16}H_{15}NO_4S$
$M_r = 317.35$
Orthorhombic
$P2_12_12_1$
$a = 6.698\,(1)$ Å
$b = 7.171\,(1)$ Å
$c = 30.604\,(5)$ Å
$V = 1470.0\,(4)$ Å^3
$Z = 4$
$D_x = 1.434$ Mg m^{-3}
$D_m = 1.423\,(3)$ Mg m^{-3}
D_m measured by flotation in xylene–CCl_4

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 8–19°$
$\mu = 0.238$ mm^{-1}
$T = 293\,(2)$ K
Equidimensional
0.14 × 0.14 × 0.14 mm
Colourless

Data collection

Siemens *R*3*m*/*V* diffractometer
ω scans
Absorption correction: none
1591 measured reflections
1527 independent reflections
1171 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.08$
$\theta_{\rm max} = 25.03°$
$h = 0 \rightarrow 7$
$k = 0 \rightarrow 8$
$l = 0 \rightarrow 33$
2 standard reflections every 98 reflections intensity decay: <1%

Refinement

Refinement on F^2
$R(F) = 0.044$
$wR(F^2) = 0.09$
$S = 1.120$
1527 reflections
199 parameters
H atoms: see text
$w = 1/[\sigma^2(F_o^2) + (0.0452P)^2 + 0.0522P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\rm max} = 0.001$
$\Delta\rho_{\rm max} = 0.219$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.217$ e Å^{-3}
Extinction correction: none
Scattering factors from *SHELXL*93 (Sheldrick, 1993)

All non-H atoms were found by direct methods and their parameters were refined with a full-matrix least-squares procedure. The H atoms were positioned geometrically and refined using the riding model.

Data collection: *R*3*m*/*V* software (Siemens, 1983). Cell refinement: *R*3*m*/*V* software. Data reduction: *SHELXTL-Plus* (Sheldrick, 1990*a*). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990*b*). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976) in *NRCVAX* (Gabe *et al.*, 1987). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BK1392). Services for accessing these data are described at the back of the journal.

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3-Methyl-1-(1,2,3,4-tetrahydroisoquinolin-2-ylcarbonyl)imidazolium iodide

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Abstract

The title compound, $C_{14}H_{16}N_3O^+\cdot I^-$, crystallizes as discrete ion pairs with close (C)—H···I contacts of 3.04 and 3.06 Å. The two C—N bonds of the urea functional group have significantly different bond lengths of 1.327 (6) and 1.466 (6) Å. This is the first crystal structure determination of a carbamoyl imidazolium salt.

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