Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.063$
$wR(F^2) = 0.227$
$S = 1.090$
3021 reflections
212 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.1572P)^2 + 0.2382P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = <0.001$
$\Delta\rho_{max} = 0.241$ e Å^{-3}
$\Delta\rho_{min} = -0.266$ e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997*a*)
Extinction coefficient: 0.0058 (14)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

N4—C8	1.344 (3)	N1—C6	1.470 (3)
N4—C5	1.464 (3)	N1—C2	1.470 (3)
N4—C3	1.465 (2)	O1—C7	1.211 (3)
O2—C8	1.219 (3)	C2—C10	1.530 (3)
N1—C7	1.345 (3)		
C8—N4—C5	122.2 (2)	C7—N1—C6	120.5 (2)
C8—N4—C3	120.8 (2)	C7—N1—C2	120.5 (2)
C5—N4—C3	116.6 (2)	C6—N1—C2	119.0 (2)

The formyl H atoms were located from the difference map; their displacement parameters were kept fixed. The H atoms of the CH, CH_2 and CH_3 groups were fixed using geometrical considerations; their overall displacement parameters were refined.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Software Corporation, 1995*a*). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1995*b*). Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*b*). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997*a*). Molecular graphics: *ZORTEP* (Zsolnai, 1997). Geometrical calculations: *PARST* (Nardelli, 1983). Software used to prepare material for publication: *SHELXL*97.

PL acknowledges Professor J. Shashidhara Prasad and Dr M. A. Sridhar, Department of Studies in Physics, University of Mysore, India, for X-ray data collection.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: VJ1091). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1999). C**55**, 411–413

Troglitazone, an euglycemic antidiabetic drug†

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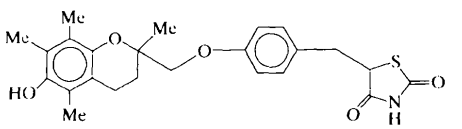
(*Received 28 May 1998; accepted 9 November 1998*)

Abstract

Troglitazone (or 5-{4-[(6-hydroxy-2,5,7,8-tetramethylchroman-2-yl)methoxy]benzyl}thiazolidine-2,4-dione, $C_{24}H_{27}NO_5S$) is the first euglycemic drug. The molecules are held together in the lattice by intermolecular hydrogen bonds between the hydroxy O atom of the chroman moiety, and the ketone O and ring N atom of the thiazolidine-2,4-dione moiety.

Comment

The title compound, (I), has been prepared according to the procedure of Horikoshi *et al.* (1994) as part of our antidiabetic research. X-ray diffraction studies have been undertaken, as the structure has not previously been reported in the literature.



(I)

The molecular structure of (I) is shown in Fig. 1. All the bond parameters are normal (Allen *et al.*, 1987). The C23—O4 and C24—O5 bond lengths are 1.198 (4) and 1.206 (4) Å, respectively. This indicates that they are carbonyl groups, as found in 1,3-thiazolidine-2,4-dione (Forn *et al.*, 1975) and in 3-phenyl-1,3-thiazolidine-2,4-dione (Stankovic & Andretti, 1979).

† Publication No. 34 from DRF.

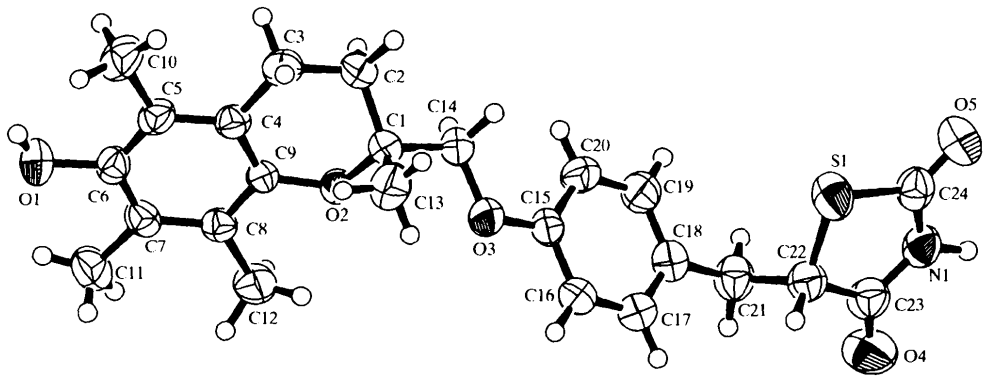


Fig. 1. The molecular structure of (I), showing 50% probability displacement ellipsoids. H atoms are shown as spheres of arbitrary radii.

The crystal lattice contains enantiomeric molecules, with *RS* and *SR* configurations at the chiral centres, C1 and C22. The thiazolidine-2,4-dione ring is essentially planar. However, the dihydropyran ring of the chroman moiety assumes a half-chair conformation, as evidenced by the endocyclic torsion angles (Duax *et al.*, 1976). The hydroxy O1 atom of the chroman moiety is involved in intermolecular hydrogen bonding with the N1 atom and one of the carbonyl O atoms, namely O5, of the thiazolidine-2,4-dione moiety. This hydrogen-bonding scheme (Table 2) stabilizes the crystal structure. The crystal packing is shown in Fig. 2. Additional stability comes from the van der Waals contacts which O1 has with N1 [3.302 (4) Å] and O5 [3.272 (4) Å] across centres of symmetry. These contacts are shown as dotted lines in Fig. 2.

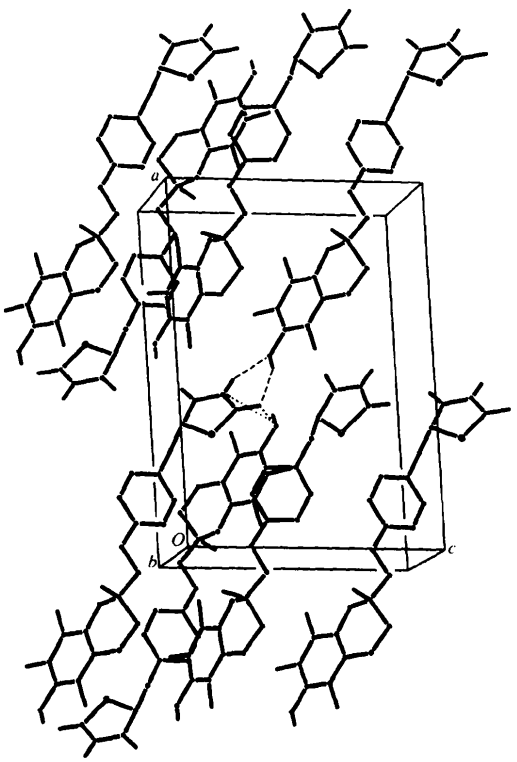


Fig. 2. Packing diagram of (I), viewed down the *b* axis. The hydrogen bonds and van der Waals contacts are shown as broken and dotted lines, respectively.

Experimental

Crystals of (I) suitable for X-ray diffraction were grown from solution in a mixture of propan-2-ol and acetone.

Crystal data

$C_{24}H_{27}NO_5S$
M_r = 441.54
Monoclinic
$P2_1/c$
a = 16.239 (3) Å
b = 11.717 (3) Å
c = 11.627 (4) Å
β = 93.69 (2)°
V = 2207.7 (9) Å^3
Z = 4
D_x = 1.328 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 20 reflections
θ = 25.0–30.9°
μ = 1.602 mm^{-1}
T = 298.2 K
Needle
0.50 × 0.30 × 0.25 mm
Colourless

Data collection

Rigaku AFC-7*S* diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.545, T_{max} = 0.670
5218 measured reflections
4421 independent reflections
3170 reflections with $I > 1\sigma(I)$

R_{int} = 0.02
θ_{max} = 70.12°
$h = -19 \rightarrow 19$
$k = -14 \rightarrow 0$
$l = 0 \rightarrow 14$
3 standard reflections
every 150 reflections
intensity decay: 0.30%

Refinement

Refinement on F
R = 0.062
wR = 0.056

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

$S = 2.039$
3170 reflections
388 parameters
All H atoms refined
$w = 1/[\sigma^2(F_o) + 0.00016|F_o|^2]$
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

S1—C22	1.814 (4)	O5—C24	1.206 (4)
S1—C24	1.756 (3)	N1—C23	1.362 (4)
O4—C23	1.198 (4)	N1—C24	1.376 (4)
C22—S1—C24	93.6 (2)	O4—C23—C22	124.3 (3)
C23—N1—C24	118.9 (3)	N1—C23—C22	111.8 (3)
S1—C22—C21	113.3 (3)	S1—C24—O5	125.2 (3)
S1—C22—C23	105.8 (2)	S1—C24—N1	109.9 (2)
O4—C23—N1	124.0 (3)	O5—C24—N1	124.9 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H2···O1^{i}	0.97 (3)	1.99 (3)	2.827 (4)	143 (3)
O1—H1···O5^{ii}	0.76 (4)	2.17 (4)	2.870 (4)	153 (5)

Symmetry codes: (i) $1 + x, y, 1 + z$; (ii) $x - 1, y, z - 1$.

The structure was solved by direct methods using *SIR*92 (Altomare *et al.*, 1993) and was refined by least-squares procedures. All calculations were performed using *TEXSAN* software (Molecular Structure Corporation, 1995).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1994). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN*. Program(s) used to solve structure: *SIR*92. Program(s) used to refine structure: *TEXSAN*. Molecular graphics: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

The authors acknowledge Drs A. Venkateswarlu and K. Anji Reddy for their interest and encouragement in this work.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: DE1099). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1999). C**55**, 413–416

Two absorption furosemide prodrugs

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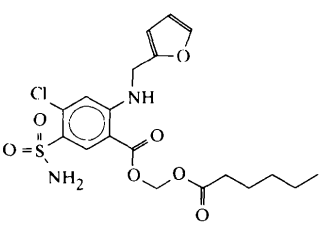
(*Received 6 March 1998; accepted 23 September 1998*)

Abstract

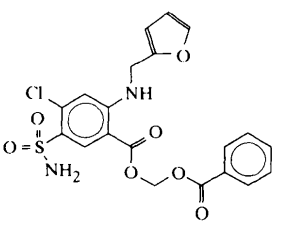
The structures of two absorption furosemide prodrugs, hexanoyloxymethyl 4-chloro-*N*-furfuryl-5-sulfamoylanthranilate ($C_{19}H_{23}ClN_2O_7S$), (I), and benzoyloxymethyl 4-chloro-*N*-furfuryl-5-sulfamoylanthranilate ($C_{20}H_{17}ClN_2O_7S$), (II), are described in this paper and compared with furosemide and four other prodrugs. The molecular conformations of both compounds are similar to those of the other prodrugs; the packing and the crystal system are the primary differences. Compound (I) crystallizes in the trigonal space group $R\bar{3}$ and compound (II) in the monoclinic space group $P2_1/n$. The packing of both structures is stabilized by a three-dimensional hydrogen-bond network.

Comment

The absorption furosemide prodrugs hexanoyloxymethyl 4-chloro-*N*-furfuryl-5-sulfamoylanthranilate, (I), and benzoyloxymethyl 4-chloro-*N*-furfuryl-5-sulfamoylanthranilate, (II), were synthesized and characterized as acyloxymethyl esters of furosemide (Prandi, Fagiolino, Manta, Llera *et al.*, 1992). The therapeutic activity of these prodrugs has been studied (Prandi, Fagiolino, Manta & Llera, 1992).



(I)



(II)

Both molecules share the original furosemide [(4-chloro-*N*-furfuryl-5-sulfamoylanthranilic acid), (III)] framework, which contains a six-membered aromatic ring (atoms C1 to C6) with the carboxylate and amine