Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Pioglitazone hydrochloride

Hemmige S. Yathirajan,[a] Basavegowda Nagaraj,[a] Padmarajaiah Nagaraja[a] and Michael Bolte[b]*

[a]Department of Studies in Chemistry, University of Mysore, Manasagangotri, Mysore 570 006, India, and [b]Institut für Anorganische Chemie, J. W. Goethe-Universität Frankfurt, Marie-Curie-Straße 11, 60439 Frankfurt/Main, Germany

Correspondence e-mail: bolte@chemie.uni-frankfurt.de

Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.005 Å
Disorder in main residue
R factor = 0.035
wR factor = 0.074
Data-to-parameter ratio = 12.5

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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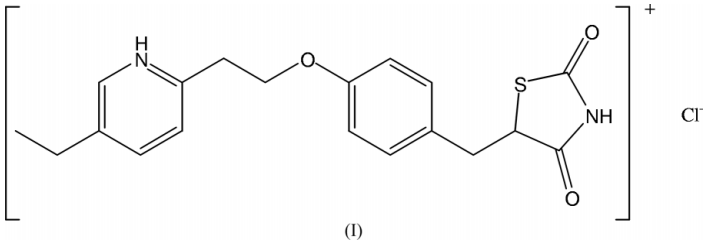
Received 10 December 2004
Accepted 14 December 2004
Online 24 December 2004

The title compound [systematic name: (±)-5-({4-[2-(5-ethyl-2-pyridinio)ethoxy]phenyl}methyl)thiazolidine-2,4-dione chloride], $C_{19}H_{21}N_2O_3S^+\cdot Cl^-$, is an oral antidiabetic agent. In the crystal structure, the molecules are linked by N—H···Cl hydrogen bonds into chains.

Comment

The title compound, (I), is an oral antidiabetic agent that acts primarily by decreasing insulin resistance. Pioglitazone hydrochloride affords a new treatment for type 2 diabetes (Lawrence & Reckless, 2001). In view of the importance of (I), the crystal structure is reported (Fig. 1). Bond lengths and angles are in the normal ranges (Cambridge Structural Database, Version 1.6 plus three updates; *MOGUL* Version 1.0; Allen, 2002).



(I)

The pivot atom, C21, of the thiazolidinedione ring and atom C17 attached to it are disordered over two sites. In both disordered orientations, the thiazolidinedione ring adopts an envelope conformation, with atoms S22, C23, N24 and C25 in a common plane (r.m.s. deviation = 0.011 Å), and from which C21 and C21′ are displaced by −0.286 (8) and 0.54 (1) Å, respectively. In the crystal structure, the molecules are linked by N—H···Cl hydrogen bonding into chains (Table 1).

Experimental

The title compound was obtained as a gift sample from Zydus Cadila, Ahmedabad, India. The compound was used without further purification. Colourless plates (m.p. 466 K) were obtained by recrystallization from methanol.

Crystal data

$C_{19}H_{21}N_2O_3S^+\cdot Cl^-$
M_r = 392.89
Monoclinic, $P2_1$
a = 10.0696 (17) Å
b = 9.4318 (16) Å
c = 10.1752 (19) Å
β = 95.178 (14)°
V = 962.4 (3) Å^3
Z = 2
D_x = 1.356 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5341 reflections
θ = 3.8–25.5°
μ = 0.33 mm^{-1}
T = 173 (2) K
Plate, colourless
0.43 × 0.28 × 0.11 mm

Data collection

Stoe IPDS-II two-circle diffractometer
ω scans
Absorption correction: multi-scan (*MULABS*; Spek, 1990; Blessing, 1995)
T_{min} = 0.872, T_{max} = 0.965
4956 measured reflections
3274 independent reflections
2480 reflections with $I > 2\sigma(I)$
R_{int} = 0.036
θ_{max} = 25.7°
$h = -11 \rightarrow 12$
$k = -11 \rightarrow 11$
$l = -12 \rightarrow 12$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.074
S = 0.83
3274 reflections
262 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0375P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Absolute structure: Flack (1983), 1405 Friedel pairs
Flack parameter = −0.07 (7)

Table 1
Selected geometric parameters (Å, °).

C21—C25	1.546 (5)	C23—N24	1.366 (4)
C21—S22	1.823 (5)	N24—C25	1.362 (4)
S22—C23	1.760 (3)		
C25—C21—S22	104.3 (3)	C25—N24—C23	117.4 (3)
C23—S22—C21	92.44 (18)	N24—C25—C21	112.0 (3)
N24—C23—S22	111.2 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N32—H32···Cl1	0.76 (3)	2.31 (3)	3.049 (3)	162 (3)
N24—H24···Cl1^{i}	0.93 (4)	2.22 (4)	3.144 (3)	176 (3)

Symmetry code: (i) $1-x, y-\frac{1}{2}, 2-z$.

H atoms bonded to carbon were positioned with idealized geometry (C—H = 1.00, 0.99, 0.98 and 0.95 Å for tertiary, secondary, methyl and aromatic CH) and refined with fixed individual displacement parameters [U_{iso}(H) = 1.2U_{eq}(tertiary, secondary, aromatic C) or 1.5U_{eq}(methyl C)] using a riding model. H atoms bonded to nitrogen were located in a difference map and refined isotropically. Atoms C21 and C17 are disordered over two sites and were refined with site-occupation factors of 0.66 (1) and 0.34 (1) for the two different orientations. Distance restraints were applied to restrain the bond distances of these two C atoms to approximately equal values.

Data collection: *X-AREA* (Stoe & Cie, 2001); cell refinement: *X-AREA*; data reduction: *X-AREA*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL-Plus* (Sheldrick, 1991); software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2003).

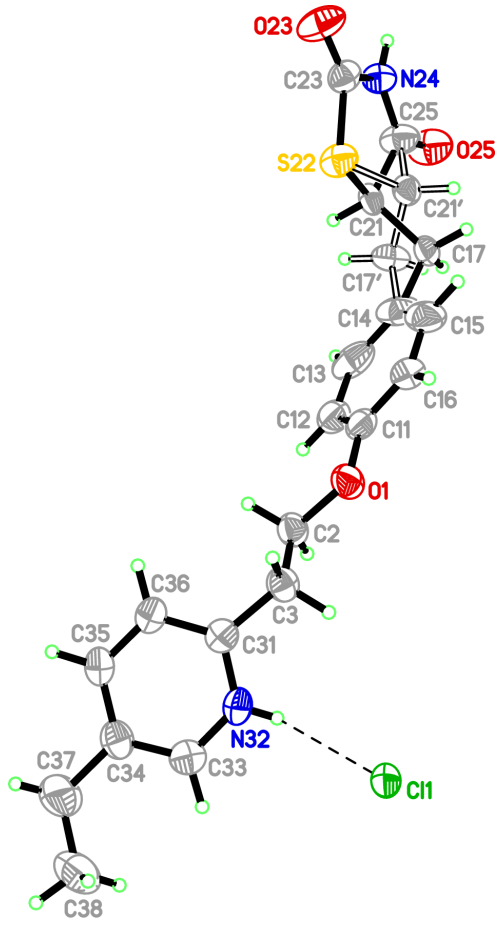


Figure 1
Perspective view of the title compound, showing the atom numbering and displacement ellipsoids drawn at the 50% probability level. The dashed line indicates a hydrogen bond. The bonds between the disordered atoms of the minor component are drawn as open bonds.

One of the authors (HSY) thanks Zydus Cadila, Ahmedabad, India, for a gift sample of pioglitazone hydrochloride.

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