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Acta Cryst. (1999). C**55**, 74–75

Gliclazide

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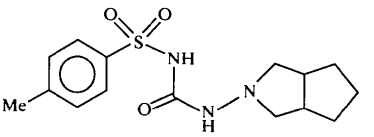
(*Received 27 May 1998; accepted 21 July 1998*)

Abstract

The crystal structure of gliclazide, *N*-[(perhydrocyclopenta[*c*]pyrrol-2-yl)aminocarbonyl]-*p*-toluenesulfonamide, $C_{15}H_{21}N_3O_3S$, a second-generation oral hypoglycemic agent, contains discrete molecules with normal molecular dimensions. Both of the five-membered fused rings adopt envelope conformations. The molecules are linked into chains by intermolecular hydrogen bonds involving amino-H atoms, with N···O separations of 2.967 (3) and 2.949 (3) Å.

Comment

Gliclazide, (I), is a second-generation oral hypoglycemic agent which is approximately 100 times more potent than the first-generation hypoglycemic agents (Lebovitz & Feinglos, 1983). It is used to assist in the control of mild to moderately severe type II diabetes mellitus (adult, maturity-onset), which does not require insulin but can be adequately controlled by diet alone, and it is the drug of choice for initiating treatment in non-insulin-dependent diabetes when diet and weight control fail. It stimulates the secretion and enhances the utilization of insulin by the appropriate tissues (Long, 1990). The pharmacokinetics and adverse effects of gliclazide are the same as those of chloropropamide and other second-generation oral hypoglycemic agents (Reynolds, 1994). However, there are conflicting data on the existence of extrapancreatic effects brought about by gliclazide (Webster & Taylor, 1996). The possible drug interactions include synergism with salicylates, cimetidine, clofibrate, fenfluramine and monoamine oxidase (MAO) type A inhibitor drugs (Stockley, 1991). In this paper, we report the crystal structure of the title compound.



(I)

The structure of (I) (Fig. 1) is composed of discrete molecules, with molecular dimensions within the expected ranges. Similar corresponding bond distances and angles have been reported in the related hypoglycemic agents 1-(4-chlorophenylsulfonyl)-3-(hexahydro-1*H*-azepin-1-yl)urea (Kamenar *et al.*, 1983) and 1-(4-methylphenylsulfonyl)-3-(hexahydro-1*H*-azepin-1-yl)urea (Kamenar *et al.*, 1983; Koo *et al.*, 1988). In the perhydrocyclopenta[*c*]pyrrole moiety in (I), the mean values of the bond distances are Csp^3—Csp^3 = 1.52 (2) and Csp^3—N = 1.469 (4) Å, and the fused five-membered cyclopentane (C10–C14) and pyrrole (N3, C9, C10, C14, C15) rings adopt C12- and N3-envelope conformations, respectively, with C12 0.574 (4) and N3 0.523 (7) Å out of the planes of the remaining atoms of the corresponding rings. The mean bond distances in the *p*-toluenesulfonyl moiety are C—$C_{aromatic}$ = 1.374 (3), S—O = 1.423 (4), Csp^3—Csp^3 = 1.497 (4) and S—Csp^2 = 1.758 (3) Å, the aromatic ring being essentially planar.

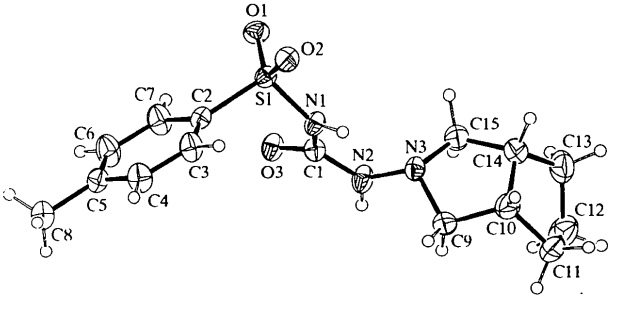


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of (I), showing the atomic numbering scheme. Displacement ellipsoids are plotted at the 30% probability level. H atoms have been shown as circles of an arbitrary radius.

There are short intermolecular hydrogen bonds involving both of the amino-H atoms and the carbonyl- and one of the sulfonyl-O atoms; the other sulfonyl-O atom is not involved in such interactions. Molecules are linked by N—H···O hydrogen bonds to give chains extending in the *c* direction (Table 2); a packing diagram is deposited with the supplementary material.

Experimental

Gliclazide powder was a gift from Ali Gohar Pharmaceuticals (Pvt) Limited, Karachi, Pakistan. It was crystallized from absolute methanol by slow evaporation at room temperature.

Crystal data

$C_{15}H_{21}N_3O_3S$
M_r = 323.41
Monoclinic
$P2_1/n$
a = 10.8326 (7) Å
b = 14.3281 (15) Å
c = 10.976 (3) Å
β = 107.026 (11)°
V = 1628.9 (4) Å^3
Z = 4
D_x = 1.319 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 25 reflections
θ = 20–30°
μ = 1.906 mm^{-1}
T = 293 (1) K
Block
0.30 × 0.26 × 0.18 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scans (North *et al.*, 1968)
T_{min} = 0.654, T_{max} = 0.710
3018 measured reflections
2871 independent reflections

2345 reflections with $I > 2\sigma(I)$
R_{int} = 0.026
θ_{max} = 68.0°
$h = 0 \rightarrow 13$
$k = 0 \rightarrow 17$
$l = -12 \rightarrow 12$
3 standard reflections
every 200 reflections
intensity decay: 1.48%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.053
$wR(F^2)$ = 0.149
S = 1.019
2871 reflections
201 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.09P)^2 + 0.65P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.605 e Å^{-3}
$\Delta\rho_{min}$ = −0.210 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

S1—O1	1.419 (2)	N1—C1	1.394 (3)
S1—O2	1.427 (2)	N2—C1	1.333 (3)
S1—N1	1.634 (2)	N2—N3	1.414 (3)
S1—C2	1.758 (3)	N3—C9	1.465 (3)
O3—C1	1.218 (3)	N3—C15	1.473 (4)
O1—S1—O2	119.46 (12)	C1—N1—S1	124.6 (2)
O1—S1—N1	108.59 (12)	C1—N2—N3	121.6 (2)
O2—S1—N1	103.22 (11)	N2—N3—C9	111.3 (2)
O1—S1—C2	108.88 (12)	N2—N3—C15	109.8 (2)
O2—S1—C2	108.56 (12)	C9—N3—C15	104.1 (2)
N1—S1—C2	107.48 (11)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O2^{i}	0.86	2.23	2.967 (3)	143
N2—H2···O3^{ii}	0.86	2.15	2.949 (3)	153

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

The space group was uniquely determined from the systematic absences.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1994). Program(s) used to solve structure: *SAPI91* (Fan, 1991). Program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997). Molecular graphics: *ORTEPII* in *TEXSAN*. Software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1499). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1999). C**55**, 75–78

N—H···π(indole) intermolecular interactions in 3,3′-benzylidenediindole

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(*Received 16 February 1998; accepted 10 August 1998*)

Abstract

In molecules of the title compound, $C_{23}H_{18}N_2$, two indole systems and one phenyl ring are connected through a common C atom. The two indole substituents are mutually orthogonal. We have identified two N—