2082 reflections
208 parameters
H atoms refined with fixed U_{iso}
Extinction correction: none
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

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

S—C(11)	1.768 (2)	N(2)—N(3)	1.398 (2)
S—C(2)	1.830 (2)	N(2)—C(2)	1.469 (2)
O(1)—C(1)	1.233 (2)	N(3)—C(11)	1.308 (3)
O(2)—C(1)	1.255 (2)	N(4)—C(11)	1.327 (3)
N(1)—C(9)	1.325 (3)	C(1)—C(2)	1.571 (3)
N(1)—C(8)	1.404 (3)	C(2)—C(3)	1.498 (3)
N(2)—C(9)	1.318 (2)	C(3)—C(4)	1.391 (3)
C(11)—S—C(2)	87.2 (1)	N(2)—C(2)—S	102.0 (1)
C(9)—N(1)—C(8)	122.5 (2)	C(3)—C(2)—C(1)	109.4 (1)
C(9)—N(2)—N(3)	121.4 (2)	C(3)—C(2)—S	115.8 (1)
C(9)—N(2)—C(2)	123.2 (2)	C(1)—C(2)—S	108.8 (1)
N(3)—N(2)—C(2)	115.1 (1)	C(8)—C(3)—C(2)	117.5 (2)
C(11)—N(3)—N(2)	108.2 (2)	C(3)—C(8)—N(1)	119.0 (2)
O(1)—C(1)—O(2)	128.7 (2)	N(2)—C(9)—N(1)	119.3 (2)
O(1)—C(1)—C(2)	116.8 (2)	N(3)—C(11)—N(4)	123.2 (2)
O(2)—C(1)—C(2)	114.3 (2)	N(3)—C(11)—S	117.5 (1)
N(2)—C(2)—C(3)	110.2 (1)	N(4)—C(11)—S	119.3 (2)
N(2)—C(2)—C(1)	110.3 (1)		

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

D—H···*A*	*D*···*A*	*D*—H···*A*
N(1)—H(3)···O(3)	2.738 (3)	175
N(4)—H(1)···O(2^{i})	2.782 (3)	173
N(4)—H(2)···N(3^{ii})	3.119 (3)	178
O(3)—H(11)···O(1^{iii})	2.775 (3)	175
O(3)—H(12)···O(2^{iv})	2.832 (2)	174

Symmetry codes: (i) $-x, 1-y, -z$; (ii) $1-x, 2-y, -z$; (iii) $1+x, y, z$; (iv) $1-x, 1-y, 1-z$.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *TEXSAN PROCESS* and *HKL* (Molecular Structure Corporation, 1989). Program(s) used to refine structure: *TEXSAN LS* and *FOURIER*. Molecular graphics: *ORTEP*II (Johnson, 1976) and *PLUTO* (Motherwell & Clegg, 1978).

Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: CF1099). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1997). C**53**, 327–329

1-Acetyl-4-[(1*R*,2*S*,5*R*)-3-menthyloxycarbonyl]piperazine-2,5-dione†

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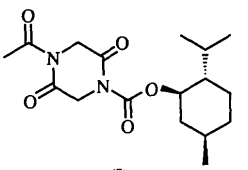
Abstract

The title compound, $C_{17}H_{26}N_2O_5$, assumes a skewed-boat conformation. The degree of folding of the piperazinedione ring given by the Hooker parameter, β, was found to be 32.06°.

Comment

X-ray crystallographic studies have shown that the presence of N and/or α-C substituents play an important role in determining the conformations of piperazine-2,5-diones (Karle, 1981). As part of our studies (Chai & King, 1995) to exploit such conformational effects to direct reactions stereoselectively, the title compound, (I), was synthesized.



(I)

The crystal structure shows that the menthyloxycarbonyl substituent extends away from the piperazinedione ring, whereas the latter adopts a skewed boat conformation. This is in contrast to the conformations adopted by glycine anhydride and its derivatives. For

† Alternative name: (1′*R*,2′*S*,5′*R*)-3-menthyl 4-acetyl-2,5-dioxopiperazine-1-carboxylate.

example, glycine anhydride adopts a planar conformation (Degeilh & Marsh, 1959), whereas sarcosine anhydride is nearly planar, adopting a flattened chair form (Groth, 1969). One measure of the degree of folding of the piperazine-2,5-dione ring is the Hooker parameter, β (Hooker, Bayley, Radding & Schellman, 1974), and this was found to be very large in the title compound, *i.e.* 32.06°. Comparable β values have been observed for sterically crowded piperazinedione derivatives, *e.g.* for *cis-N,N'*-diacetylated alanine anhydride (30°) and *cis-N,N'*-dimethylated valine anhydride (41°) (Benedetti, Marsh & Goodman, 1976). To our knowledge, this is the largest β value reported for glycine anhydride derivatives. The conformational parameters [following the convention of the IUPAC–IUB Commission on Biochemical Nomenclature (1970)] for peptides are summarized in Table 2.

From the ω values which measure the deviation of the amide bond from planarity, it is apparent that twisting about the endocyclic amide bond C2—N1 is slight [7 (1)°] in contrast to that about the endocyclic amide bond C5—N4 [16.2 (9)°]. The endocyclic amide bonds (N1—C2 and N4—C5) adjacent to the *N*-acetyl and the *N*-menthyloxycarbonyl substituents, respectively, appear slightly longer [1.375 (9) and 1.365 (9) Å] compared with the amide bonds of glycine and sarcosine anhydride [1.325 (7) and 1.348 (3) Å]. The diminished double-bond character in the former cases can be attributed to delocalization of the lone pair of electrons on the N atoms onto the exocyclic amide bond. It is also noteworthy that both of these endocyclic amide bonds are shorter compared with the exocyclic amide bonds, with N1—C7 [1.418 (9) Å] longer than N4—C9 [1.403 (8) Å]. The carbonyl groups in the title piperazinedione have bond lengths of 1.18 (1), 1.204 (9), 1.22 (1) and 1.229 (9) Å. The latter values are comparable with the C=O bond lengths of 1.239 (7) and 1.234 (3) Å in glycine anhydride and sarcosine anhydride, respectively, whereas the former are shorter. The internal bond angles C2—N1—C6 [119.4 (6)°] and C3—N4—C5 [117.2 (7)°] are also slightly compressed as compared with the values of 126.0 (3)° in glycine anhydride and 124.6 (2)° in sarcosine anhydride.

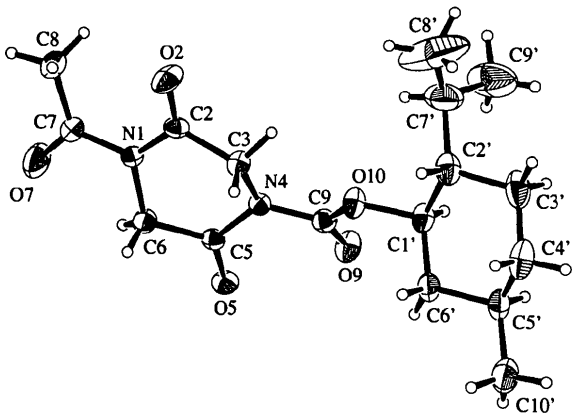


Fig 1. View of the title compound showing the labelling of all non-H atoms. Displacement ellipsoids are shown at 20% probability levels. H atoms are shown as circles of arbitrary radii.

Experimental

1-Acetylpiperazine-2,5-dione was synthesized from glycine anhydride following the procedure of Akimova, Petrova & Gavrilov (1954). The piperazine-2,5-dione was then treated with menthyl chloroformate (1.2 equivalents) and *N,N*-dimethylaminopyridine (1.2 equivalents) in CH_2Cl_2 and the progress of the reaction was monitored by thin-layer chromatography. Upon completion of the reaction, the reaction mixture was washed successively with water and brine, following which the organic layer was dried over sodium sulfate and concentrated *in vacuo*. The desired product was isolated by flash column chromatography as a colourless solid in 55% yield. Recrystallization from ethyl acetate and petroleum spirit gave suitable crystals for X-ray analysis.

Crystal data

$C_{17}H_{26}N_2O_5$
M_r = 338.40
Monoclinic
$P2_1$
a = 9.977 (4) Å
b = 5.757 (4) Å
c = 16.047 (3) Å
β = 96.26 (2)°
V = 916.2 (8) Å^3
Z = 2
D_x = 1.227 Mg m^{-3}
D_m not measured
Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 25 reflections
θ = 20.9–26.0°
μ = 0.747 mm^{-1}
T = 296 (1) K
Needle
0.36 × 0.08 × 0.04 mm
Colourless

Data collection

Rigaku AFC-6*R* diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical based on azimuthal (ψ) scans (North, Phillips & Mathews, 1968)
T_{min} = 0.86, T_{max} = 0.97
1622 measured reflections
1525 independent reflections
1521 reflections with $I > 0$
R_{int} = 0.031
θ_{max} = 60.02°
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 6$
$l = -18 \rightarrow 17$
3 standard reflections every 150 reflections
intensity decay: negligible

Refinement

Refinement on F
R = 0.0983
wR = 0.0448
S = 1.989
1521 reflections
217 parameters
H atoms not refined
$w = 4F_o^2/[\sigma^2(F_o^2) + (0.007F_o^2)^2]$
$(\Delta/\sigma)_{max}$ = 0.0188
$\Delta\rho_{max}$ = 0.39 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}
Extinction correction: Zachariasen type 2, Gaussian isotropic
Extinction coefficient: 1.3 (7) × 10^{-6}
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

O(2)—C(2)	1.204 (9)	N(1)—C(7)	1.418 (9)
O(5)—C(5)	1.229 (9)	N(4)—C(5)	1.365 (9)
O(10)—C(1′)	1.478 (7)	N(4)—C(9)	1.403 (8)
N(1)—C(2)	1.375 (9)		
C(2)—N(1)—C(6)	119.4 (6)	N(4)—C(3)—C(2)	115.0 (7)
C(3)—N(4)—C(5)	117.2 (7)	N(4)—C(5)—C(6)	117.7 (8)
N(1)—C(2)—C(3)	116.4 (7)	N(1)—C(6)—C(5)	117.4 (6)

Table 2. *Torsion angles (°)*

C(2)—N(1)—C(6)—C(5)	φ_1	−32.4 (9)
C(5)—N(4)—C(3)—C(2)	φ_2	−41.0 (8)
N(1)—C(6)—C(5)—N(4)	ψ_1	20.1 (9)
N(4)—C(3)—C(2)—N(1)	ψ_2	28.9 (9)
C(3)—C(2)—N(1)—C(6)	ω_1	7 (1)
C(6)—C(5)—N(4)—C(3)	ω_2	16.2 (9)

The θ-scan width used was $(1.30 + 0.30\tan\theta)°$ at a speed of 16° min^{-1} (in ω). The weak reflections were rescanned a maximum of four times and the counts accumulated to ensure good counting statistics. Stationary background counts were made on each side of the reflection with a 2:1 ratio of peak to background counting time. The maximum limit of 120° in 2θ was used. Higher-angle data collection was not possible and would have resulted in hardware collision. Owing to the small size and weakly diffracting nature of the crystal, collection of data to any higher angle would not have significantly improved the data to parameter ratio in this particular case. The reader should however treat with discretion the somewhat detailed comparisons given in the discussion. The structure was solved by the direct methods program *SIR*92 (Altomare *et al.*, 1994) and expanded using Fourier techniques (*DIRDIF*92; Beurskens *et al.*, 1992). H atoms were located from a difference map and fixed at ideal positions with C—H = 0.96 Å and U_{iso} = $1.2U_{eq}$(C).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1992*a*). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1992*b*). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: TA1117). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Glimepiride

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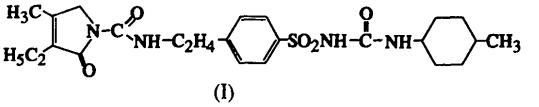
(*Received 17 October 1995; accepted 16 November 1996*)

Abstract

Glimepiride, 1-{4-[2-(3-ethyl-4-methyl-2-oxo-3-pyrroline-1-carboxyamido)ethyl]phenylsulfonyl}-3-(*trans*-4-methylcyclohexyl)urea, $C_{24}H_{34}N_4O_5S$, is a drug used in the treatment of non-insulin dependent diabetes mellitus.

Comment

Glimepiride, (I), is a second-generation sulfonylurea compound used in the treatment of non-insulin dependent diabetes mellitus (Holmes, Heel, Brogden, Speight & Avery, 1984). Structural data on glimepiride is limited and so far only one stable polymorphic form is known; its solubility is 1.2 mg l^{-1} (293 K) at pH 7 (Iwata, 1997). The crystal structure of this stable form determined by X-ray crystallographic analysis is reported here.



(I)