Acta Crystallographica Section E
**Structure Reports Online**
ISSN 1600-5368

# A new polymorph of chlorpropamide: 4-chloro-*N*-(propylaminocarbonyl)benzenesulfonamide

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**Key indicators**

Single-crystal X-ray study
*T* = 295 K
Mean σ(C–C) = 0.010 Å
*R* factor = 0.089
*wR* factor = 0.223
Data-to-parameter ratio = 19.6

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

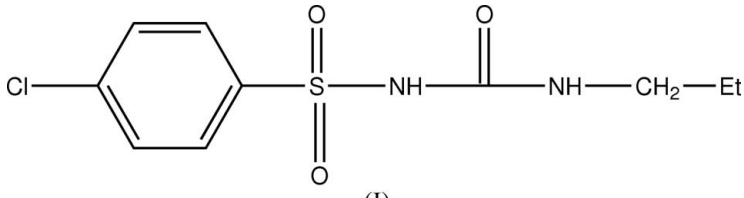


Received 22 August 2006
Accepted 3 September 2006

The title compound, $C_{10}H_{13}ClN_2O_3S$, known as chlorpropamide, was crystallized from a heptane–ethyl acetate solution in a new polymorphic form. The conformations of molecules and their packing in the new polymorph differ significantly from those in the previously reported structure, although the intermolecular hydrogen-bond patterns in both polymorphs are very similar.

## Comment

Chlorpropamide, (I), is an oral antidiabetic agent. Several chlorpropamide polymorphs and a benzene solvate have been reported (Simmons *et al.*, 1973; Burger, 1975; Al-Saieq & Riley, 1982; Ueda *et al.*, 1984; De Villiers & Wurster, 1999; Vemavarapu *et al.*, 2002). However, the crystal structure is known for only one polymorph [refcode BEDMIG (Koo *et al.*, 1980) in the Cambridge Structural Database (Version 5.27; Allen, 2002)]. We report here the structure of a new polymorph, (I), in the centrosymmetric space group *Pbcn*. We suggest naming this polymorph β-chlorpropamide and the only polymorph, among numerous previously reported ones, for which the crystal structure is known as α-chlorpropamide (Koo *et al.*, 1980).




(I)

The asymmetric unit of the β-polymorph contains one molecule, and its conformation differs noticeably from that in the α-form, mainly in the orientation of the alkyl 'tail' with respect to the benzene ring and the N1,C7,N2,O3 plane (Fig. 1 and Table 1). The benzene ring and alkyl chain are on the same side of the plane defined by atoms N1,C7,N2,O3 in the β-polymorph (Fig. 1, Table 1), but are on opposite sides of this plane in the α-polymorph (Koo *et al.*, 1980).

The main intermolecular hydrogen-bonding pattern in the β-polymorph (Fig. 2) is the same as in the α-form, and the distances and angles between the atoms in the hydrogen bonds differ only slightly (Table 2). The main difference is in the relative orientation of the aromatic rings and the alkyl chains of the neighbouring molecules in the bands (Figs. 2 and 3). In the β-polymorph, the hydrogen-bonded chains are directed along the *b* axis, and all the benzene rings are on the same side of a chain, when viewed along the chain axis (Fig. 3). This is

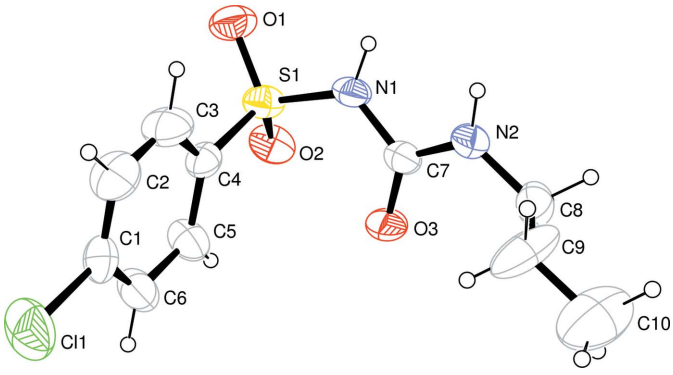



**Figure 1**
A view of the molecular structure of $\beta$-chlorpropamide with the atom-labeling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as spheres of arbitrary radii.

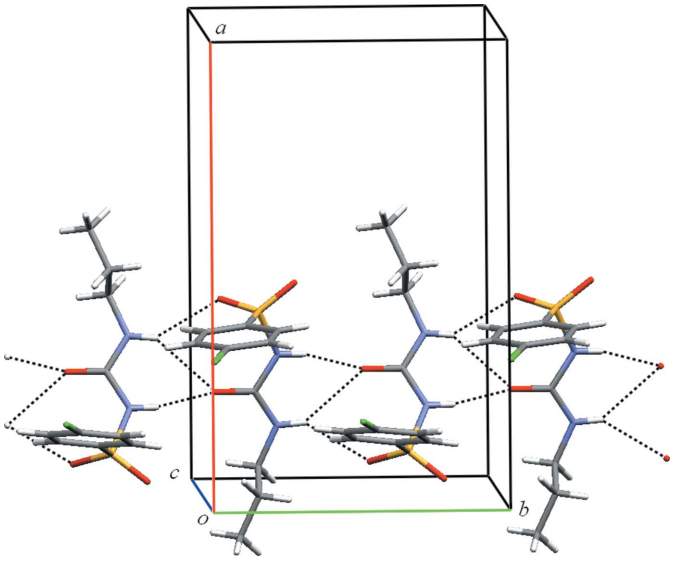



**Figure 2**
The hydrogen-bonded bands in (I), with hydrogen bonds drawn as dashed lines.

very different from the $\alpha$-polymorph, in which the hydrogen-bonded chains along the *a* axis have the benzene rings alternating on opposite sides of a chain when viewed along the chain axis. The $\beta$-form is about 5% less dense than the $\alpha$-form.

The powder diffraction pattern calculated from the single-crystal diffraction data for the $\beta$-form (Kraus & Nolze, 1999) reasonably matches entry 35–1970 in the PDF (set 50, International Center for Diffraction Data) based on a private communication from H. Ueda, 1984.

## Experimental

Chlorpropamide, 87 mg (Sigma Chemical Co., batch #31H0722) was dissolved in boiling heptane (2.5 ml). The solution was filtered hot and kept at room temperature in a sealed flask. After cooling to room temperature, small transparent plates were precipitated, from which a single crystal suitable for X-ray diffraction was selected. Powder diffraction analysis showed the sample to consist of one phase only.

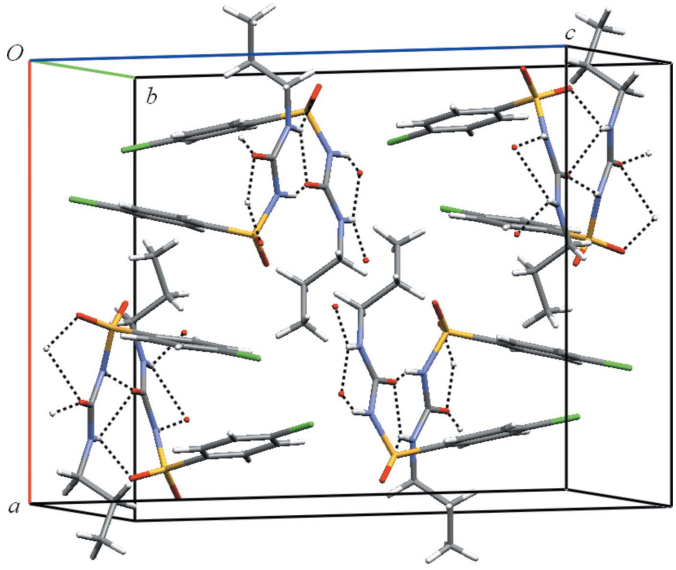



**Figure 3**
The crystal packing of the bands in (I).

*Crystal data*

$C_{10}H_{13}ClN_2O_3S$
$M_r$ = 276.74
Orthorhombic, *Pbcn*
*a* = 14.777 (3) Å
*b* = 9.316 (4) Å
*c* = 19.224 (5) Å
*V* = 2646.4 (14) Å$^3$
*Z* = 8
$D_x$ = 1.389 Mg m$^{-3}$
Mo *K*$\alpha$ radiation
$\mu$ = 0.44 mm$^{-1}$
*T* = 295 (2) K
Block, colorless
0.46 × 0.31 × 0.12 mm

*Data collection*

Stoe Stadi-4 four-circle D094 diffractometer
$2\theta$–$\omega$ scans
Absorption correction: $\psi$ scan (*X-RED*; Stoe & Cie, 1997)
$T_{min}$ = 0.834, $T_{max}$ = 0.948
5718 measured reflections
3040 independent reflections
1365 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.051
$\theta_{max}$ = 27.5°
3 standard reflections
frequency: 240 min
intensity decay: 5.8%

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.089
$wR(F^2)$ = 0.223
*S* = 1.11
3040 reflections
155 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.061P)^2 + 3.1551P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.29 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.27 e Å$^{-3}$

**Table 1**
Selected torsion angles (°).

| | | | |
|---|---|---|---|
| O2—S1—N1—C7 | −53.8 (5) | O1—S1—C4—C3 | −34.7 (6) |
| O1—S1—N1—C7 | 176.7 (4) | N1—S1—C4—C3 | 75.7 (5) |
| C4—S1—N1—C7 | 63.0 (5) | O2—S1—C4—C5 | 12.6 (6) |
| C8—N2—C7—O3 | 2.4 (9) | O1—S1—C4—C5 | 144.5 (5) |
| C8—N2—C7—N1 | −178.7 (5) | N1—S1—C4—C5 | −105.2 (5) |
| S1—N1—C7—O3 | 10.1 (8) | C7—N2—C8—C9 | −94.5 (7) |
| S1—N1—C7—N2 | −168.8 (4) | N2—C8—C9—C10 | −179.7 (7) |
| O2—S1—C4—C3 | −166.6 (5) | | |

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N1—H1$A$···O3$^{i}$ | 0.86 | 1.95 | 2.740 (5) | 152 |
| N2—H2$A$···O2$^{i}$ | 0.86 | 2.41 | 3.130 (6) | 142 |
| N2—H2$A$···O3$^{i}$ | 0.86 | 2.58 | 3.280 (6) | 140 |

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

The displacement ellipsoids are large for two 'tail' atoms, C9 and C10, indicating possible static/dynamic disorder (Mueller *et al.*, 2006). A model with partially occupied positions for disordered atoms (C9 and C10) was tried, but did not give better refinement results. H atoms were positioned geometrically and refined using a riding model, with C—H = 0.93 (aromatic), 0.96 ($CH_3$) and 0.97 Å ($CH_2$), N—H = 0.86 Å, and $U_{iso}$(H) = 1.2$U_{eq}$(C,N) or 1.5$U_{eq}$(methyl C).

Data collection: *STADI4* (Stoe & Cie, 1997); cell refinement: *STADI4*; data reduction: *X-RED* (Stoe & Cie, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *MERCURY* (Bruno *et al.*, 2002); software used to prepare material for publication: *SHELXL97* (Sheldrick, 1997) and *X-RED* (Stoe & Cie, 1997).

This work was supported by grant No 05–03-32468 from the RFBR, grants NO-008-XI and Y3-C-08–01 from BRHE, and grant No. 2.2.2.3.2007 from the Russian Ministry of Education and Science.

## References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Al-Saieq, S. S. & Riley, G. S. (1982). *Pharm. Acta Helv.* **57**, 8–11.
Bruno, I. J., Cole, J. C., Edgington, P. R., Kessler, M., Macrae, C. F., McCabe, P., Pearson, J. & Taylor, R. (2002). *Acta Cryst.* B**58**, 389–397.
Burger, A. (1975). *Sci. Pharm.* **43**, 152–161.
De Villiers, M. M. & Wurster, D. E. (1999). *Acta Pharm.* **49**, 79–88.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Koo, C. H., Cho, S. I. & Yeon, Y. H. (1980). *Arch. Pharmacol. Res.* **3**, 37–49.
Kraus, W. & Nolze, G. (1999). *Powder Cell Software.* Version 2.4. Federal Institute for Material Research and Testing, Berlin, Germany.
Mueller, P., Herbst-Irmer, R., Spek, A. L., Schneider, T. R. & Sawaya, M. R. (2006). *Crystal Structure Refinement. A Crystallographer's Guide to SHELXL*. IUCr Texts on Crystallography, 8. Oxford Science Publications. Oxford University Press.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Simmons, D. L., Ranz, R. J. & Guanchandani, N. D. (1973). *Can. J. Pharm. Sci.* **8**, 125–127.
Stoe & Cie (1997). STADI4 and *X-RED*. Stoe & Cie GmbH, Darmstadt, Germany.
Ueda, H., Nambu, N. & Nagai, T. (1984). *Chem. Pharm. Bull.* **32**, 244–250.
Vemavarapu, C., Mollan, M. J. & Needham, T. E. (2002). *AAPS PharmSciTech*, 3 article 29 (URL: http://www.aapspharmsci.org).