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Powder study of chlorothiazide *N*,*N*-dimethylformamide solvate

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Key indicators

Powder X-ray study
T = 100 K
Mean σ(C–C) = 0.045 Å
R factor = 0.039
wR factor = 0.050

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

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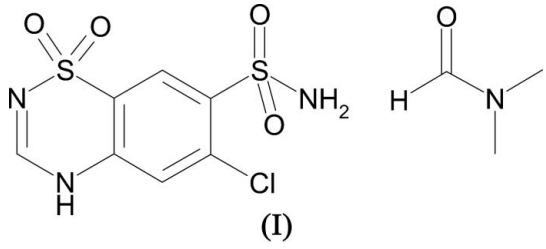
The crystal structure of the title compound [systematic name: 6-chloro-4*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide–*N*,*N*-dimethylformamide (1/1)], $C_7H_6ClN_3O_4S_2\cdot C_3H_7NO$, was solved by simulated annealing from laboratory X-ray powder diffraction data collected at 100 K. Subsequent Rietveld refinement, using data collected to 1.5 Å resolution, yielded an R_{wp} of 0.050. Hydrogen bonds to *N*,*N*-dimethylformamide form the rungs of a ladder motif, which is further stabilized by a $\pi\cdots$halogen dimer interaction. The benzene rings in adjacent ladders engage with each other in an offset face-to-face π–π interaction.

Comment

The diuretic chlorothiazide (CT) promotes the excretion of water and electrolytes by the kidneys and was developed for the treatment of conditions such as oedema and congestive heart failure. The title compound, (I), was crystallized from *N*,*N*-dimethylformamide (DMF) during a preliminary solvent screen in preparation for an automated parallel crystallization study of CT. The sample was identified as a new form using multi-sample foil transmission X-ray powder diffraction analysis (Florence *et al.*, 2003).



(I)

The crystal structure of (I) (Fig. 1) was determined after recollecting powder diffraction data from a sample of (I) in a rotating capillary (Fig. 2). The intermolecular interactions in (I) combine to create the ladder motif shown in Fig. 3. The stiles of the ladder comprise infinite $[1\bar{1}0]$ chains of CT molecules linked by N1$\cdots$N3 hydrogen bonds, with rungs formed by hydrogen bonds N1$\cdots$O4*A* and N2$\cdots$O4*A* to DMF (Table 1). This motif is further stabilized by a $\pi\cdots$halogen dimer interaction (Rahman *et al.*, 2004), wherein two CT molecules associate by means of one aromatic offset face-face interaction, supplemented by two aromatic $\pi\cdots$halogen interactions, to create the centrosymmetric building block (Fig. 3), with the following geometric parameters (*Cg*2 is the centroid of ring *R*2; atoms C1/C5/C6/C4/C2/C7): *Cg*2$\cdots$*Cg*2′ = 4.44 (2) Å, Cl1$\cdots$*Cg*2′ = 3.84 (1) Å and C6—Cl1$\cdots$*Cg*2′ = 79 (1)°; primed atoms are generated by the symmetry opera-

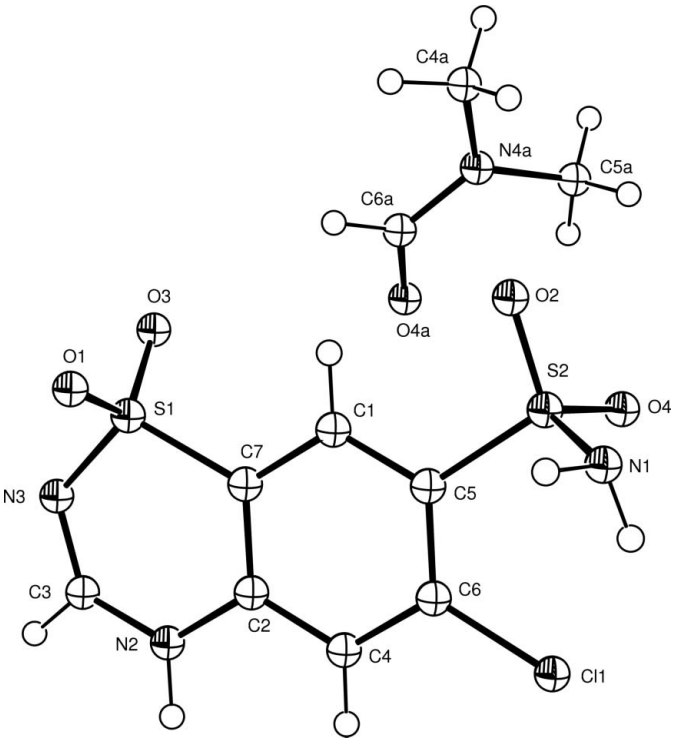


Figure 1
The molecular structure of (I). Displacement ellipsoids are shown at the 50% probability level.

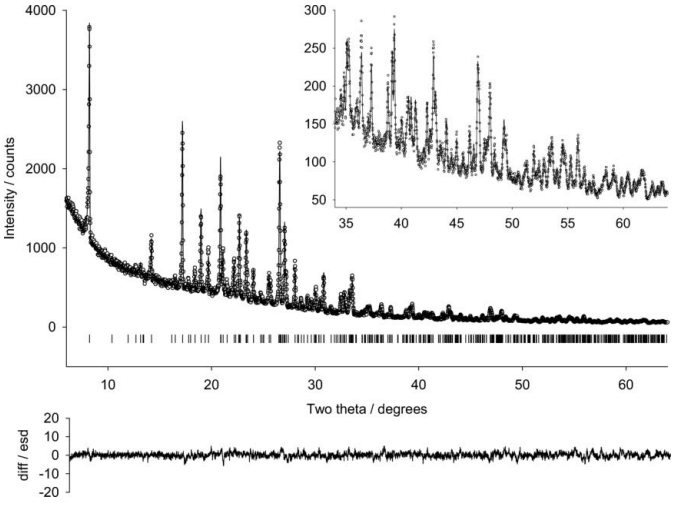


Figure 2
Final observed (points), calculated (line) and difference [$(y_{obs} - y_{calc})/\sigma(y_{obs})$] profiles for the Rietveld refinement of (I).

tion ($2 - x$, $2 - y$, $1 - z$). The benzene rings in adjacent ladders engage with each other in an offset face-to-face π–π interaction, with $Cg2\cdots Cg2^{i}$ = 4.26 (2) Å [symmetry code: (i) $1 - x$, $2 - y$, $1 - z$].

Experimental

A polycrystalline sample of (I) was purchased from Sigma–Aldrich (CAS 58–94-6) and recrystallized from a dimethylformamide solution by slow evaporation over 48 h at 278 K.

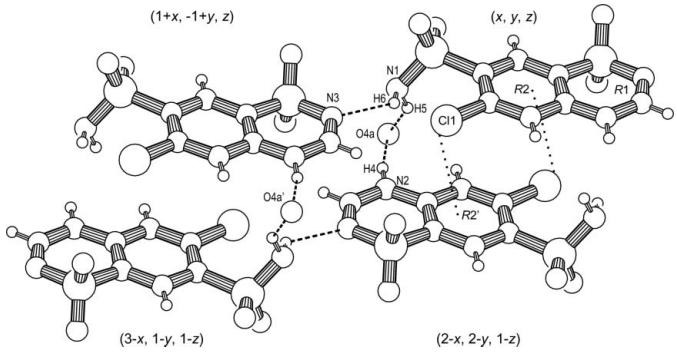


Figure 3
The hydrophilic and hydrophobic interactions in (I). In the $\pi\cdots$halogen dimer interaction, two Cl atoms are positioned over the π-systems of the $R2$ and $R2'$ rings. Atoms O4A and O4A' are in the dimethylformamide molecules at $(1 + x, y, z)$ and $(2 - x, 1 - y, 1 - z)$, respectively.

Crystal data

$C_7H_6ClN_3O_4S_2\cdot C_3H_7NO$
M_r = 368.83
Triclinic, $P\overline{1}$
a = 7.9822 (4) Å
b = 8.8830 (5) Å
c = 11.1075 (6) Å
α = 86.689 (3)°
β = 75.078 (3)°
γ = 73.196 (3)°
V = 728.41 (7) Å^3
Z = 2
D_x = 1.682 Mg m^{-3}
Cu $K\alpha_1$ radiation
μ = 5.30 mm^{-1}
T = 100 K
Specimen shape: cylinder
10 × 0.7 × 0.7 mm
Specimen prepared at 0 kPa
Specimen prepared at 293 K
Particle morphology: needle, colourless

Data collection

Bruker D8 Advance diffractometer
Specimen mounting: 0.7 mm borosilicate capillary
Specimen mounted in transmission mode
Scan method: step
Absorption correction: none
$2\theta_{min}$ = 6, $2\theta_{max}$ = 64°
Increment in 2θ = 0.014°

Refinement

Refinement on F^2
R_p = 0.039
R_{wp} = 0.050
R_{exp} = 0.036
R_B = 3.2
S = 1.41
Wavelength of incident radiation: 1.54056 Å
Excluded region(s): none
Profile function: fundamental parameters with axial divergence correction
108 parameters
Only H-atom coordinates refined
Weighting scheme based on measured s.u.'s, $1/\sigma(y_o)^2$
$(\Delta/\sigma)_{max}$ = 0.049
Preferred orientation correction: none

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H4···O4A^{i}	0.9 (2)	1.8 (2)	2.71 (3)	164
N1—H5···O4A^{ii}	0.9 (3)	2.0 (2)	2.78 (3)	140
N1—H6···N3^{iii}	0.9 (2)	2.4 (2)	3.05 (3)	129

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

The sample was loaded into a 0.7 mm borosilicate glass capillary and rotated throughout the data collection to minimize preferred orientation effects. Data were collected using a variable count time (VCT) scheme in which the step time is increased with 2θ (Shankland *et al.*, 1997; Hill & Madsen, 2002). The diffraction pattern indexed to a

triclinic cell [$F(22)$ = 64.2, $M(22)$ = 22.9; *DICVOL91* (Boultif & Louer, 1991)], and space group $P\overline{1}$ was assigned from volume considerations and a lack of systematic absences. The data set was background-subtracted and truncated to 51.35° 2θ for Pawley fitting (Pawley, 1981; $\chi^2_{\rm Pawley}$ = 1.33) and the structure was solved using the simulated annealing (SA) global optimization procedure, described previously (David *et al.*, 1998), which is now implemented in the *DASH* computer program (David *et al.*, 2001).

The SA structure solution used 273 reflections and involved the optimization of two fragments (including H atoms) totaling 14 degrees of freedom, with the internal degrees of freedom allowing rotations around the S2—C5 and N4*A*—C6*A* bonds. The sulfonamide conformation was fixed throughout the optimization, with anti-periplanar torsion angles assigned to H5—N1—S2—O4 and H6—N1—S2—O2, consistent with the conformation observed in the single-crystal structure of non-solvated CT (Johnston *et al.*, 2006). The tautomeric H atom was placed on N2 (not N3), consistent with density functional calculations (Latosińska, 2003) and with the single-crystal structure of CT. The best SA solution had a favourable $\chi^2_{\rm SA}/\chi^2_{\rm Pawley}$ ratio of 2.3 and a chemically reasonable lattice packing arrangement, with no significant misfit to the diffraction data. The solved structure was then refined against the full data set (6–64° 2θ) using a restrained Rietveld method (Rietveld, 1969), as implemented in *TOPAS* (Coelho, 2003), with $R_{\rm wp}$ falling from 0.1369 to 0.0504 during the refinement. All atomic positions (including H atoms) were refined, subject to a series of restraints on bond lengths, bond angles and, where appropriate, planarity. The distance and angle restraints were based on the CT single-crystal structure. As reported elsewhere for famotidine (Shankland *et al.*, 2002), rotating the CT sulfonamide group in increments of 120° about the S2—C5 bond (Fig. 1) results in three orientations that are similar in the sense that the X-ray scattering power of N1(H2) is on a par with that of atoms O2 and O4. In this case, the correctness of the orientation shown in Fig. 1 was confirmed by the superior $R_{\rm wp}$ and intermolecular hydrogen-bonding pattern, compared with the two alternatives.

Data collection: *DIFFRAC* plus *XRD Commander* (Kienle & Jacob, 2003); cell refinement: *TOPAS* (Coelho, 2003); data reduction: *DASH* (David *et al.*, 2001); program(s) used to solve structure: *DASH*; program(s) used to refine structure: *TOPAS*; molecular graphics: *PLATON* (Version 011105; Spek, 2003); software used to prepare material for publication: *enCIFer* (Version 1.1; Allen *et al.*, 2004).

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