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Hydrochlorothiazide *N*,*N*-dimethylformamide solvate

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Key indicators

Single-crystal synchrotron study
T = 150 K
Mean σ(C–C) = 0.003 Å
R factor = 0.040
wR factor = 0.107
Data-to-parameter ratio = 10.4

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

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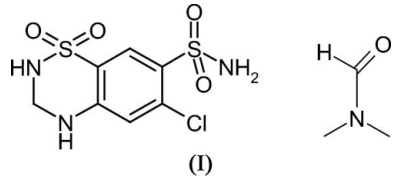
Hydrochlorothiazide forms a 1:1 solvate with *N*,*N*-dimethylformamide (systematic name: 6-chloro-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide-1,1-dioxide dimethylformamide solvate), $C_7H_8ClN_3O_4S_2\cdot C_3H_7NO$. The compound crystallizes with two molecules of hydrochlorothiazide and two solvent molecules in the asymmetric unit and displays an extensive hydrogen-bonding network.

Comment

Hydrochlorothiazide (HCT) is a thiazide diuretic which is known to crystallize in at least two non-solvated forms, form I (Dupont & Dideberg, 1972) and form II (Florence *et al.*, 2005). Form (I) was produced during an automated parallel crystallization polymorph screen on HCT. The sample was identified as a novel form using multi-sample X-ray powder diffraction analysis of all recrystallized samples (Florence *et al.*, 2003). Subsequent manual recrystallization from a saturated *N*,*N*-dimethylformamide (DMF):acetone solution by slow evaporation at 278 K yielded samples of the HCT DMF solvate suitable for a synchrotron microcrystal study (Cernik *et al.*, 1997, 2000).



(I)

The compound crystallizes as a 1:1 solvate with $Z' = 2$ (Fig. 1). The benzothiadiazine ring of HCT adopts a non-planar conformation in both residues, with the largest deviations from the least-squares plane through atoms C2–C7 observed for atoms S1 and N1 in residue *A* [0.278 (1) and 0.770 (2) Å respectively] and atom N1*A* in residue *B* [0.6802 (2) Å]. In residue *A*, the sulphonamide side chain adopts a torsion angle N3—S2—C5—C6 of −57.7 (2)° such that the NH_2 group is located on the same side of the molecule as the H atom (H1N) bonded to N1, a similar arrangement to that in both of the non-solvated forms of HCT. The corresponding torsion angle in residue *B* is 60.76 (2)°, such that the NH_2 group lies on the opposite side of the molecule to the H atom (H5N) bonded to N1*A*.

The crystal structure is stabilized by a network of seven N—H···O and one N—H···N intermolecular hydrogen bonds (Table 1). These contacts interconnect (*a*) HCT molecules (Fig. 2, contacts 1, 2, 4 and 6) and (*b*) HCT and solvent molecules (Fig. 2 contacts 3, 4, 5, 7 and 8). Residues *A* and *B* form parallel *C*(8) (Etter, 1990) hydrogen-bonded chains in the direction of the *b* axis *via* contacts 2 and 6, respectively (Fig. 3),

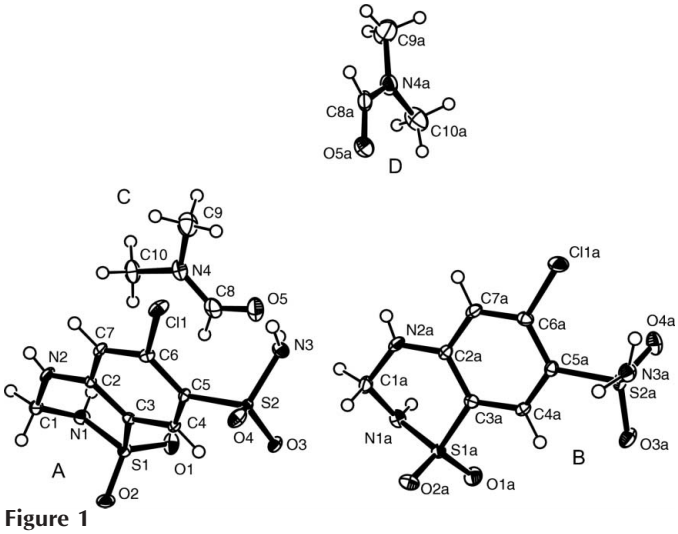


Figure 1
The asymmetric unit, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

with the chains interconnected *via* C—H···O contacts to form layers in the *ab* plane. The layers stack along the *c* axis with solvent residue *C* lying between layers of HCT molecules, interconnected *via* contacts 3 and 6 to HCT residues *A* and *B*, respectively. The remaining solvent molecule (residue *D*) lies approximately perpendicular to the *ab* plane and forms hydrogen bonds with HCT residue *B* (Fig. 2, contacts 5 and 8). The structure is further stabilized by seven C—H···O contacts (Table 1).

Experimental

The sample of HCT used to prepare the solvate was used as received from Sigma–Aldrich. This was recrystallized from a 50:50 DMF/acetone solution by isothermal solvent evaporation at 278 K.

Crystal data

$C_7H_8ClN_3O_4S_2\cdot C_3H_7NO$	V = 1509.50 (7) Å^3
M_r = 370.83	Z = 4
Triclinic, $P\overline{1}$	D_x = 1.632 Mg m^{-3}
a = 7.3028 (2) Å	Synchrotron radiation
b = 9.1492 (2) Å	λ = 0.8466 Å
c = 23.6989 (6) Å	μ = 0.56 mm^{-1}
α = 86.194 (1)°	T = 150 (2) K
β = 89.841 (1)°	Plate, colourless
γ = 72.855 (1)°	0.18 × 0.10 × 0.03 mm

Data collection

Bruker SMART APEX2 CCD diffractometer	4574 independent reflections
	4311 reflections with $I > 2\sigma(I)$
ω scans	R_{int} = 0.018
Absorption correction: none	θ_{max} = 29.0°
10824 measured reflections	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0721P)^2 + 1.2599P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.040	
$wR(F^2)$ = 0.107	
S = 1.05	$(\Delta/\sigma)_{max}$ = 0.001
4574 reflections	$\Delta\rho_{max}$ = 0.52 e Å^{-3}
441 parameters	$\Delta\rho_{min}$ = −0.52 e Å^{-3}
H atoms treated by a mixture of independent and constrained refinement	

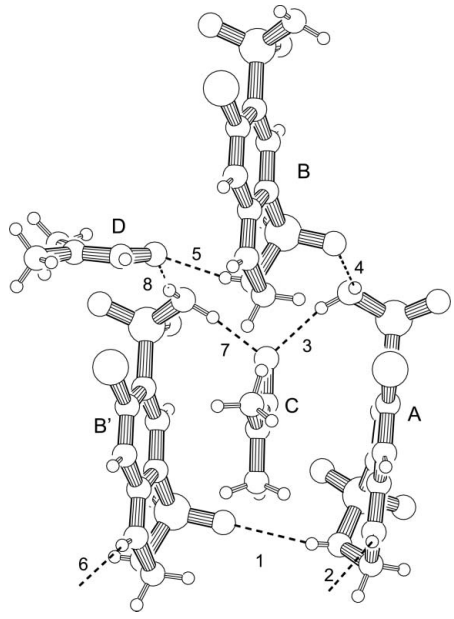


Figure 2
A packing diagram illustrating hydrogen bonds in (I). Unique contacts are labelled as follow: 1 = N1···O2A^{i}; 2 = N2···O4^{i}; 3 = N3···O5; 4 = N3···O2A^{ii}; 5 = N1A···O5A^{iii}; 6 = N2A^{i}···N3A(x, −2 + y, z); 7 = N3A—H7N···O5^{iv}; 8 = N3A—H8N···O5A^{iv} (see Table 1 for symmetry codes and geometry). Contacts calculated and illustrated using *PLATON* (Spek, 2003; program version 280604). Contact 6 is shown outwith the asymmetric unit for clarity.

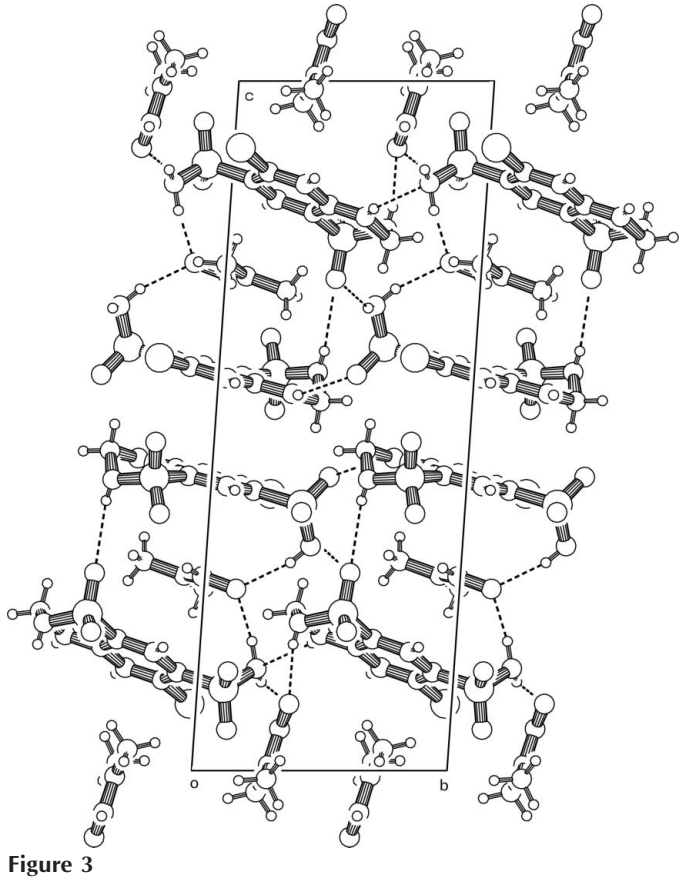


Figure 3
The crystal packing in (I), viewed down the *a* axis, showing the alternating layers of HCT and DMF molecules stacked along *c*. Hydrogen bonds are shown as dashed lines.

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···O2A^{i}	0.80 (3)	2.60 (3)	3.290 (3)	146 (3)
N2—H2N···O4^{i}	0.74 (3)	2.47 (3)	3.023 (3)	134 (3)
N3—H3N···O5	0.90 (3)	2.07 (3)	2.954 (3)	165 (3)
N3—H4N···O2A^{ii}	0.85 (4)	2.35 (4)	3.092 (3)	146 (3)
N1A—H5N···O5A^{iii}	0.78 (4)	2.12 (4)	2.882 (3)	167 (3)
N2A—H6N···N3A^{i}	0.77 (4)	2.48 (4)	3.177 (3)	150 (3)
N3A—H7N···O5^{iv}	0.95 (4)	1.89 (4)	2.820 (3)	164 (3)
N3A—H8N···O5A^{iv}	0.86 (3)	2.12 (3)	2.942 (3)	163 (2)
C1A—H1A1···O3A^{i}	0.99	2.42	3.157 (3)	131
C1—H1A···O3^{i}	0.99	2.56	3.235 (3)	125
C1A—H1A2···O3	0.99	2.51	3.467 (3)	162
C7—H7···O2^{ii}	0.95	2.56	3.466 (3)	159
C7A—H7A···O1A^{ii}	0.95	2.45	3.163 (3)	132
C9—H9B···O1^{ii}	0.98	2.54	3.442 (3)	152
C10—H10C···O1^{ii}	0.98	2.51	3.323 (3)	141

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

The amine and aldehyde H atoms were located by difference synthesis and refined isotropically. The remaining H atoms were positioned geometrically and a riding model with $U_{iso}(H) = 1.2U_{eq}(C)$ or $1.5U_{eq}(C_{methyl})$ was used during the refinement process (C—H distances 0.95, 0.99 and 0.98 Å for CH, CH_2 and CH_3 groups, respectively).

Data collection: *APEX2* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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