

Andrea Johnston,^a Alastair J.
 Florence^{a*} and Alan R. Kennedy^b
^aDepartment of Pharmaceutical Sciences,
 University of Strathclyde, 27 Taylor Street,
 Glasgow G4 0NR, Scotland, and ^bWestCHEM,
 Department of Pure and Applied Chemistry,
 University of Strathclyde, 295 Cathedral Street,
 Glasgow G1 1XL, Scotland

 Correspondence e-mail:
 alastair.florence@strath.ac.uk

Key indicators

Single-crystal synchrotron study

 $T = 150\text{ K}$

 Mean $\sigma(\text{C}-\text{C}) = 0.003\text{ \AA}$
 R factor = 0.040

 wR factor = 0.107

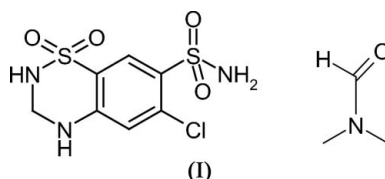
Data-to-parameter ratio = 10.4

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

Hydrochlorothiazide *N,N*-dimethylformamide solvate

 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), $\text{C}_7\text{H}_8\text{ClN}_3\text{O}_4\text{S}_2 \cdot \text{C}_3\text{H}_7\text{NO}$. 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).

 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 $-57.7 (2)^\circ$ 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 $60.76 (2)^\circ$, 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),

Received 23 March 2006

Accepted 28 March 2006

Online 7 April 2006

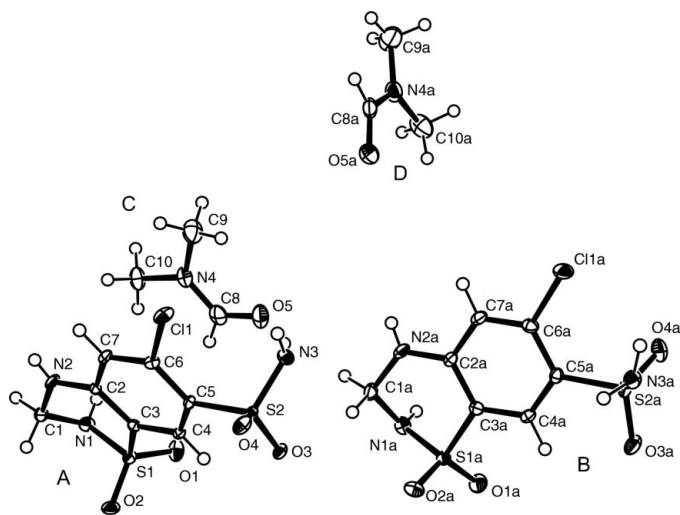


Figure 1
The asymmetric unit, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

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

$C_7H_8ClN_3O_4S_2 \cdot C_3H_7NO$
 $M_r = 370.83$
 Triclinic, $P\bar{1}$
 $a = 7.3028$ (2) Å
 $b = 9.1492$ (2) Å
 $c = 23.6989$ (6) Å
 $\alpha = 86.194$ (1)°
 $\beta = 89.841$ (1)°
 $\gamma = 72.855$ (1)°

$V = 1509.50$ (7) Å³
 $Z = 4$
 $D_x = 1.632$ Mg m⁻³
 Synchrotron radiation
 $\lambda = 0.8466$ Å
 $\mu = 0.56$ mm⁻¹
 $T = 150$ (2) K
 Plate, colourless
 $0.18 \times 0.10 \times 0.03$ mm

Data collection

Bruker SMART APEX2 CCD
 diffractometer
 ω scans
 Absorption correction: none
 10824 measured reflections

4574 independent reflections
 4311 reflections with $I > 2\sigma(I)$
 $R_{int} = 0.018$
 $\theta_{max} = 29.0^\circ$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.040$
 $wR(F^2) = 0.107$
 $S = 1.05$
 4574 reflections
 441 parameters
 H atoms treated by a mixture of
 independent and constrained
 refinement

$w = 1/[\sigma^2(F_o^2) + (0.0721P)^2 + 1.2599P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} = 0.001$
 $\Delta\rho_{max} = 0.52$ e Å⁻³
 $\Delta\rho_{min} = -0.52$ e Å⁻³

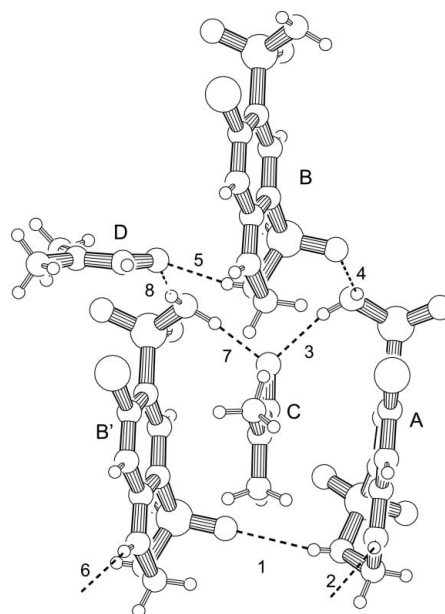


Figure 2
A packing diagram illustrating hydrogen bonds in (I). Unique contacts are labelled as follows: 1 = N1···O2Aⁱ; 2 = N2···O4ⁱ; 3 = N3···O5; 4 = N3···O2Aⁱⁱ; 5 = N1A···O5Aⁱⁱⁱ; 6 = N2Aⁱ···N3A(*x*, *-2* + *y*, *z*); 7 = N3A—H7N···O5^{iv}; 8 = N3A—H8N···O5A^{iv} (see Table 1 for symmetry codes and geometry). Contacts calculated and illustrated using PLATON (Spek, 2003; program version 280604). Contact 6 is shown outwith the asymmetric unit for clarity.

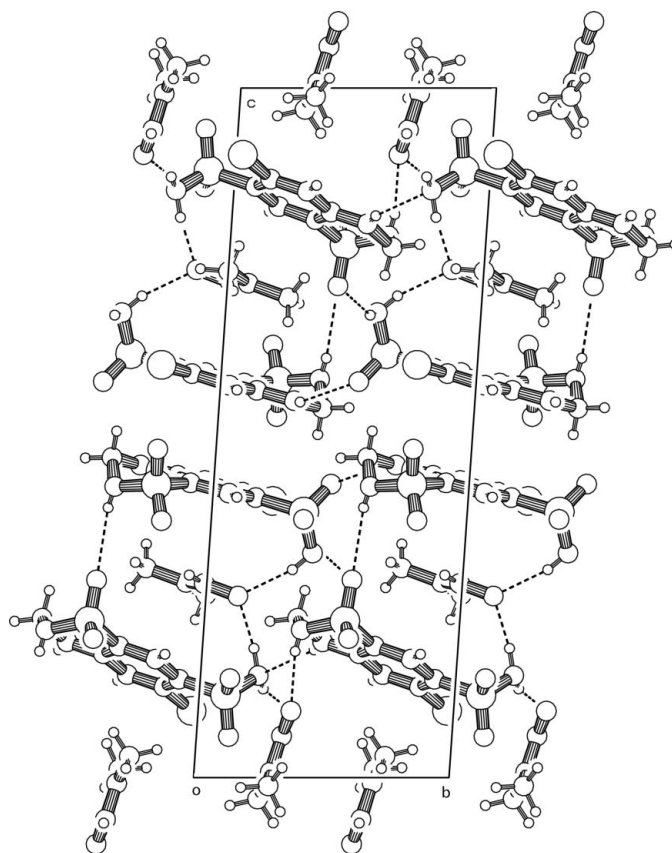


Figure 3
The crystal packing in (I), viewed down the *a* axis, showing the alternating layers of HCT and DMF molecules stacked along *c*. Hydrogen bonds are shown as dashed lines.

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

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
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 $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ or $1.5U_{\text{eq}}(\text{C}_{\text{methyl}})$ was used during the refinement process (C—H distances 0.95, 0.99 and 0.98 Å for CH, CH₂ and CH₃ 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*.

The authors thank the Basic Technology programme of the UK Research Councils for funding this work under the project Control and Prediction of the Organic Solid State (URL: <http://www.cposs.org.uk>). Thanks are also due to the CCLRC for provision of a beamtime grant at Daresbury SRS.

References

- Bruker (2004). *APEX2* (Version 1.14) and *SAINT* (Version 7.06a). Bruker AXS Inc., Madison, Wisconsin, USA.
- Cernik, R. J., Clegg, W., Catlow, C. R. A., Bushnell-Wye, G., Flaherty, J. V., Greaves, G. N., Burrows, I., Taylor, D. J., Teat, S. J. & Hamichi, M. (1997). *J. Synchrotron Rad.* **4**, 279–286.
- Cernik, R. J., Clegg, W., Catlow, C. R. A., Bushnell-Wye, G., Flaherty, J. V., Greaves, G. N., Burrows, I., Taylor, D. J., Teat, S. J. & Hamichi, M. (2000). *J. Synchrotron Rad.* **7**, 40.
- Dupont, L. & Dideberg, O. (1972). *Acta Cryst.* **B28**, 2340–2347.
- Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.
- Florence, A. J., Baumgartner, B., Weston, C., Shankland, N., Kennedy, A. R., Shankland, K. & David, W. I. F. (2003). *J. Pharm. Sci.* **92**, 1930–1938.
- Florence, A. J., Johnston, A., Fernandes, P., Shankland, K., Stevens, H. N. E., Osmunsden, S. & Mullen, A. B. (2005). *Acta Cryst.* **E61**, o2798–o2800.
- Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
- Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.