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Hydrochlorothiazide *N*,*N*-dimethylacetamide disolvate

Andrea Johnston,[a] Alastair J. Florence[a]* and Alan R. Kennedy[b]

[a]Department of Pharmaceutical Sciences, University of Strathclyde, 27 Taylor Street, Glasgow G4 0NR, Scotland, and [b]WestCHEM, Department of Pure & Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow G1 1XL, Scotland

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

Key indicators

Single-crystal X-ray study
T = 123 K
Mean σ(C–C) = 0.004 Å
Disorder in solvent or counterion
R factor = 0.058
wR factor = 0.121
Data-to-parameter ratio = 16.5

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

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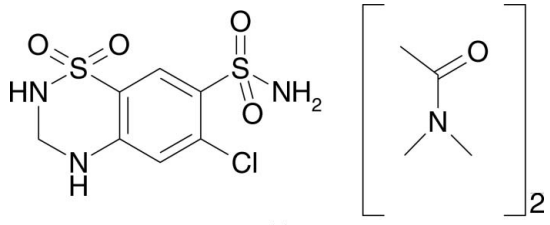
Hydrochlorothiazide forms a 1:2 solvate with *N*,*N*-dimethylacetamide (systematic name: 6-chloro-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide dimethylacetamide disolvate), $C_7H_8ClN_3O_4S_2\cdot 2C_4H_9NO$. The compound crystallizes with one hydrochorothiazide and two disordered solvent molecules in the asymmetric unit, with a hydrogen-bonding network comprising four N—H···O contacts.

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). Compound (I) was produced during an automated parallel crystallization study on HCT. The sample was identified as a new 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*-dimethylacetamide (DMA) solution by slow evaporation at 298 K yielded samples of the HCT DMA disolvate suitable for single-crystal diffraction (Fig. 1).



(I)

The compound crystallizes with one HCT and two DMA molecules in the asymmetric unit. Both solvent molecules are disordered over two sites though the positions of the acetyl O atoms (O1*S* and O2*S*) and one methyl group from each solvent (C2*S* and C10*S*) are modelled as coincident. The S1/N1/C1/N2/C2/C7 six-membered ring in HCT adopts a non-planar conformation with atoms S1 and N1 having deviations of 0.105 (1) and 0.684 (3) Å, respectively, from the least-squares plane through atoms C2/C3/C4/C5/C6/C7. The sulfonamide side chain adopts a torsion angle N3—S2—C5—C4 of 60.7 (3)°, such that O3 eclipses H6, and O4 and N3 are staggered with respect to Cl1.

The structure contains four N—H···O hydrogen bonds, with N1, N2 and N3 of HCT donating contacts to adjacent acetyl O atoms of DMA (Fig. 2). In addition, there are two C—H···O contacts between HCT and solvent, with a third, *viz*. C3—H3···O1(x, 1 + y, z), forming an infinite chain of HCT molecules in the *b*-axis direction. Adjacent HCT chains

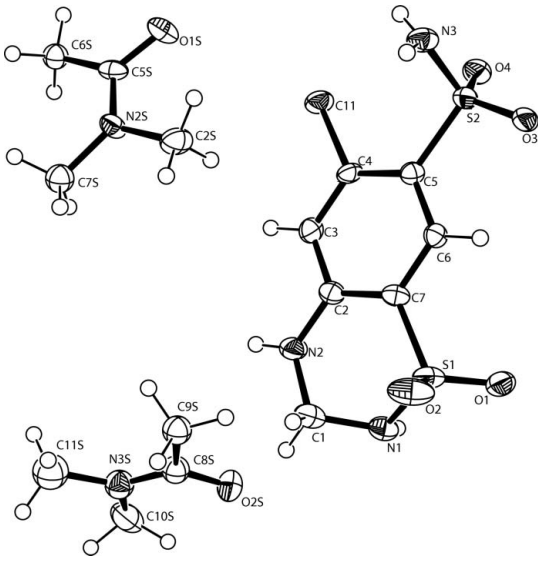


Figure 1
Drawing of the asymmetric unit, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. The minor occupancy disordered atom sites have been omitted for clarity.

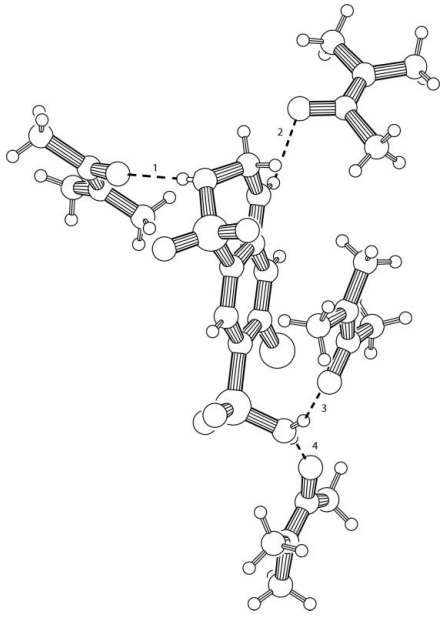


Figure 2
A partial packing diagram illustrating unique hydrogen bonds (dashed lines). Contacts are labelled as follow: 1 = N1···O2*S*($1-x, -\frac{1}{2}+y, \frac{1}{2}-z$) of 2.834 (4) Å; 2 = N2···O2*S* of 2.912 (4) Å; 3 = N3···O1*S*($x, -1+y, z$) of 2.873 (4) Å; 4 = N3···O1*S*($-x, -\frac{1}{2}+y, \frac{1}{2}-z$) of 2.881 (4) Å. Contacts illustrated using *PLATON* (Spek, 2003; Version 280604).

pack as layers in the *ab* plane and form an alternating stacked arrangement with layers of solvent molecules in the direction of the *c* axis (Fig. 3).

Experimental

A single-crystal sample of the title compound was recrystallized from a saturated dimethylacetamide solution by isothermal solvent evaporation at 298 K.

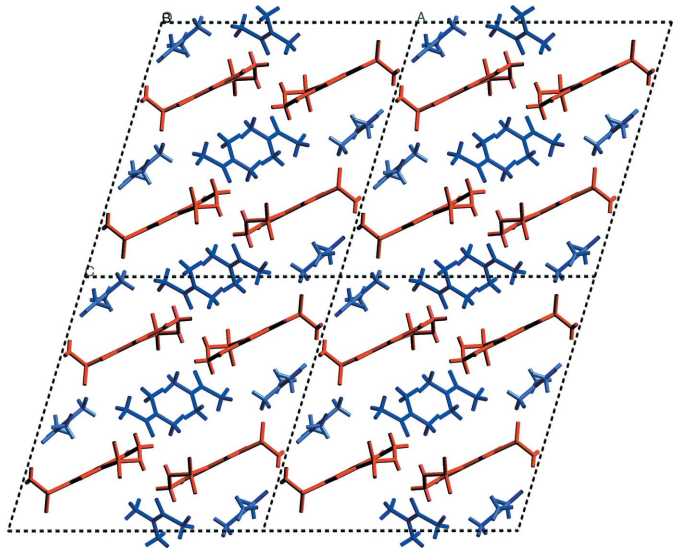


Figure 3
The crystal packing in the structure of (I), viewed down the *b* axis, showing the alternating layers of HCT and DMA molecules.

Crystal data

$C_7H_8ClN_3O_4S_2\cdot 2C_4H_9NO$
$M_r = 471.98$
Monoclinic, $P2_1/c$
$a = 17.0841\ (6)$ Å
$b = 7.3905\ (3)$ Å
$c = 17.7937\ (7)$ Å
$\beta = 106.875\ (2)^\circ$
$V = 2149.89\ (14)$ Å^3
$Z = 4$
$D_x = 1.458$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.41$ mm^{-1}
$T = 123\ (2)$ K
Prism, colourless
0.20 × 0.14 × 0.08 mm

Data collection

Nonius KappaCCD diffractometer
ω and φ scans
Absorption correction: none
7559 measured reflections
4744 independent reflections
2544 reflections with $I > 2\sigma(I)$
$R_{int} = 0.067$
$\theta_{max} = 27.1^\circ$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.058$
$wR(F^2) = 0.121$
$S = 1.01$
4744 reflections
288 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0486P)^2 + 0.4808P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.38$ e Å^{-3}
$\Delta\rho_{min} = -0.38$ e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1*N*···O2*S*^{i}	0.75 (3)	2.08 (3)	2.834 (4)	175 (3)
N2—H2*N*···O2*S*	0.84 (4)	2.26 (4)	2.912 (4)	135 (3)
N3—H3*N*···O1*S*^{ii}	0.84 (4)	2.05 (4)	2.881 (4)	170 (3)
N3—H4*N*···O1*S*^{iii}	0.81 (3)	2.11 (4)	2.873 (4)	156 (3)
C1—H1*A*···O2*S*	0.99	2.56	3.100 (4)	114
C3—H3···O1^{iv}	0.95	2.42	3.275 (4)	149

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

Both DMA molecules were modelled as disordered over two sites. Occupancy factors refined to 0.61 (1):0.39 (1) for the molecule including atom O1*S* and to 0.56 (1):0.44 (1) for that including O2*S*. The DMA atoms N1*S*, N3*S*, N4*S*, C1*S*, C3*S*, C4*S*, C7*S*, C8*S*, C9*S*, C11*S*, C12*S*, C13*S* and C14*S* were treated isotropically. The amine H atoms were found through difference syntheses and refined [isotropically for those on N2 and N3, and with $U_{iso}(H) = 1.2U_{eq}(N1)$ for H1*N*]. All other H atoms were constrained to idealized positions using a riding model; $U_{iso}(H) = 1.2U_{eq}$ for CH and CH_2, $U_{iso}(H) = 1.5U_{eq}$ for CH_3, and C—H = 0.95, 0.99 and 0.98 Å for CH, CH_2 and CH_3, respectively.

Data collection: *COLLECT* (Hooft, 1988) and *DENZO* (Otwinowski & Minor, 1997); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO*; 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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References

Dupont, L. & Dideberg, O. (1972). *Acta Cryst.* B**28**, 2340–2347.
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.* E**61**, o2798–o2800.
Hooft, R. (1988). *COLLECT*. Nonius BV, Delft, The Netherlands.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp 307–326. New York: Academic Press.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.