# organic papers

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**Key indicators**

Single-crystal X-ray study
$T = 123$ K
Mean $\sigma$(C–C) = 0.002 Å
$R$ factor = 0.034
$wR$ factor = 0.084
Data-to-parameter ratio = 23.1

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

# Hydrochlorothiazide–aniline (1/1)

Hydrochlorothiazide forms a 1:1 solvate with aniline, $C_7H_8ClN_3O_4S_2\cdot C_6H_7N$. The crystal structure contains a hydrogen-bonding network comprising two N—H$\cdots$N and three N—H$\cdots$O contacts.

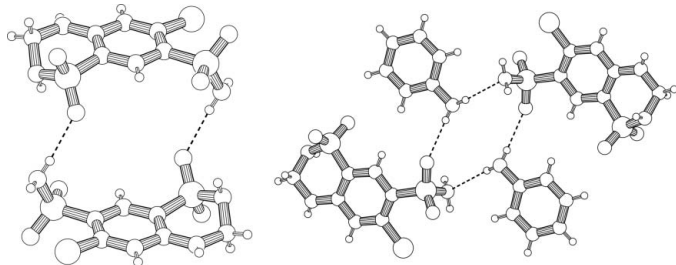## Comment

Hydrochlorothiazide (HCT) is a thiazide diuretic which is known to crystallize in at least one non-solvated form (Dupont & Dideberg, 1972). The aniline solvate, (I), was produced during an automated parallel crystallization polymorph screen on HCT. The sample was identified as a novel form using multisample X-ray powder diffraction analysis of all recrystallized samples (Florence et al., 2003). Subsequent manual recrystallization from a saturated 1:1 acetone–aniline solution by slow evaporation at 278 K yielded samples of (I) suitable for single-crystal X-ray analysis (Fig. 1).



(I)
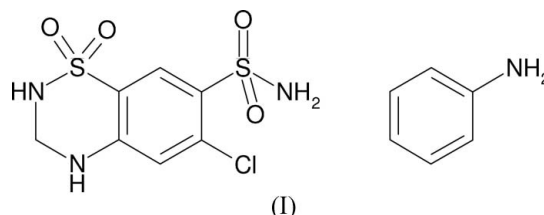
In (I), the N1—S1—C1—N2—C2—C7 six-membered ring in HCT adopts a non-planar conformation, with atoms S1 and N1 having deviations of 0.271 (1) and 0.843 (1) Å, respectively, from the least-squares plane through atoms C2–C7. The sulfonamide side chain adopts a torsion angle N3—S2—C5—C4 of 69.05 (12)°, such that atom O4 eclipses H6 and atoms O3
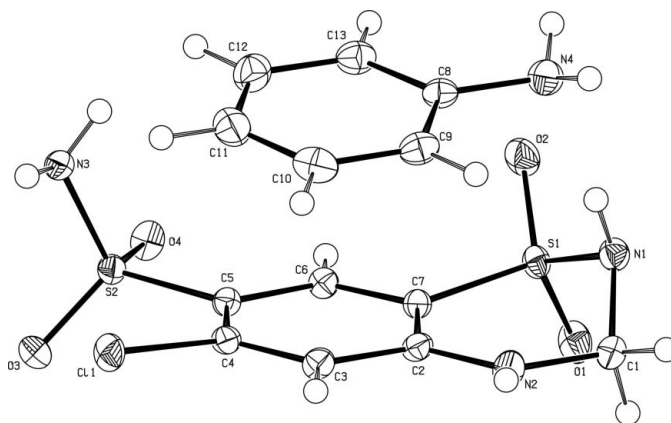


**Figure 1**
Plot of the asymmetric unit contents with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.
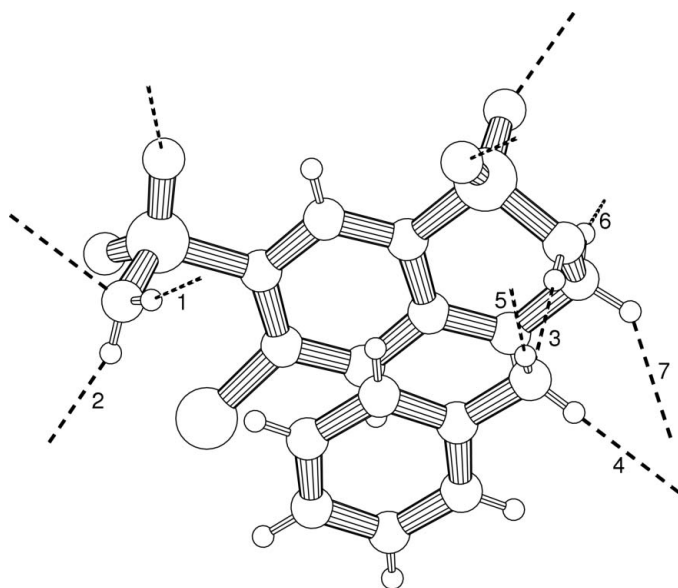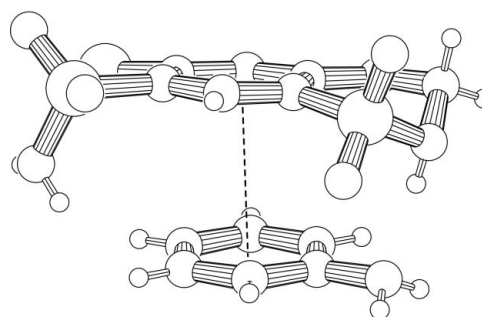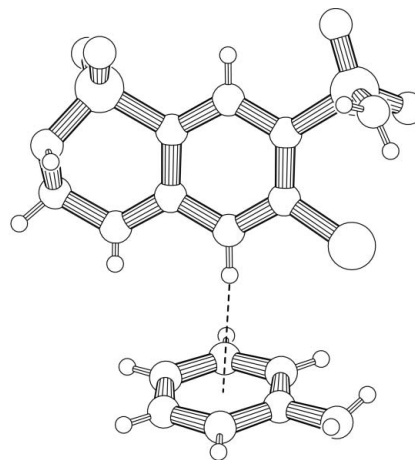
**Figure 2**
A packing diagram of (I). Dashed lines indicate hydrogen bonds and unique contacts are labelled as follows: 1 = N3···O2 [2.9725 (16) Å, O2 in the molecule at $(1 - x, 1 - y, 2 - z)$]; 2 = N3···O1 [2.9390 (15) Å, O1 in the molecule at $(\frac{1}{2} + x, \frac{1}{2} - y, -\frac{1}{2} + z)$]; 3 = N1···N4 [2.9652 (17) Å]; 4 = N4···N3 [3.3944 (18) Å, in the molecule at $(-1 + x, y, z)$]; 5 = N4···O4 [3.1000 (17) Å, O4 in the molecule at $(1 - x, 1 - y, 2 - z)$]; 6 = C1···O3 [3.2535 (18) Å, O3 in the molecule at $(1 - x, -y, 2 - z)$]; 7 = C1···O3 [3.2852 (17) Å, O3 in the molecule at $(-1 + x, y, z)$]. Contacts calculated and illustrated using *PLATON* (Spek, 2003; program version 280604)



**Figure 3**
The $R_2^2(16)$ (left) and $R_4^4(12)$ hydrogen-bond motifs in the crystal structure of (I).



**Figure 4**
Hydrophobic interactions in (I), showing a C3—H3···centroid contact to the centroid of the benzene ring of aniline [C3···centroid = 3.618 (2) Å] (top) and a $\pi$–$\pi$ off-stacking interaction between HCT and aniline with a centroid–centroid distance of 3.6955 (8) Å (bottom). Contacts are illustrated using dashed lines.

and N3 are staggered with respect to Cl1. In the non-solvated structure (Dupont & Dideberg, 1972), this group is rotated by approximately 130° compared to (I) such that the amine group lies on the opposite side of the benzothiadiazine moiety. The aniline molecule is planar, the greatest deviation of any non-H atom from the least-squares plane through C8–C13/N4 being 0.013 (1) Å for C8.

The crystal structure is stabilized by a network of hydrogen bonds interconnecting (a) HCT molecules (Fig. 2, contacts 1 and 2) and (b) HCT and solvent molecules (contacts 3, 4 and 5). Two C—H···O contacts also exist between HCT molecules (contacts 6 and 7). Contact 1 (N3—H3N···O2) forms a centrosymmetric $R_2^2(16)$ motif between molecules of HCT, whilst contacts 4 and 5 (N4—H5N···N3 and N4—H6N···O4) combine to form an $R_4^4(12)$ motif between aniline and HCT (Fig. 3). Hydrophobic interactions between HCT and aniline include a C—H···$\pi$ contact and an offset face-to-face (off) $\pi$–$\pi$ approach (Fig. 4).

## Experimental

A single-crystal sample of the title compound was recrystallized from a 1:1 acetone–aniline solution by slow evaporation at 278 K.

### Crystal data

| | |
|---|---|
| C₇H₈ClN₃O₄S₂·C₆H₇N | $D_x = 1.621$ Mg m⁻³ |
| $M_r = 390.86$ | Mo $K\alpha$ radiation |
| Monoclinic, $P2_1/n$ | Cell parameters from 5824 |
| $a = 9.7757$ (3) Å | reflections |
| $b = 10.5004$ (3) Å | $\theta = 1.0$–32.0° |
| $c = 15.6093$ (4) Å | $\mu = 0.53$ mm⁻¹ |
| $\beta = 91.692$ (2)° | $T = 123$ (2) K |
| $V = 1601.58$ (8) Å³ | Prism, colourless |
| $Z = 4$ | $0.38 \times 0.30 \times 0.18$ mm |

### Data collection

| | |
|---|---|
| Nonius KappaCCD diffractometer | $R_{int} = 0.027$ |
| $\omega$ and $\varphi$ scans | $\theta_{max} = 32.0°$ |
| Absorption correction: none | $h = -14 \rightarrow 14$ |
| 10766 measured reflections | $k = -15 \rightarrow 15$ |
| 5573 independent reflections | $l = -23 \rightarrow 23$ |
| 4379 reflections with $I > 2\sigma(I)$ | |

| | |
|---|---|
| Refinement on $F^2$ | $w = 1/[\sigma^2(F_o^2) + (0.036P)^2$ |
| $R[F^2 > 2\sigma(F^2)] = 0.034$ | $+ 0.781P]$ |
| $wR(F^2) = 0.084$ | where $P = (F_o^2 + 2F_c^2)/3$ |
| $S = 1.02$ | $(\Delta/\sigma)_{max} = 0.002$ |
| 5573 reflections | $\Delta\rho_{max} = 0.48$ e Å$^{-3}$ |
| 241 parameters | $\Delta\rho_{min} = -0.53$ e Å$^{-3}$ |
| H atoms treated by a mixture of | |
| independent and constrained | |
| refinement | |

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

| $D-\mathrm{H}\cdots A$ | $D-\mathrm{H}$ | $\mathrm{H}\cdots A$ | $D\cdots A$ | $D-\mathrm{H}\cdots A$ |
|---|---|---|---|---|
| N1—H1$N\cdots$N4 | 0.87 (2) | 2.10 (2) | 2.9652 (17) | 174 (2) |
| N3—H3$N\cdots$O2$^{i}$ | 0.85 (2) | 2.13 (2) | 2.9725 (16) | 169 (2) |
| N3—H4$N\cdots$O1$^{ii}$ | 0.90 (2) | 2.09 (2) | 2.9390 (15) | 157 (2) |
| N4—H5$N\cdots$N3$^{iii}$ | 0.89 (2) | 2.52 (2) | 3.3944 (18) | 169 (2) |
| N4—H6$N\cdots$O4$^{i}$ | 0.83 (2) | 2.28 (2) | 3.1000 (17) | 173 (2) |
| C1—H1$A\cdots$O3$^{iv}$ | 0.99 | 2.37 | 3.2535 (18) | 148 |
| C1—H1$B\cdots$O3$^{iii}$ | 0.99 | 2.47 | 3.2852 (17) | 139 |
| C6—H6$\cdots$O4 | 0.95 | 2.38 | 2.8101 (16) | 107 |

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

The N-bound H atoms were found in difference maps and refined freely [N—H = 0.77 (2)–0.90 (2) Å]. The remaining H atoms were positioned geometrically at distances of 0.95 (CH) and 0.99 Å (CH$_2$) from the parent C atoms; a riding model was used [$U_{iso}(\mathrm{H}) = 1.2U_{eq}(\mathrm{C})$] during the refinement process.

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*.

## References

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