

Paracetamol monohydrate at 150 K

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Key indicators

Single-crystal X-ray study

$T = 150\text{ K}$

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

R factor = 0.062

wR factor = 0.153

Data-to-parameter ratio = 13.1

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

The crystal structure of a new monohydrate of paracetamol (4-hydroxyacetanilide), $\text{C}_8\text{H}_9\text{NO}_2 \cdot \text{H}_2\text{O}$, is reported at 150 K. It consists of paracetamol and water molecules bound by hydrogen bonding into columns; further hydrogen bonds between paracetamol molecules connect the columns to form a three-dimensional array.

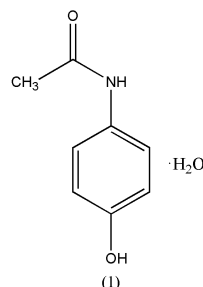
Received 22 October 2002

Accepted 31 October 2002

Online 8 November 2002

Comment

Paracetamol is an important drug molecule with two structurally characterized phases [monoclinic phase I (Nichols & Frampton, 1998) and orthorhombic phase II (Di Martino *et al.*, 1997)] and an elusive phase III. Solvates of paracetamol have also recently been studied in some detail, with the structural elucidation of a trihydrate (McGregor *et al.*, 2002) and the publication of a series of structures of cocrystals with organic hydrogen-bond acceptors (Oswald *et al.*, 2002). We report here the crystal structure of a monohydrate, (1), of paracetamol.



The habit of the crystals is needle-like and distinctly different from the hexagonal blocks of the monoclinic anhydrous phase I and the rectangular blocks of the orthorhombic anhydrous phase II, making optical identification

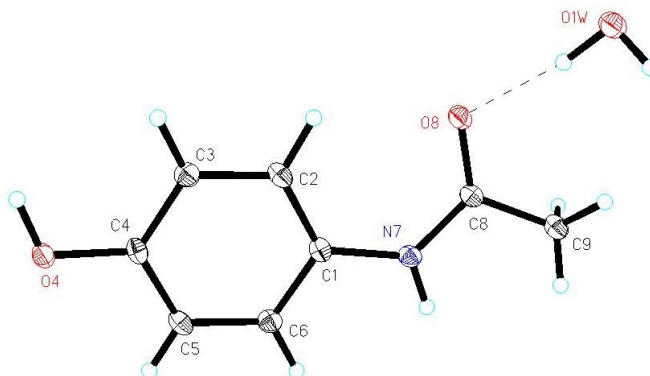


Figure 1

A view of paracetamol monohydrate, with the atom labelling. Displacement ellipsoids are drawn at the 30% probability level.

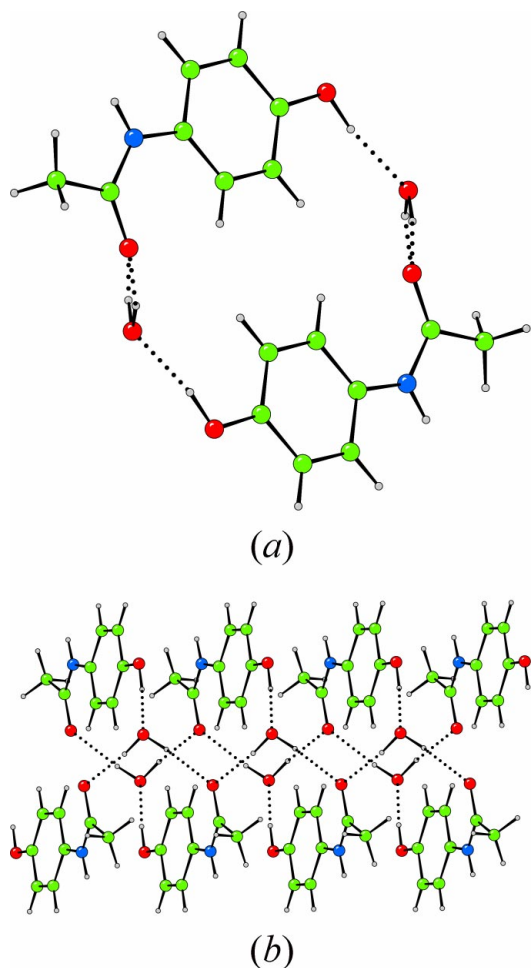


Figure 2

(a) View of the water-bound stack along the *a* axis. The *b* and *c* axes, respectively, lie vertically and horizontally in this figure. Colour scheme: C green, N blue, O red, and H grey. The stack forms an $R^4_4(22)$ ring. (b) The same stack as (a), with the *a* axis vertical.

simple. Under ambient conditions, the crystals are unstable with respect to loss of water, and dehydrate within five minutes on exposure to air, giving monoclinic paracetamol (identified by X-ray powder diffraction).

The crystal structure of the monohydrate shows that the paracetamol molecule is not completely planar, with a dihedral angle of $10.29(14)^\circ$ between the phenolic and amide fragments. This dihedral angle is highly variable (Oswald *et al.*, 2002); for example, values of 20.5 and 17.7° are observed in the monoclinic and orthorhombic forms of anhydrous paracetamol, respectively (Nichols & Frampton, 1998), and a value of 45.9° is observed in the trihydrate (McGregor *et al.*, 2002).

The paracetamol molecules are stacked along the *a* axis and linked by interleaving water molecules, which act as hydrogen-bond donors to the carbonyl-O atoms above and below. This forms a $C^1_2(4)$ chain at the binary level (Bernstein *et al.*, 1995). Related to this by the inversion centre at $(\frac{1}{2}, \frac{1}{2}, 0)$ is a second stack, and this is linked to the first by hydrogen bonds between the phenolic OH (donor) and the water O (acceptor) (Figs. 2*a* and 2*b*). This scheme satisfies all the hydrogen-bonding

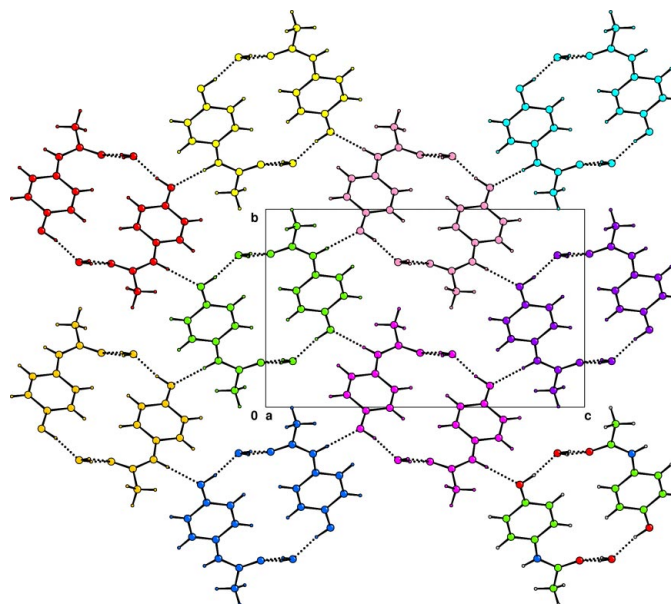


Figure 3

Packing in the crystal structure of paracetamol monohydrate. The stacks shown in Fig. 2 are shown here in different colours, although the colour scheme used in Fig. 2 are displayed here in the case of the stack in the bottom right. In addition to the small $R^4_4(22)$ rings of the water-bound stacks, larger $R^8_8(30)$ patterns are observed between four of these stacks.

potential of the water, with the exception of the second acceptor functionality of the oxygen. This motif is far from uncommon (Jeffrey, 1997).

The remaining donor and acceptor capacity of the paracetamol molecules comprises an amidic NH (donor) and a phenolic O atom (acceptor). Interactions between these moieties link the water-bound stacks together. This interaction, which is the longest hydrogen bond in the structure, is the only direct link between paracetamol molecules. Its effect is to create $C(7)$ chains. These linkages are depicted in Fig. 3, in which different water-bound stacks are colour-coded.

Experimental

Paracetamol (0.108 g, 0.714 mmol; Sigma–Aldrich) and disodium terephthalate (0.180 g, 0.857 mmol; Sigma–Aldrich) were dissolved in deionized water (3.25 ml) by warming to 333 K. The solution was cooled rapidly to 273 K, at which point colourless crystals were produced. Prior to data collection, it was necessary to mount the crystals quickly under perfluoropolyether oil in order to minimize dehydration.

Crystal data

$C_8H_9NO_2 \cdot H_2O$
 $M_r = 169.18$
 Monoclinic, $P2_1/n$
 $a = 4.5039(6) \text{ \AA}$
 $b = 10.5391(14) \text{ \AA}$
 $c = 17.048(2) \text{ \AA}$
 $\beta = 96.399(3)^\circ$
 $V = 804.18(19) \text{ \AA}^3$
 $Z = 4$

$D_x = 1.397 \text{ Mg m}^{-3}$
 Mo $K\alpha$ radiation
 Cell parameters from 1700 reflections
 $\theta = 2.2\text{--}26.4^\circ$
 $\mu = 0.11 \text{ mm}^{-1}$
 $T = 150(2) \text{ K}$
 Needle, colourless
 $0.45 \times 0.07 \times 0.06 \text{ mm}$

Data collection

Bruker SMART APEX CCD area-detector diffractometer	4516 measured reflections
φ and ω scans	1650 independent reflections
Absorption correction: multi-scan [SADABS (Sheldrick, 1997), based on a procedure formulated by Blessing (1995)]	1232 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.864$, $T_{\max} = 0.962$	$R_{\text{int}} = 0.052$
	$\theta_{\text{max}} = 26.4^\circ$
	$h = -5 \rightarrow 5$
	$k = -13 \rightarrow 13$
	$l = -18 \rightarrow 21$

Refinement

Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.062$	$w = 1/[\sigma^2(F_o^2) + (0.0834P)^2]$
$wR(F^2) = 0.153$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 0.97$	$(\Delta/\sigma)_{\text{max}} < 0.001$
1650 reflections	$\Delta\rho_{\text{max}} = 0.35 \text{ e } \text{\AA}^{-3}$
126 parameters	$\Delta\rho_{\text{min}} = -0.28 \text{ e } \text{\AA}^{-3}$

Table 1

Hydrogen-bonding geometry (\AA , $^\circ$).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
$N7-H7 \cdots O4^i$	0.88 (3)	2.04 (3)	2.918 (3)	174 (2)
$O4-H4 \cdots O1W^{ii}$	0.93 (3)	1.76 (3)	2.673 (2)	170 (2)
$O1W-H1W \cdots O8^{iii}$	0.93 (4)	1.85 (4)	2.780 (3)	171 (3)
$O1W-H2W \cdots O8^{iv}$	0.90 (4)	1.97 (4)	2.866 (3)	171 (3)

Symmetry codes: (i) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$; (ii) $\frac{3}{2} - x, y - \frac{1}{2}, \frac{1}{2} - z$; (iii) $\frac{1}{2} + x, \frac{3}{2} - y, \frac{1}{2} + z$; (iv) $x - \frac{1}{2}, \frac{3}{2} - y, \frac{1}{2} + z$.

H atoms bound to carbon were placed in calculated positions and refined as riding or rotating groups. The amide, hydroxyl and water H atoms were located in a difference map and freely refined, giving an

N—H bond length of 0.88 (3) \AA and O—H bond lengths between 0.90 (4) and 0.93 (4) \AA .

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL* and *CAMERON* (Watkin *et al.*, 1993); software used to prepare material for publication: *SHELXTL*.

We thank the EPSRC for funding and Professor A. Harrison for use of a powder diffractometer.

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