C5—C4—C9	119.1 (4)	C5′—C4′—C9′	119.2 (4)
C4—C5—C6	121.0 (5)	C4′—C5′—C6′	120.9 (5)
C5—C6—C7	120.1 (4)	C5′—C6′—C7′	119.7 (5)
C6—C7—C8	119.5 (5)	C6′—C7′—C8′	120.4 (5)
C7—C8—C9	121.3 (5)	C7′—C8′—C9′	121.0 (5)
C1—C9—C4	121.3 (3)	C1′—C9′—C4′	121.7 (4)
C1—C9—C8	119.7 (4)	C1′—C9′—C8′	119.5 (4)
C4—C9—C8	118.9 (4)	C4′—C9′—C8′	118.8 (4)
C1—C10—C11	121.8 (3)	C1′—C10′—C11′	121.3 (4)
C1—C10—C15	120.5 (3)	C1′—C10′—C15′	120.0 (4)
C11—C10—C15	117.7 (4)	C11′—C10′—C15′	118.7 (5)
C10—C11—C12	121.2 (4)	C10′—C11′—C12′	120.8 (4)
C11—C12—C13	119.4 (4)	C11′—C12′—C13′	119.5 (5)
C12—C13—C14	120.4 (4)	C12′—C13′—C14′	120.5 (5)
C13—C14—C15	120.0 (4)	C13′—C14′—C15′	119.8 (5)
C10—C15—C14	121.3 (4)	C10′—C15′—C14′	120.6 (5)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H2···Cl1	0.90	2.23	3.126 (3)	172
N1—H3···Cl1^{i}	1.01	2.09	3.084 (3)	167
N1′—H2′···Cl1′	0.90	2.22	3.116 (4)	176
N1′—H3′···Cl1′^{ii}	1.11	1.98	3.074 (4)	168

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

The intensity data for *hkl* and $\bar{h}\bar{k}\bar{l}$ were alternately measured every five reflections during the data collection. After structure determination, 40 reflections with large differences in F_c values between the Bijvoet reflections were chosen and their intensity data were measured more precisely. The structure was solved by direct methods and all non-H atoms were refined anisotropically by full-matrix least-squares techniques. Although all H atoms were located on a difference Fourier map, their positions were not refined. Their displacement parameters were assumed to be 1.2 times B_{eq} of the attached atom. For the *R*-factor ratio test, all atoms were refined again by full-matrix least-squares techniques with the reflections *hkl* and $\bar{h}\bar{k}\bar{l}$ (total of 4919 reflections). The angles of the least-squares planes were calculated using the program *LISTUP* (Takenaka, 1990) and the other structural parameters were calculated using the program *TEXSAN* (Molecular Structure Corporation, 1997).

Data collection: *Rigaku/AFC Diffractometer Control Software* (Rigaku Corporation, 1995). Cell refinement: *Rigaku/AFC Diffractometer Control Software*. Data reduction: *TEXSAN*. Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994). Program(s) used to refine structure: *TEXSAN*. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *TEXSAN*.

We thank Professor A. Takenaka for help of various sorts.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: OA1027). Services for accessing these data are described at the back of the journal.

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The Monoclinic Form of Acetaminophen at 150 K

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(*Received 21 August 1997; accepted 1 December 1997*)

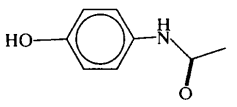
Abstract

The crystal structure of the anti-inflammatory agent acetaminophen [*N*-(4-hydroxyphenyl)acetamide, $C_8H_9NO_2$] has been refined using a Siemens SMART three-circle automatic diffractometer with a charge-coupled device (CCD) detector at 150 K. Monoclinic crystals of acetaminophen were grown from ethanol solution (m.p. 443–444 K). The crystal structure exhibits two kinds of hydrogen bonds [2.656 (2) Å, OH donates to O=C; 2.914 (2) Å, HO accepts from HN]. The molecules form a pleated sheet parallel to the (101) plane. The sheets are stacked along [010]. The molecules within a stack are held together by van der Waals interactions. Molecules from different sheets form 'head-to-tail'-type dimers.

Comment

Acetaminophen, (I), is the most prominent pain-relieving drug among acetanilide derivatives. Its physical and chemical properties have been intensively studied by Grant & Chow (1991). Precise data on its crystal structure are required for controlling processes such as dissolution and sublimation, which are important

for optimizing bioavailability and therapeutic activity of the drug, as well as its administration and storage (Vasilchenko *et al.*, 1997).



(I)

The first structural studies of acetaminophen crystals were reported about 20 years ago. The Powder Diffraction File (1982) contains three patterns for acetaminophen; however, the structures of only two polymorphs were described in the literature. The orthorhombic form was reported to be obtained by slow evaporation of an ethanol solution (Haisa *et al.*, 1974) and the monoclinic form was obtained from aqueous solution (Haisa *et al.*, 1976).

Diffraction data for the monoclinic polymorph (Haisa *et al.*, 1976) were collected using Weissenberg photographs from two single crystals at ambient temperature. The precision of the results was not very high; the value of $R(F)$ was 0.072 for 1382 non-zero reflections.

We tried to reproduce the crystal growth of both polymorphs following the procedure described in the literature in order to obtain more precise structural data, but could obtain only the monoclinic polymorph, whatever solvent was used. This may be the phenomenon termed as 'disappearance of polymorphs' (Dunitz & Bernstein, 1995).

In the present contribution, we report the results of a precise low-temperature single-crystal structural analysis of the monoclinic polymorph only. Using a SMART diffractometer allowed us to decrease the time of data collection to 7 h without loss of the quality of the refinement.

The values of the lattice parameters and the general pattern of the structure of acetaminophen at 150 K (present study) are in reasonable agreement with the room-temperature data reported previously (Haisa *et al.*, 1976). The matrix for the transformation from the data set of Haisa *et al.* (1976) to our data set is (00$\bar{1}$,010,101). No phase transitions were observed in the temperature range 290–150 K. The precision of the present data is higher than the precision of the data of Haisa *et al.* (1976).

The data on the molecular geometry of the acetaminophen obtained in our study are in good agreement with the results of Haisa *et al.* (1976), while being more precise than the latter. The benzene ring is practically flat (deviations of C atoms from the common plane do not exceed 0.007 Å). The dihedral angle between the benzene ring and the acetamido group is 20.5°. The hydroxy H1′ atom does not lie in the plane of the benzene ring (dihedral angle 17.2°). The hydroxy group and the acetamido group lie in the same plane (Fig. 1).

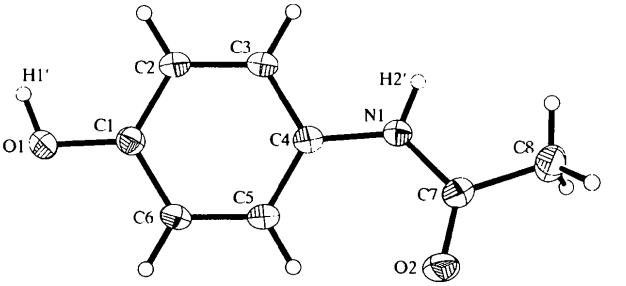


Fig. 1. The molecular structure of acetaminophen. Displacement ellipsoids are plotted at the 50% probability level.

Each molecule in the structure is surrounded by six molecules that are linked together by two types of hydrogen bond [2.656 (2) Å, OH donates to O=C; 2.914 (2) Å, HO accepts from H—N]. The molecules form a pleated sheet parallel to the (101) plane. The sheets are stacked along [010]. The molecules in a stack are held together by van der Waals interactions. The distances between benzene rings (along [010]) are 3.286 (8) and 3.253 (8) Å. The molecules in different sheets form 'head-to-tail'-type dimers. The N1 atom of the first molecule is located above the centre of the benzene ring of the second molecule (at a distance of 3.33 Å). The distance between C4 atoms of different molecules is 3.35 Å. Hydrogen-bonded chains $\cdots$H—N—C=O$\cdots$H—O$\cdots$H—N—C=O$\cdots$ along [100] are present in the structure. Several types of molecular

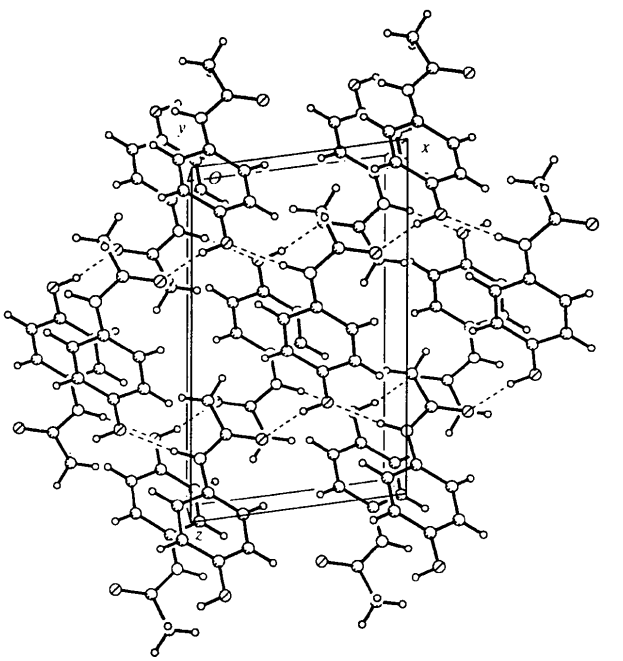


Fig. 2. Packing diagram of the crystal structure of acetaminophen viewed along [010].

chains can be distinguished in the structure: along the [100] direction, along the [101] direction and along the [$\bar{1}$01] direction. According to our data, the directions of the hydrogen-bonded chains of molecules in the structure can be well correlated with the anisotropy of the shape pits by sublimation of the title compound, as well as with its dissolution in different solvents (Vasilchenko *et al.*, 1996).

Experimental

Crystals were grown by decreasing the temperature (from 303 K at a rate 3 K per day) of an ethanol solution.

Crystal data

$C_8H_9NO_2$
M_r = 151.16
Monoclinic
$P2_1/n$
a = 7.0939 (6) Å
b = 9.2625 (8) Å
c = 11.657 (1) Å
β = 97.672 (1)°
V = 759.09 (11) Å^3
Z = 4
D_x = 1.323 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 289 reflections
θ = 10–20°
μ = 0.096 mm^{-1}
T = 150 (2) K
Prism
0.38 × 0.22 × 0.20 mm
Colourless

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: by integration (*XPREP*; Siemens, 1995)
T_{min} = 0.969, T_{max} = 0.983
4122 measured reflections
1890 independent reflections
1672 reflections with $I > 2\sigma(I)$
R_{int} = 0.036
θ_{max} = 29.85°
$h = -9 \rightarrow 9$
$k = -12 \rightarrow 10$
$l = -9 \rightarrow 16$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.112
S = 1.185
1890 reflections
115 parameters
For H1′ and H2′, all parameters refined
$w = 1/[\sigma^2(F_o^2) + 0.6011P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.265 e Å^{-3}
$\Delta\rho_{min}$ = −0.190 e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.082 (6)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

O1—C1	1.375 (2)	C4—N1	1.420 (2)
C1—C2	1.396 (2)	N1—C7	1.346 (2)
C2—C3	1.385 (2)	C7—O2	1.236 (2)
C3—C4	1.396 (2)	C7—C8	1.509 (2)
C4—C5	1.396 (2)	O1—H1′	0.92 (3)
C5—C6	1.388 (2)	N1—H2′	0.92 (2)
C6—C1	1.389 (2)		
H1′—O1—C1	111.0 (17)	C6—C1—O1	118.47 (14)
O1—C1—C2	122.13 (14)	C6—C1—C2	119.40 (15)
C1—C2—C3	119.9 (2)	C4—N1—C7	128.41 (14)
C2—C3—C4	120.89 (15)	C4—N1—H2′	116.0 (13)
C3—C4—C5	118.98 (15)	H2′—N1—C7	115.4 (13)
C3—C4—N1	116.82 (14)	N1—C7—O2	123.2 (2)
C5—C4—N1	124.18 (14)	N1—C7—C8	115.11 (14)
C4—C5—C6	120.09 (15)	O2—C7—C8	121.72 (15)
C5—C6—C1	120.72 (15)		

Data were collected using ω scans with a scan rate of 0.9° min^{-1}. The scan width was 0.3°.

Data collection: *SMART* (Siemens, 1994*a*). Cell refinement: *SMART*. Data reduction: *SAINT* (Siemens, 1994*b*). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *SHELXTL* (Siemens, 1994*c*). Software used to prepare material for publication: *SHELXL*93.

The crystals were grown at the Institute of Solid State Chemistry SD RAS, Novosibirsk, Russia. The structural study was carried out at the University of Durham (Chemistry Department, Crystallography Group) during a research stay of DYN in the group of JAKH. DYN is grateful to the University of Durham for hospitality and financial support of the study. The authors are grateful to V. V. Boldyrev for stimulating the study and to E. V. Boldyreva and T. P. Shakhtshneider for helpful comments.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV1018). Services for accessing these data are described at the back of the journal.

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