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γ-Indomethacin at 120 K

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.003 Å
R factor = 0.044
wR factor = 0.105
Data-to-parameter ratio = 16.4

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

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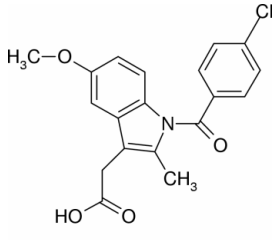
The crystal structure of γ-indomethacin, $C_{19}H_{16}ClNO_4$, is supported, not only by O—H···O interactions, but also by C—H···π and π–π interactions.

Comment

Room-temperature crystal structures of γ-indomethacin, (I), have been reported previously (Kistenmacher & Marsh, 1972; Galdecki & Glówka, 1976) and the crystal structure of the metastable α form at 203 K is also known (Chen *et al.*, 2002). The compound presents an unusual case in which the more stable γ form is reported to have the lower density. Also, the known dimer formation between the carboxylic acid groups would be difficult to predict in the presence of other donors and acceptors. Only in the metastable α form does the carbonyl atom O1 act as an acceptor, whereby trimers are formed in the space group $P2_1$ with $Z = 6$.



(I)

Apart from the previously reported O—H···O interactions, we have now examined other non-covalent interactions between γ-indomethacin molecules. Both crystal structures of γ-indomethacin reported previously used different cell settings, so to avoid confusion, we have used reduced cell dimensions throughout our study.

The molecular structure of (I) is shown in Fig. 1. The dihedral angle between the mean planes of the indole ring system and the chlorophenyl ring is 66.51 (5)°. The geometry of the $R_2^2(8)$ hydrogen bonding between centrosymmetrically related carboxylic acid groups is given in Table 2 and the interaction is shown in Fig. 2.

As well as the classical hydrogen bonding involved in dimer formation, the supramolecular structure is also supported by edge-to-face C—H···π interactions, as listed in Table 3 and shown in Fig. 3. Here the methylene H atoms on C18 and methyl atom H20*A* interact with the π systems of the indole rings.

Completing the molecular attractions is a π–π interaction between centrosymmetrically related chlorophenyl rings, as shown in Fig. 4 and detailed in Table 4.

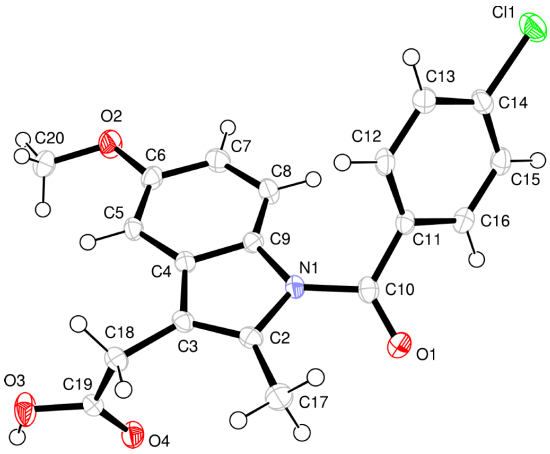


Figure 1
The molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level.

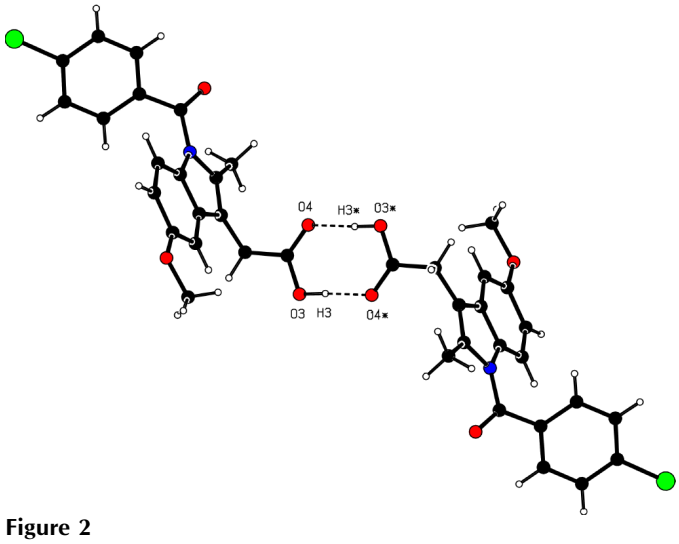


Figure 2
Dimer formation between carboxylic acid groups. Atoms marked with an asterisk (*) are at the symmetry position $(-1-x, 1-y, -z)$.

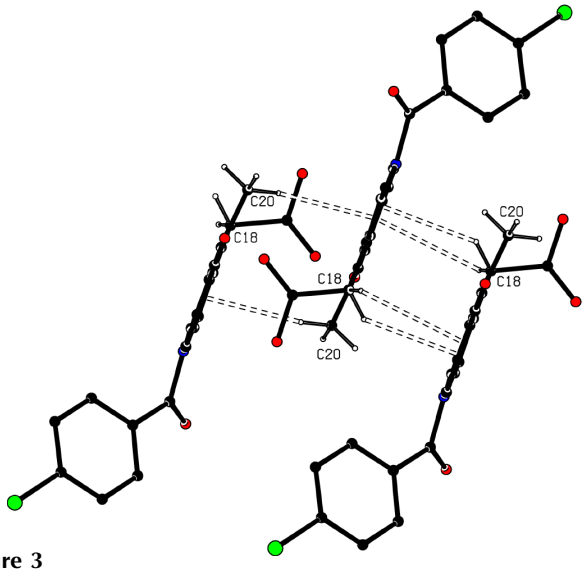


Figure 3
The C—H$\cdots\pi$ hydrogen bonding, shown as double-dashed lines, between molecules related by a centre of symmetry.

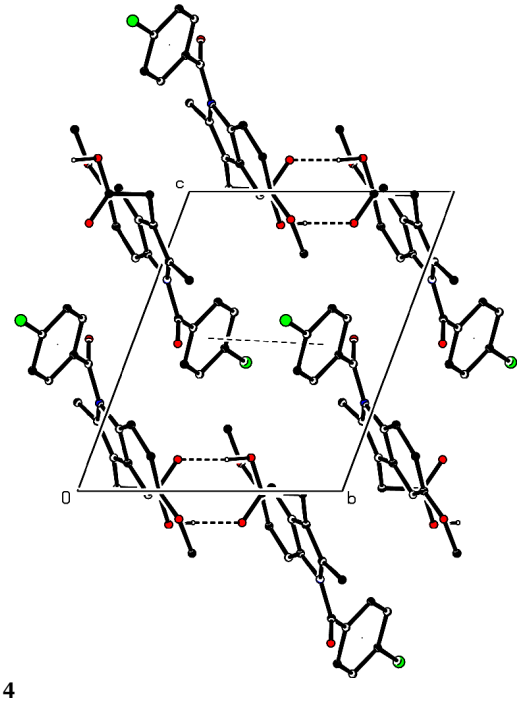


Figure 4
A crystal packing diagram showing the π–π interaction, as a dashed line, between chlorophenyl rings stacked across a centre of symmetry. The ring centre is indicated by a dot. Dimer formation is also shown.

Morphological evaluation of γ-indomethacin has also been performed (Slavin *et al.*, 2002).

Experimental

Indomethacin was purchased from Sigma and was recrystallized from 4-methylpentan-2-one, to produce the γ-polymorph.

Crystal data

$C_{19}H_{16}ClNO_4$
M_r = 357.78
Triclinic, $P\overline{1}$
a = 9.236 (5) Å
b = 9.620 (5) Å
c = 10.887 (5) Å
α = 69.897 (5)°
β = 87.328 (5)°
γ = 69.501 (5)°
V = 847.9 (7) Å^3
Z = 2
D_x = 1.401 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4841 reflections
θ = 2.9–27.5°
μ = 0.25 mm^{-1}
T = 120 (2) K
Plate, colourless
0.23 × 0.20 × 0.02 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995, 1997)
T_{min} = 0.956, T_{max} = 0.992
10585 measured reflections
3800 independent reflections
2586 reflections with $I > 2\sigma(I)$
R_{int} = 0.056
θ_{max} = 27.5°
$h = -11 \rightarrow 11$
$k = -11 \rightarrow 12$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.105
S = 1.01
3800 reflections
232 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0439P)^2 + 0.0875P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.27 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.012 (2)

Table 1
Selected geometric parameters (Å, °).

Cl1—C14	1.740 (2)	O4—C19	1.218 (2)
O1—C10	1.216 (2)	C18—C19	1.505 (3)
O3—C19	1.313 (2)		
C9—C4—C3	107.74 (16)	C8—C9—N1	131.83 (17)
C5—C4—C3	131.18 (17)	C4—C9—N1	107.23 (16)
C10—N1—C2—C17	−9.2 (3)	C2—N1—C10—O1	−25.9 (3)
C17—C2—C3—C18	3.2 (3)	O1—C10—C11—C12	135.90 (19)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3···O4^{i}	0.91 (3)	1.75 (3)	2.651 (3)	173 (3)

Symmetry code: (i) $-1-x, 1-y, -z$.

Table 3
C—H...π interactions (Å,°).

C—H	*CgI*	symmetry code	H···*CgI*	C—H···*CgI*	C···*CgI*
C18—H18*A*	2	$-x, -y, -z$	3.12	118	3.687 (3)
C18—H18*B*	1	$-x, -y, -z$	2.72	166	3.692 (3)
C20—H20*A*	2	$-x, 1-y, -z$	2.68	142	3.511 (3)

Cg is the centre of gravity of rings in the indole system: *Cg*1 five-membered ring and *Cg*2 six-membered ring. The symmetry applies to the *CgI* position.

Table 4
π–π interactions (Å,°).

CgI	*CgJ*	symmetry code	*Cg*···*CgI*	dihedral angle	interplanar	offset
3	3	$1-x, -1-y, 1-z$	3.922 (2)	0.0	3.411 (2)	1.942

*Cg*3 is the centre of gravity of the chlorophenyl ring. The symmetry applies to the *CgJ* position.

The coordinates of the hydroxy H atom were freely refined; the other H atoms were placed in calculated positions and allowed to ride on their parent atoms. For all H atoms, U_{iso} values were set at 1.2 (non-methyl) or 1.3 (methyl) times U_{eq} of the parent atom.

Data collection: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT* (Hooft, 1998); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: WinGX (Farrugia, 1999).

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