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Indomethacin methyl ester

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Key indicators

Single-crystal X-ray study
T = 180 K
Mean $\sigma(\text{C}-\text{C}) = 0.003 \text{ \AA}$
R factor = 0.047
wR factor = 0.117
Data-to-parameter ratio = 13.0

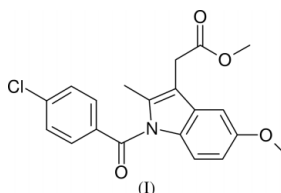
For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

Indomethacin methyl ester

The crystal structure of the title compound [systematic name: methyl 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indole-3-acetate], $\text{C}_{20}\text{H}_{18}\text{ClNO}_4$, exhibits a short axis similar to another indomethacin analogue. Also observed in the structure is a packing of molecules influenced by weak $\text{C}-\text{H}\cdots\text{O}$ hydrogen bonds.

Comment

As part of an investigation into the crystallization of pharmaceutical compounds, the crystal structures of indomethacin derivatives are of interest. Numerous studies have been reported on various crystal structures of the drug indomethacin (γ -form: Kistenmacher & Marsh, 1972; α -form: Chen *et al.*, 2002; *t*-butanol and methanol solvates: Joshi *et al.*, 1998). In contrast, the structure of its methyl ester, (I), has not been reported to date. We report here its crystal structure and describe the intermolecular interactions involved.



The asymmetric unit of (I) comprises one molecule (Fig. 1). Although the crystal structure of the indomethacin methyl ester differs significantly from that of the parent carboxylic acid, it bears some similarity to the structure of another indomethacin derivative, iodoindomethacin (Loll *et al.*, 1996). Both crystal structures exhibit a relatively short axis [4.8326 (1) Å for the methyl ester derivative *versus* 4.7250 (10) Å for the iodo derivative]. In addition, both crystal structures show a halogen contact to a carbonyl O atom [$\text{Cl1}\cdots\text{O4} = 3.575 (2) \text{ \AA}$ *versus* $\text{I1}\cdots\text{O4} = 3.162 (5) \text{ \AA}$].

In the absence of the carboxylic acid group of indomethacin, no strong $\text{O}-\text{H}\cdots\text{O}$ hydrogen bonding can be expected in the crystal structure of the methyl ester. Instead, $\text{C}-\text{H}\cdots\text{O}$ hydrogen bonds form a three-dimensional supramolecular network, as shown in Fig. 2. Hydrogen-bond distances and angles are provided in Table 1.

Experimental

Indomethacin and anhydrous benzenesulfonic acid were obtained from Sigma-Aldrich and were used as received. Indomethacin (130 mg, 0.364 mmol) and benzenesulfonic acid (115 mg, 0.727 mmol) were dissolved in methanol with heating. Crystals precipitated as the

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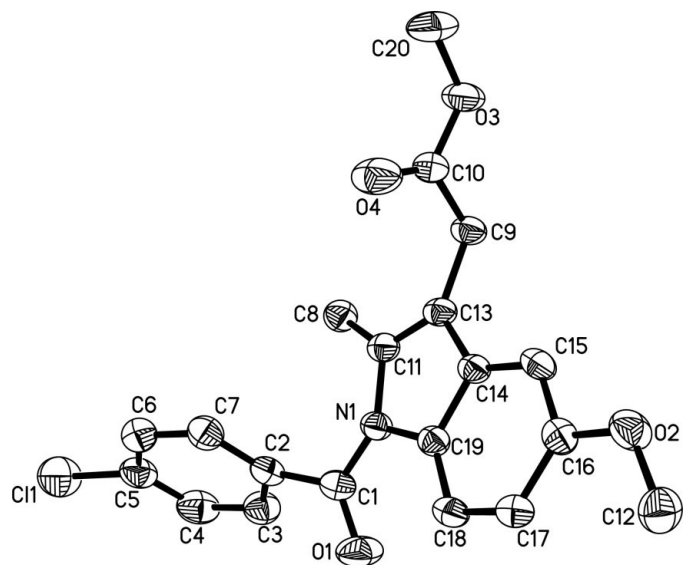


Figure 1
Molecular unit showing displacement ellipsoids at the 50% probability level.

solution cooled to room temperature and were immediately isolated and dried.

Crystal data

$C_{20}H_{18}ClNO_4$	$D_x = 1.404 \text{ Mg m}^{-3}$
$M_r = 371.82$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 6724 reflections
$a = 19.0206 (5) \text{ \AA}$	$\theta = 1.0\text{--}25.0^\circ$
$b = 4.8326 (1) \text{ \AA}$	$\mu = 0.24 \text{ mm}^{-1}$
$c = 19.3092 (8) \text{ \AA}$	$T = 180 (2) \text{ K}$
$\beta = 97.739 (1)^\circ$	Needle, yellow
$V = 1758.72 (9) \text{ \AA}^3$	$0.46 \times 0.07 \times 0.05 \text{ mm}$
$Z = 4$	

Data collection

Nonius KappaCCD diffractometer	2410 reflections with $I > 2\sigma(I)$
ω and φ scans	$R_{\text{int}} = 0.035$
Absorption correction: multi-scan (<i>SORTAV</i> ; Blessing, 1995)	$\theta_{\text{max}} = 25.0^\circ$
$T_{\text{min}} = 0.946$, $T_{\text{max}} = 0.985$	$h = -22 \rightarrow 22$
10 009 measured reflections	$k = -5 \rightarrow 5$
3086 independent reflections	$l = -22 \rightarrow 23$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0481P)^2 + 1.0445P]$
$R[F^2 > 2\sigma(F^2)] = 0.047$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.117$	$(\Delta/\sigma)_{\text{max}} = 0.002$
$S = 1.04$	$\Delta\rho_{\text{max}} = 0.31 \text{ e \AA}^{-3}$
3086 reflections	$\Delta\rho_{\text{min}} = -0.39 \text{ e \AA}^{-3}$
238 parameters	
H-atom parameters constrained	

Table 1

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

$D\text{--}H\cdots A$	$D\text{--}H$	$H\cdots A$	$D\cdots A$	$D\text{--}H\cdots A$
$C18\text{--}H18\cdots O1^i$	0.95	2.34	3.260 (3)	162
$C3\text{--}H3\cdots O1^{ii}$	0.95	2.59	3.480 (3)	156
$C9\text{--}H9A\cdots O4^{iii}$	0.99	2.62	3.565 (3)	160
$C15\text{--}H15\cdots O2^{iv}$	0.95	2.48	3.419 (2)	170

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

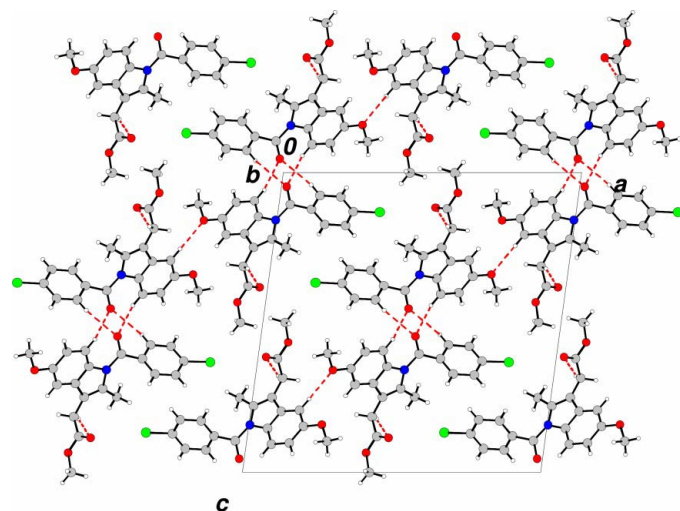


Figure 2
Projection on to (010), showing the packing involving $C\text{--}H\cdots O$ interactions. The intermolecular $C9\text{--}H9A\cdots O4(x, y - 1, z)$ hydrogen bond projects parallel to the b axis.

All H atoms were placed geometrically and treated using a riding model. The U_{iso} values for methyl H atoms were fixed at $1.5U_{\text{eq}}$ of the carrier atom. For all other H atoms, $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}$ (carrier atom). The $C\text{--}H$ distances of methyl groups were fixed at 0.98 \AA ; all other $C\text{--}H$ distances were fixed at 0.95 \AA .

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *HKL SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *HKL DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* (Sheldrick, 1993) and *DIAMOND* (Brandenburg, 1999); software used to prepare material for publication: *SHELXL97*.

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