Acta Crystallographica Section E
**Structure Reports Online**
ISSN 1600-5368

# Indomethacin *tert*-butanol solvate at 120 K

**Philip J. Cox* and Pamela L. Manson**

School of Pharmacy, The Robert Gordon University, Schoolhill, Aberdeen AB10 1FR, Scotland

Correspondence e-mail: p.j.cox@rgu.ac.uk

**Key indicators**

Single-crystal X-ray study
$T$ = 120 K
Mean $\sigma$(C–C) = 0.002 Å
$R$ factor = 0.036
$wR$ factor = 0.091
Data-to-parameter ratio = 17.6

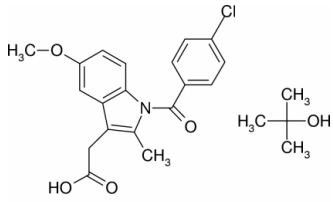
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Crystals of the title compound, $C_{19}H_{16}ClNO_4\cdot C_4H_{10}O$, contain O—H···O, C—H···O and C—H···$\pi$ interactions.

Received 1 July 2003
Accepted 7 July 2003
Online 31 July 2003

## Comment

The crystal structure of indomethacin *tert*-butanol solvate, (I), has been previously determined at 293 K but reported only briefly (Joshi *et al.*, 1998; Stowell *et al.*, 2002). We now present details of the structure determined at 120 K.




(I)

The molecular structure is shown in Fig. 1. The dihedral angle between the mean planes passing through the C atoms of the indole ring system and the chlorophenyl ring is 69.33 (3)°, similar to the value of 66.51 (5)° reported for unsolvated indomethacin at 120 K (Cox & Manson, 2003). The molecular geometry is also similar to that reported for the room-temperature structure of indomethacin (Kistenmacher & Marsh, 1972).

Classical O—H···O hydrogen bonding enables two *tert*-butanol molecules to link to two indomethacin molecules. Hydroxy atom O5 of the solvent acts as both a donor and acceptor in the formation of an $R_4^4(12)$ ring across a centre of symmetry. This is shown in Fig. 2 and details of the geometry of this hydrogen bonding, together with a weaker C—H···O interaction, are given in Table 2. This weaker interaction extends the hydrogen bonding to link four indomethacin molecules and four solvent molecules in an $R_6^6(30)$ ring formation (Fig. 3). There is no disorder in the methyl groups of the solvent, and five weak C—H···$\pi$ interactions involving the alcohol and indomethacin are present, as listed in Table 3 and shown in Fig. 4. Two further C—H···$\pi$ interactions are present. There is also a short intermolecular Cl1···Cl1$^{iv}$ [symmetry code: (iv) $1-x, -y, -z$] contact of 3.3745 (4) Å that compares with the sum of the van der Waals radii (3.50 Å; Bondi, 1964), but there are no significant $\pi$–$\pi$ interactions.

## Experimental

Indomethacin was purchased from Sigma and was recrystallized from *tert*-butanol to produce the title solvate.

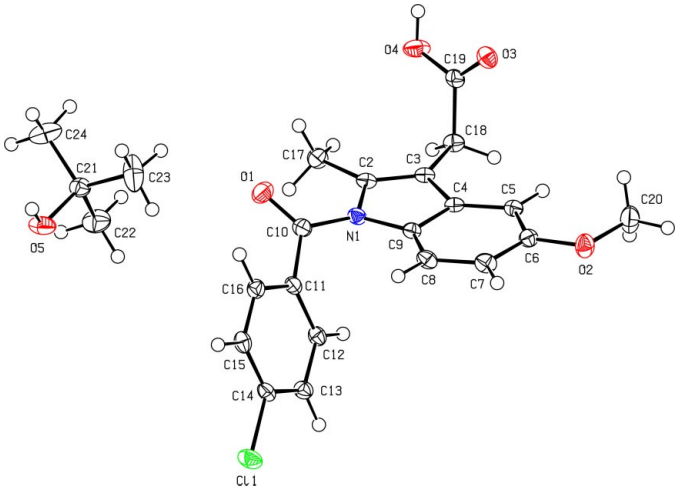



**Figure 1**
The structure of the asymmetric unit of (I). Displacement ellipsoids are drawn at the 50% probability level.

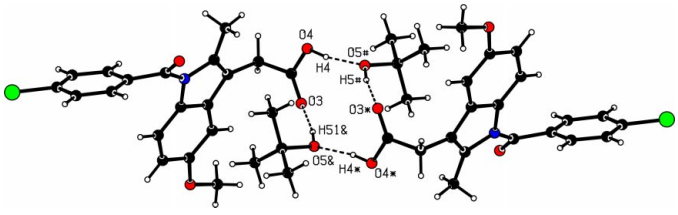



**Figure 2**
Classical hydrogen bonding between carboxylic acid groups of two indomethacin molecules and hydroxy groups of two solvent molecules. Atoms marked with an ampersand (&), hash (#) and asterisk (*) are at symmetry positions $(1-x, 1-y, 1-z)$, $(x, 1+y, z)$ and $(1-x, 2-y, 1-z)$, respectively.

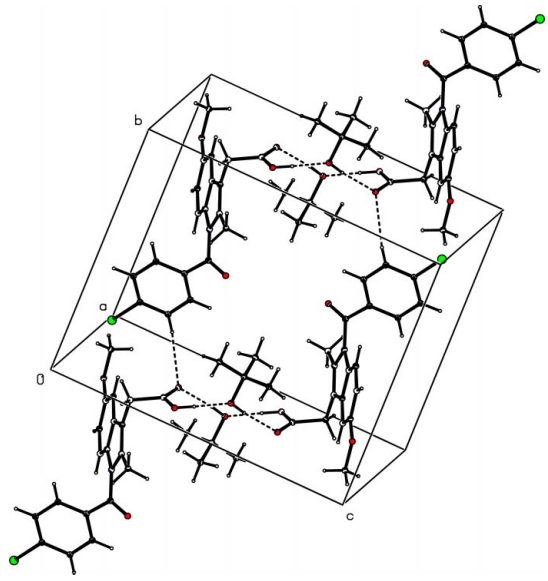



**Figure 3**
A partial packing diagram, showing extended hydrogen bonding linking four indomethacin molecules and four solvent molecules.

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

| | | | |
|---|---|---|---|
| Cl1—C14 | 1.7422 (12) | O4—C19 | 1.3183 (15) |
| O3—C19 | 1.2170 (15) | O5—C21 | 1.4514 (16) |
| C5—C4—C3 | 131.57 (11) | C8—C9—N1 | 131.44 (11) |
| C9—C4—C3 | 107.46 (10) | C4—C9—N1 | 107.31 (10) |
| C10—N1—C2—C17 | −8.62 (18) | C2—N1—C10—O1 | −29.24 (18) |
| C17—C2—C3—C18 | 1.0 (2) | O1—C10—C11—C12 | 138.60 (13) |

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

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O4—H4···O5$^{i}$ | 0.89 (2) | 1.71 (2) | 2.586 (1) | 170 (2) |
| O5—H51···O3$^{ii}$ | 0.88 (2) | 1.94 (2) | 2.814 (1) | 170 (2) |
| C15—H15···O3$^{iii}$ | 0.95 | 2.54 | 3.368 (1) | 145 |

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

**Table 3**
C—H···$\pi$ interactions (Å,°).

| C—H | *CgI* | Symmetry code | H···*CgI* | C—H···*CgI* | C···*CgI* |
|---|---|---|---|---|---|
| C13—H13 | 2 | $1-x, 1-y, -z$ | 2.63 | 164 | 3.556 (1) |
| C17—H17*C* | 3 | $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$ | 2.82 | 134 | 3.576 (1) |
| C22—H22*A* | 1 | $\frac{1}{2}-x, -\frac{1}{2}+y, \frac{1}{2}-z$ | 3.20 | 119 | 3.776 (2) |
| C23—H23*B* | 1 | $1-x, 1-y, 1-z$ | 3.21 | 135 | 3.960 (2) |
| C24—H24*A* | 1 | $1-x, 1-y, 1-z$ | 3.13 | 130 | 3.828 (2) |
| C24—H24*B* | 2 | $1-x, 1-y, 1-z$ | 3.03 | 124 | 3.663 (2) |
| C24—H24*C* | 3 | $-\frac{1}{2}+x, \frac{1}{2}-, \frac{1}{2}+z$ | 2.93 | 149 | 3.805 (2) |

† *CgI* represent the centre of gravity of a ring, with $I=1$ for the five-membered ring, $I=2$ for the six-membered ring (indole system) and $I=3$ for the chlorophenyl ring. The symmetry applies to the *CgI* position.

*Crystal data*

$C_{19}H_{16}ClNO_4\cdot C_4H_{10}O$
$M_r = 431.9$
Monoclinic, $P2_1/n$
$a = 11.9806$ (1) Å
$b = 12.2749$ (1) Å
$c = 14.7679$ (2) Å
$\beta = 91.561$ (4)°
$V = 2170.97$ (4) Å$^3$
$Z = 4$
$D_x = 1.321$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 27 193 reflections
$\theta = 2.9$–27.5°
$\mu = 0.21$ mm$^{-1}$
$T = 120$ (2) K
Prism, colourless
0.56 × 0.40 × 0.24 mm

*Data collection*

Nonius KappaCCD area-detector
$\varphi$ and $\omega$ scans
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995, 1997)
$T_{min} = 0.877$, $T_{max} = 0.957$
26 128 measured reflections
4955 independent reflections
4405 reflections with $I > 2\sigma(I)$
$R_{int} = 0.047$
$\theta_{max} = 27.5°$
$h = -15 \rightarrow 14$
$k = -15 \rightarrow 15$
$l = -19 \rightarrow 17$

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.036$
$wR(F^2) = 0.092$
$S = 1.02$
4955 reflections
282 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0405P)^2 + 0.9973P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.27$ e Å$^{-3}$
$\Delta\rho_{min} = -0.31$ e Å$^{-3}$

The coordinates of the hydroxy H atoms were freely refined; the other H atoms were placed in calculated positions and allowed to ride

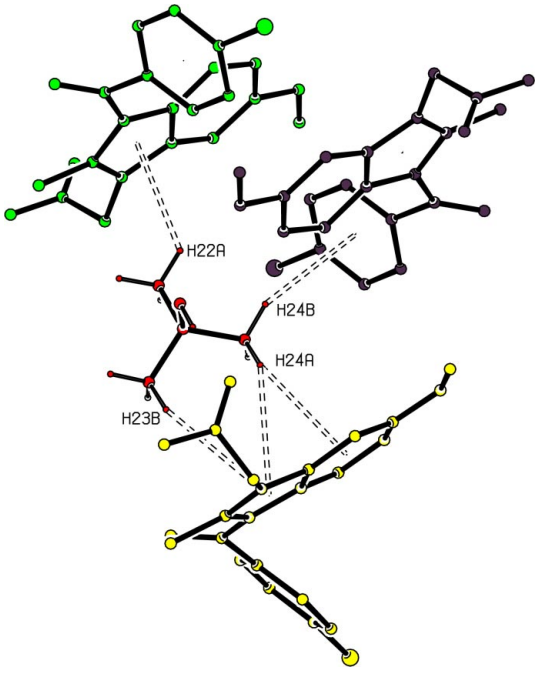



**Figure 4**
Five C—H···$\pi$ interactions (shown as double-dashed lines) involving methyl H atoms of the solvent. Ring centres are marked with a dot.

on their parent atoms. For all H atoms, $U_{iso}$ is 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: *PLATON* (Spek, 2002); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

We thank the EPSRC for use of the National Crystallographic Service at Southampton University (X-ray data collection), and for the use of the Chemical Database Service at Daresbury (Fletcher *et al.*, 1996).

## References

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.
Blessing, R. H. (1995). *Acta Cryst.* A**51**, 33–38.
Blessing, R. H. (1997). *J. Appl. Cryst.* **30**, 421–426.
Bondi, A. (1964). *J. Phys. Chem.* **68**, 441–451.
Cox, P. J. & Manson, P. L. (2003). *Acta Cryst.* E**59**, o986–o988.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Fletcher, D. A., McMeeking, R. F. & Parkin, D. (1996). *J. Chem. Inf. Comput. Sci.* **36**, 746–749.
Hooft, R. (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.
Joshi, V., Stowell, J. G. & Byrn, S. R. (1998). *Mol. Cryst. Liq. Cryst.* **313**, 265–270.
Kistenmacher, T. J. & Marsh, R. E. (1972). *J. Am. Chem. Soc.* 94 1340–1345.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Sheldrick, G. M. (1997). *SHELX*97–2. University of Göttingen, Germany.
Spek, A. L. (2002). *PLATON*. Version 80702. University of Utrecht, The Netherlands.
Stowell, J. G., Byrn, S. R. & Huang, K.-S. (2002). Private communication to the Cambridge Structural Database. Refcode BANMOT. Crystallographic Data Centre, 12 Union Road, Cambridge, England.