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A pseudopolymorph of valdecoxib

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Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.003 Å
Disorder in solvent or counterion
R factor = 0.044
wR factor = 0.131
Data-to-parameter ratio = 14.6

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

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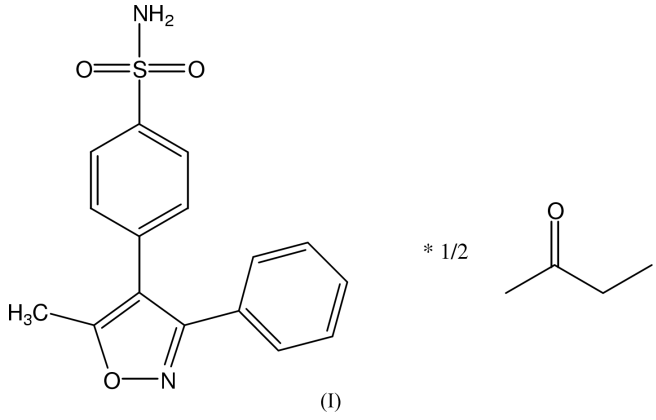
Valdecoxib, $C_{16}H_{14}N_2O_3S$, is a non-steroidal anti-inflammatory drug containing a planar isoxazole heterocycle which is substituted at the C atoms with two aromatic rings and a methyl group. In addition to one molecule of valdecoxib, there is half a molecule of ethyl methyl ketone in the asymmetric unit of the title compound [systematic name: 4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide ethyl methyl ketone hemisolvate], *viz*. $C_{16}H_{14}N_2O_3S{\cdot}0.5C_4H_8O$. The crystal packing is stabilized by N—H···O hydrogen bonds. Apart from the orientation of the sulfonamide group, the conformation of the title compound agrees well with that of the recently published orthorhombic polymorph which does not contain any solvent.

Comment

The title compound [systematic name: 4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide], (I), is a non-steroidal anti-inflammatory drug. A review on various aspects of valdecoxib has recently been reported (Chavez & Dekorte, 2003). The crystal structure of valdecoxib not containing any solvent, (II), has already been reported (Malathy Sony *et al.*, 2005).



(I)

A perspective view of (I) is shown in Fig. 1. Bond lengths and angles can be regarded as normal (Cambridge Structural Database, Version 1.6 plus three updates; *MOGUL* Version 1.0; Allen, 2002). The isoxazole heterocycle is planar (r.m.s. deviation = 0.003 Å). The dihedral angle between the heterocycle and the phenyl ring is 34.56 (8)° [22.2 (1)° in (II)], and 56.18 (8)° [54.3 (1)° in (II)] with the benzenesulfonamide ring. The only remarkable difference between the molecular conformations of (I) and (II) is the orientation of the sulfonamide group. In (I), the amino group is on the same side as the methyl group of the isoxazole ring. By contrast, in (II), the amino group is on the same side as the phenyl ring

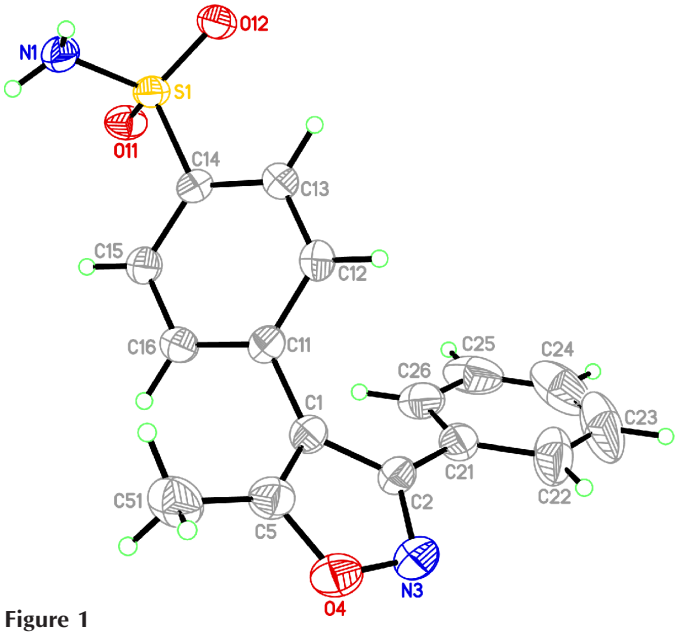


Figure 1
Perspective view of the title compound, with the atom numbering. Displacement ellipsoids are drawn at the 50% probability level. The ethyl methyl ketone molecule is not shown.

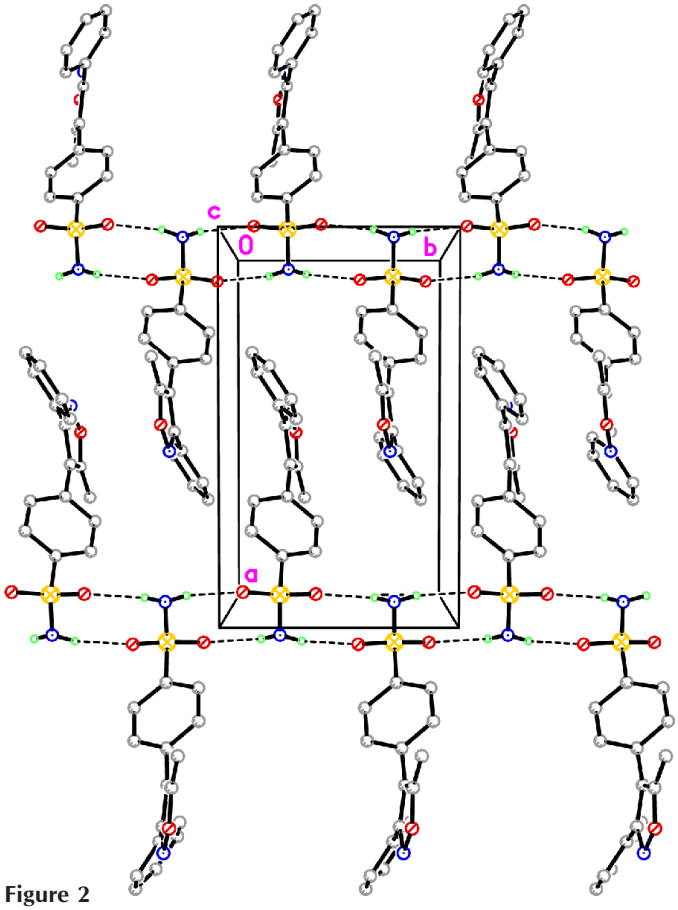


Figure 2
Packing diagram of the title compound, showing the hydrogen bonds as dashed lines. The view is on to the *ab* plane. The solvent molecules have been omitted for clarity.

attached to the isoxazole ring. The amino H atoms in (I) are hydrogen bonded to sulfonyl O atoms of two different molecules. As a result, ribbons are formed along the *b* axis (Fig. 2). In (II), only one H atom of the amino group forms a hydrogen bond to a sulfonyl O atom. The other one forms an N—H$\cdots\pi$ bond to the centre of the unsubstituted phenyl ring. These two structures provide a good example of how the inclusion of solvent molecules has an impact on either the molecular conformation of a molecule or the formation of hydrogen bonds.

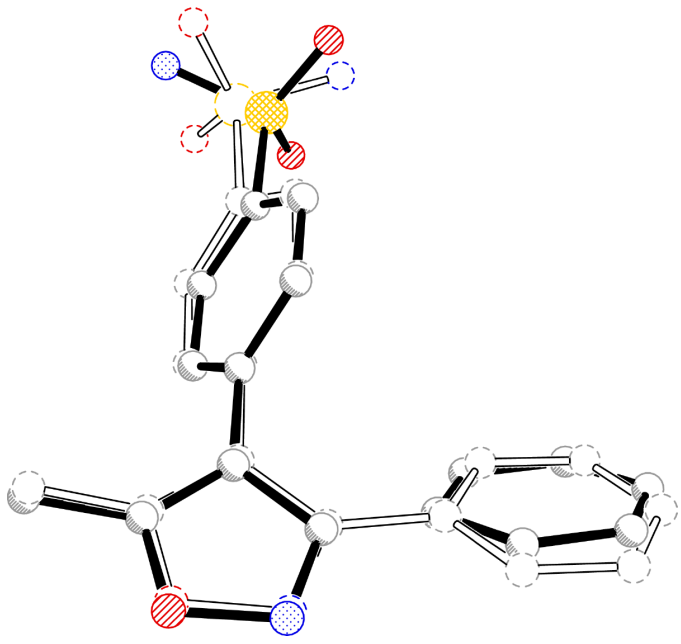


Figure 3
A least-squares fit (r.m.s. deviation = 0.238 Å for all atoms, except for the S-bound O and N atoms) of the title compound (full bonds) with its orthorhombic polymorph (open bonds).

Experimental

The title compound was obtained as a gift sample from Astral Pharmaceuticals, Mumbai, India, and was used without further purification. Colourless plates were obtained from ethyl methyl ketone by slow evaporation.

Crystal data

$C_{16}H_{14}N_2O_3S\cdot0.5C_4H_8O$
M_r = 350.40
Monoclinic, $P2_1/c$
a = 13.0201 (14) Å
b = 7.7930 (5) Å
c = 17.3305 (19) Å
β = 94.373 (9)°
V = 1753.3 (3) Å^3
Z = 4
D_x = 1.327 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 24 673 reflections
θ = 3.5–25.7°
μ = 0.21 mm^{-1}
T = 173 (2) K
Plate, colourless
0.40 × 0.37 × 0.14 mm

Data collection

Stoe IPDS-II two-circle diffractometer
ω scans
Absorption correction: multi-scan (*MULABS*; Spek, 2003; Blessing, 1995)
T_{min} = 0.912, T_{max} = 0.962
24 057 measured reflections
3345 independent reflections
2768 reflections with $I > 2\sigma(I)$
R_{int} = 0.057
θ_{max} = 25.8°
h = −15 → 15
k = −9 → 9
l = −21 → 21

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0755P)^2 + 0.4033P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.044$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.131$	$\Delta\rho_{max} = 0.60$ e Å^{-3}
$S = 1.06$	$\Delta\rho_{min} = -0.56$ e Å^{-3}
3345 reflections	
229 parameters	
H atoms treated by a mixture of independent and constrained refinement	

Table 1
Selected bond lengths (Å).

S1—O11	1.4280 (13)	C1—C2	1.428 (3)
S1—O12	1.4311 (13)	C2—N3	1.309 (3)
S1—N1	1.6036 (18)	N3—O4	1.402 (2)
S1—C14	1.7628 (18)	O4—C5	1.354 (2)
C1—C5	1.348 (3)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O12^{i}	0.85 (3)	2.05 (3)	2.881 (2)	165 (2)
N1—H1B···O11^{ii}	0.81 (3)	2.09 (3)	2.863 (2)	160 (3)

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

The H atoms bonded to nitrogen were refined isotropically. Other H atoms were refined with fixed individual displacement parameters [U_{iso}(H) = 1.2U_{eq}(C)] using a riding model, with C—H = 0.98 and 0.95 Å for methyl and aromatic CH groups, respectively. In addition, the methyl group was allowed to rotate but not to tip. There is half a molecule of ethyl methyl ketone per asymmetric unit, which is disordered about a centre of inversion.

Data collection: *X-AREA* (Stoe & Cie, 2001); cell refinement: *X-AREA*; data reduction: *X-AREA*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL-Plus* (Sheldrick, 1991); software used to prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2003).

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References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Blessing, R. H. (1995). *Acta Cryst.* A**51**, 33–38.
Chavez, M. L. & Dekorte, C. J. (2003). *Clin. Ther.* **25**, 817–851.
Malathy Sony, S. M., Charles, P., Ponnuswamy, M. N. & Yathirajan, H. S. (2005). *Acta Cryst.* E**61**, o108–o110.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1991). *SHELXTL-Plus.* Release 4.1. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Stoe & Cie (2001). *X-AREA*. Stoe & Cie, Darmstadt, Germany.