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Diflunisal–hexane (4/1)

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Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.008 Å
Disorder in main residue
R factor = 0.066
wR factor = 0.200
Data-to-parameter ratio = 9.8

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

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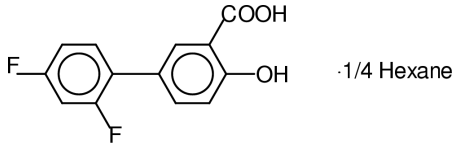
2′,4′-Difluoro-4-hydroxybiphenyl-3-carboxylic acid (diflunisal, $C_{13}H_8F_2O_3$) 0.25-hexane solvate forms a monoclinic crystal lattice with special channels parallel to the twofold screw axes along the *b* direction. These channels are occupied by disordered hexane molecules. The crystal lattice consists of the dimers of diflunisal, in which two molecules are linked together by a pair of hydrogen bonds between their respective carboxyl groups.

Comment

Diflunisal is a difluorophenyl derivative of acetylsalicylic acid (aspirin), which is used therapeutically as an anti-inflammatory drug similarly to aspirin. The structure of unsolvated diflunisal was described earlier (Yang Bae Kim & Il Yeong Park, 1996). However, this new investigation displays properties of clathrate materials and includes in the crystal lattice solvent molecules. Here, the structure of its hexane solvate, (I), is reported.



(I)

The investigated structure is characterized as a packing of the diflunisal dimers, which are obtained by energetically equivalent hydrogen bonds between two adjacent molecules (Table 1). Probably, the atom O2 takes part in forming not only the intermolecular bonds but also the intramolecular ones O1—H10···O2.

The conformation state of a diflunisal molecule may be characterized as follows: The phenyl planes are tilted round the C1—C8 bond by a dihedral angle of 43.4 (1)°. Similar values of angles have been reported for π-stacking interactions in nucleic acids (Langlet *et al.*, 1981; Rein, 1978; Claverie, 1978). For comparison, the planes of benzene molecules in an orthorhombic crystal, which are situated 5.81 Å apart from each other, form a dihedral angle of 29° (Bacon *et al.*, 1964). It should be noted that theoretical analysis of the structure of benzene clusters (Sun & Bernstein, 1996) derives dihedral angles between planes of benzene molecules corresponding to approximately 40°, where the molecules are packed in a herringbone arrangement.

In diflunisal, the hydroxyl group is tilted towards the phenyl group: the torsion angle C3—C4—O1—H1O is 7 (3)°. The

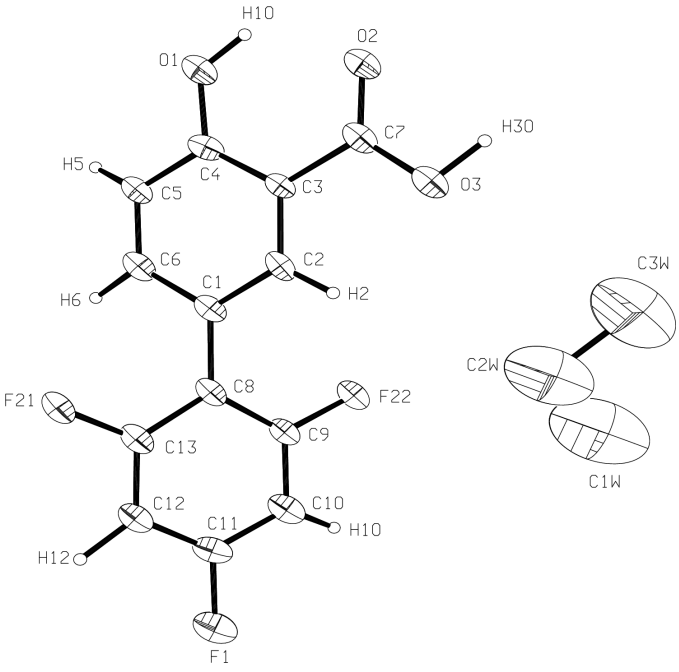


Figure 1
A view of diflunisal with the atomic numbering scheme. Displacement ellipsoids are drawn at the 20% probability level.

geometry of the carboxyl group slightly differs from a planar arrangement [torsion angle O2—C7—O3—H3O is 12 (2)]° and is approximately coplanar with the phenyl fragment [torsion angle O3—C7—C3—C2 is 0 (2)°]. Fluorine atoms in positions 2′- and 6′- are disordered.

The phenyl groups of neighbouring parallel molecules are stacked face-to-face and shifted by R_{shift} = 1.6 Å. The distance between these planes of the phenyl rings is R_b = 3.73 Å. These parameters are in good agreement with the values for the local energetic minimum calculated for benzene dimers: R_{shift}^* = 1.6 Å and R_b^* = 3.85 Å (Hobza *et al.*, 1993; Hobza *et al.*, 1994), and the relative orientation and packing of phenyl rings in diflunisal follow in general the rules for packing of benzene dimers. Out of four energetic minima calculated for benzene arrangement (parallel staggered, PS; parallel displaced, PD; herring-bone, H; T-shape, T), in the present case two such local energetic minima are realised (PD and H).

The characteristic (specific) property of the crystal lattice of diflunisal is the existence of channels along the twofold screw axes and parallel to the *b* direction. The geometry of these channels allows accommodation of solvent molecules of appropriate sizes. In the present case, the channels are filled by hexane molecules, which are situated in a disordered state.

Our suppositions about the existence of a hexane solvate and not an acetone molecule, are based on the following. The results of TG-measurements show that the stoichiometry of an acetone solvate would have to be 3:1 for diflunisal:acetone. The C═O stretching vibration frequency for acetone is 1725 (5) cm^{-1}, and is. sufficiently far from the C═O frequency for diflunisal (1671 cm^{-1}) to be distinguishable. Thus there

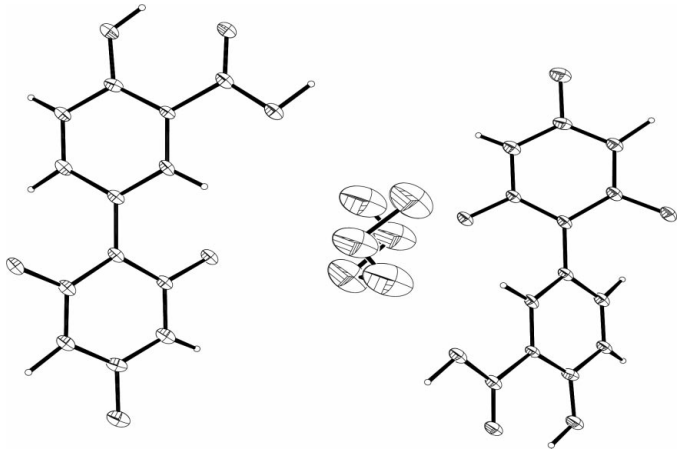


Figure 2
A complete *n*-hexane molecule lying between two diflunisal molecules. The molecules are generated over a twofold screw axis. Displacement ellipsoids are drawn at the 10% probability level.

should be an additional absorption band around 1725 cm^{-1} with an intensity about one-third that for the diflunisal absorption band. However, experiments show no peaks in this region. We therefore conclude that the described solvate contains hexane molecules. Furthermore, difference Fourier maps show three peaks about the same size around a twofold screw axis, generating a polymeric chain along this symmetry element, consistent with disordered hexane.

A diflunisal hydrate was described by us earler (Hansen *et al.*, 2001). It seems from the current data that the hexane molecule may occupy two different sites. It should be noted that the investigated solvate is stable under ambient conditions. In order to check the stoichiometry of the solvate DSC and TG-measurements were carried out at various heating rates (v = 1–20 $Kmin^{-1}$). The heat change occurring during desolvation at v = 10 $Kmin^{-1}$ and temperature interval from 365 to 389 K is 10 Jg^{-1}. The average mass loss is 7.3%, corresponding to a diflunisal:hexane stoichiometry of 4:1. This result is in a good agreement with the X-ray experiment.

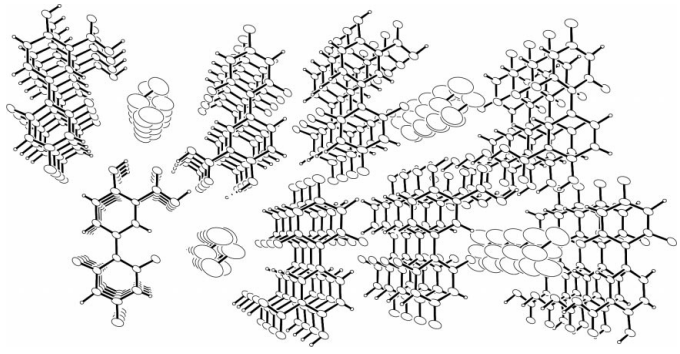


Figure 3
Fragment of the crystal packing looking down the *b* axis.

Experimental

The solvate was grown by crystallization from a saturated solution of diflunisal in acetone by vapour diffusion of hexane (Guillory, 1999).

Crystal data

$C_{14.5}H_7F_2O_3$
M_r = 267.21
Monoclinic, $C2/c$
a = 34.826 (17) Å
b = 3.7296 (16) Å
c = 20.703 (10) Å
β = 110.63 (5)°
V = 2517 (2) Å^3
Z = 8
D_x = 1.410 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 26 reflections
θ = 12–16°
μ = 0.12 mm^{-1}
T = 298 (2) K
Needle, white
0.30 × 0.20 × 0.10 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: none
2312 measured reflections
2220 independent reflections
715 reflections with $I > 2\sigma(I)$
R_{int} = 0.045
θ_{max} = 25.0°
$h = -40 \rightarrow 38$
$k = -1 \rightarrow 4$
$l = -1 \rightarrow 24$
3 standard reflections
frequency: 120 min
intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.066
$wR(F^2)$ = 0.200
S = 1.04
2220 reflections
227 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0837P)^2\mathrm{P}]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.183
$\Delta\rho_{max}$ = 0.27 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °) for the diflunisal molecules.

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3O···O2^{i}	1.02 (5)	1.69 (5)	2.665 (6)	159 (3)
O1—H1O···O2	0.92 (5)	2.01 (6)	2.630 (6)	123 (3)

Symmetry code: (i) $\frac{1}{2} - x, \frac{1}{2} - y, 1 - z$.

All programs used in the solution (Sheldrick, 1997), refinement (Sheldrick, 1997) and display (Burnett & Johnson, 1996) of the structures are included in the *OSCAIL* program package (McArdle, 1993).

Data collection, cell refinement and data reduction: *CAD*-4 *Software* (Enraf–Nonius, 1989); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *OSCAIL* (McArdle, 1993).

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