

Acta Crystallographica Section E

## Structure Reports

Online

ISSN 1600-5368

## 2,6-Difluorobenzoic acid

 Mohammad T. M. Al-Dajani,<sup>a</sup> Habibah A Wahab,<sup>b</sup>  
 Nornisah Mohamed,<sup>a</sup> Chin Sing Yeap<sup>c,‡</sup> and Hoong-Kun  
 Fun<sup>c,\*§</sup>

<sup>a</sup>School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia, <sup>b</sup>Malaysian Institute of Pharmaceuticals and Nutraceuticals, Ministry of Science, Technology and Innovation, Blok A, 10 Persiaran Bukit Jambul, 11900 Bayan Lepas, Penang, Malaysia, and <sup>c</sup>X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia  
 Correspondence e-mail: hkfun@usm.my

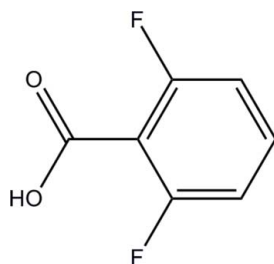
Received 17 July 2010; accepted 19 July 2010

Key indicators: single-crystal X-ray study;  $T = 100$  K; mean  $\sigma(\text{C}-\text{C}) = 0.002$  Å;  
 R factor = 0.049;  $wR$  factor = 0.143; data-to-parameter ratio = 18.9.

In the title compound,  $\text{C}_7\text{H}_4\text{F}_2\text{O}_2$ , the dihedral angle between the benzene ring and the carboxylate group is  $33.70$  ( $14$ )°. In the crystal structure, inversion dimers linked by pairs of  $\text{O}-\text{H}\cdots\text{O}$  hydrogen bonds occur, generating  $R_2^2(8)$  loops. The dimers are linked into sheets lying parallel to  $(102)$  by  $\text{C}-\text{H}\cdots\text{F}$  hydrogen bonds.

## Related literature

For general background to 2,6-difluorobenzylchloride derivatives, see: Beavo (1995); Beavo & Reifsnnyder (1990); Nicholson *et al.* (1991). For the stability of the temperature controller used in the data collection, see: Cosier & Glazer (1986).



## Experimental

## Crystal data

 $\text{C}_7\text{H}_4\text{F}_2\text{O}_2$ 
 $M_r = 158.10$ 

Monoclinic,  $P2_1/c$   
 $a = 3.6517$  (4) Å  
 $b = 14.1214$  (15) Å  
 $c = 12.2850$  (13) Å  
 $\beta = 95.651$  (3)°  
 $V = 630.42$  (12) Å<sup>3</sup>

$Z = 4$   
 Mo  $K\alpha$  radiation  
 $\mu = 0.16$  mm<sup>-1</sup>  
 $T = 100$  K  
 $0.73 \times 0.19 \times 0.09$  mm

## Data collection

Bruker APEXII DUO CCD  
 diffractometer  
 Absorption correction: multi-scan  
 (SADABS; Bruker, 2009)  
 $T_{\min} = 0.841$ ,  $T_{\max} = 0.986$

6112 measured reflections  
 2190 independent reflections  
 1895 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.029$

## Refinement

$R[F^2 > 2\sigma(F^2)] = 0.049$   
 $wR(F^2) = 0.143$   
 $S = 1.12$   
 2190 reflections

116 parameters  
 All H-atom parameters refined  
 $\Delta\rho_{\text{max}} = 0.47$  e Å<sup>-3</sup>  
 $\Delta\rho_{\text{min}} = -0.31$  e Å<sup>-3</sup>

Table 1

Hydrogen-bond geometry (Å, °).

| $D-H\cdots A$                             | $D-H$    | $H\cdots A$ | $D\cdots A$ | $D-H\cdots A$ |
|---|----------|-------------|-------------|---------------|
| $\text{O2}-\text{H1O2}\cdots\text{O3}^i$  | 0.95 (4) | 1.68 (4)    | 2.6318 (14) | 174 (4)       |
| $\text{C3}-\text{H3}\cdots\text{F2}^{ii}$ | 0.98 (2) | 2.54 (2)    | 3.3428 (16) | 138.7 (16)    |

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

Data collection: APEX2 (Bruker, 2009); cell refinement: SAINT (Bruker, 2009); data reduction: SAINT; program(s) used to solve structure: SHELXTL (Sheldrick, 2008); program(s) used to refine structure: SHELXTL; molecular graphics: SHELXTL; software used to prepare material for publication: SHELXTL and PLATON (Spek, 2009).

NM gratefully acknowledges funding from Universiti Sains Malaysia (USM) under the University Research Grant (No. 1001/PFARMASI/815025). HKF and CSY thank USM for the Research University Golden Goose Grant (No. 1001/PFIZIK/811012). CSY also thanks USM for the award of a USM Fellowship.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HB5558).

## References

- Beavo, J. A. (1995). *Physiol. Rev.* **75**, 725–748.  
 Beavo, J. A. & Reifsnnyder, D. H. (1990). *Trends Pharmacol. Sci.* **11**, 150–155.  
 Bruker (2009). APEX2, SAINT and SADABS. Bruker AXS Inc., Madison, Wisconsin, USA.  
 Cosier, J. & Glazer, A. M. (1986). *J. Appl. Cryst.* **19**, 105–107.  
 Nicholson, C. D., Chaliss, R. A. & Shalid, M. (1991). *Trends Pharmacol. Sci.* **12**, 19–27.  
 Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.  
 Spek, A. L. (2009). *Acta Cryst.* **D65**, 148–155.

<sup>‡</sup> Thomson Reuters ResearcherID: A-5523-2009.

<sup>§</sup> Thomson Reuters ResearcherID: A-3561-2009.

---

## supporting information

*Acta Cryst.* (2010). E66, o2109 [https://doi.org/10.1107/S1600536810028758]

### 2,6-Difluorobenzoic acid

**Mohammad T. M. Al-Dajani, Habibah A Wahab, Nornisah Mohamed, Chin Sing Yeap and Hoong-Kun Fun**

#### S1. Comment

The derivatives of 2,6-difluorobenzylchloride involved in the inhibition of phosphodiesterases (PDEs) are enzymes which catalyze PDEs. These derivatives are classified into seven families, five of which, PDE1–PDE5, have been characterized (Beavo, 1995). The hydrolysis of cyclic nucleotides was evaluated according to the methods in given the references (Beavo & Reifsnnyder, 1990; Nicholson *et al.*, 1991).

The molecule of the title compound, (I), (Fig. 1) is not planar with the dihedral angle between the benzene ring and the carboxylate group being 33.70 (14)°. In the crystal structure, the molecules are linked into pairs of centrosymmetric dimers by intermolecular O2—H1O2···O3 hydrogen bonds (Table 1). These dimers are linked into two-dimensional plane by the intermolecular C3—H3A···F2 hydrogen bonds (Fig. 2, Table 1) parallel to (102).

#### S2. Experimental

2,6-Difluorobenzylchloride (0.01 mol, 1.7 g) was added drop-wise with stirring into a round bottom flask containing 25 ml water and then refluxed for two and half hours. The gum compound precipitate formed was filtered and dissolved in alkaline water. Hydrochloric acid was then added drop-wise with stirring. The white precipitate formed was dissolved in methanol. Colourless needles of (I) were formed at room temperature overnight and filtrated and dried at 333 K.

#### S3. Refinement

All hydrogen atoms were located in a difference Fourier map and refined freely.

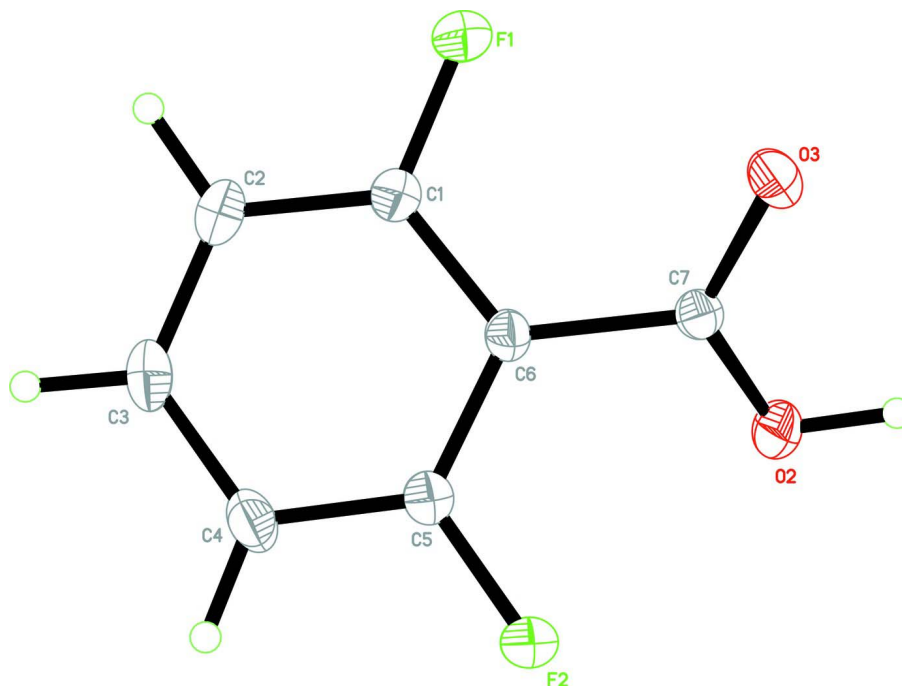


Figure 1

The molecular structure of (I) with 50% probability ellipsoids for non-H atoms.

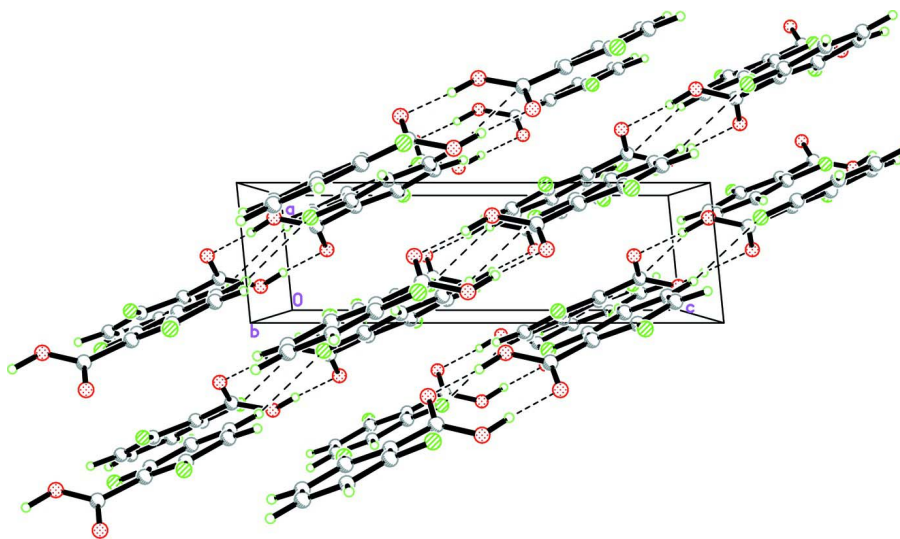


Figure 2

The crystal packing of (I), viewed down the  $b$  axis, showing two 2-D planes.

### 2,6-Difluorobenzoic acid

#### Crystal data

$C_7H_4F_2O_2$

$M_r = 158.10$

Monoclinic,  $P2_1/c$

Hall symbol:  $-P\ 2_1/c$

$a = 3.6517(4)\ \text{\AA}$

$b = 14.1214(15)\ \text{\AA}$

$c = 12.2850(13)\ \text{\AA}$

$\beta = 95.651(3)^\circ$

$V = 630.42(12)\ \text{\AA}^3$

$Z = 4$

$F(000) = 320$   
 $D_x = 1.666 \text{ Mg m}^{-3}$   
 Mo  $K\alpha$  radiation,  $\lambda = 0.71073 \text{ \AA}$   
 Cell parameters from 3166 reflections  
 $\theta = 3.3\text{--}32.1^\circ$

$\mu = 0.16 \text{ mm}^{-1}$   
 $T = 100 \text{ K}$   
 Needle, colourless  
 $0.73 \times 0.19 \times 0.09 \text{ mm}$

#### Data collection

Bruker APEXII DUO CCD  
 diffractometer  
 Radiation source: fine-focus sealed tube  
 Graphite monochromator  
 $\varphi$  and  $\omega$  scans  
 Absorption correction: multi-scan  
 (SADABS; Bruker, 2009)  
 $T_{\min} = 0.841$ ,  $T_{\max} = 0.986$

6112 measured reflections  
 2190 independent reflections  
 1895 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.029$   
 $\theta_{\text{max}} = 32.1^\circ$ ,  $\theta_{\text{min}} = 2.2^\circ$   
 $h = -5 \rightarrow 5$   
 $k = -20 \rightarrow 20$   
 $l = -18 \rightarrow 18$

#### Refinement

Refinement on  $F^2$   
 Least-squares matrix: full  
 $R[F^2 > 2\sigma(F^2)] = 0.049$   
 $wR(F^2) = 0.143$   
 $S = 1.12$   
 2190 reflections  
 116 parameters  
 0 restraints  
 Primary atom site location: structure-invariant  
 direct methods

Secondary atom site location: difference Fourier  
 map  
 Hydrogen site location: inferred from  
 neighbouring sites  
 All H-atom parameters refined  
 $w = 1/[\sigma^2(F_o^2) + (0.0668P)^2 + 0.3079P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\text{max}} < 0.001$   
 $\Delta\rho_{\text{max}} = 0.47 \text{ e \AA}^{-3}$   
 $\Delta\rho_{\text{min}} = -0.31 \text{ e \AA}^{-3}$

#### Special details

**Experimental.** The crystal was placed in the cold stream of an Oxford Cryosystems Cobra open-flow nitrogen cryostat (Cosier & Glazer, 1986) operating at 100.0 (1) K.

**Geometry.** All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

**Refinement.** Refinement of  $F^2$  against ALL reflections. The weighted  $R$ -factor  $wR$  and goodness of fit  $S$  are based on  $F^2$ , conventional  $R$ -factors  $R$  are based on  $F$ , with  $F$  set to zero for negative  $F^2$ . The threshold expression of  $F^2 > \sigma(F^2)$  is used only for calculating  $R$ -factors(gt) etc. and is not relevant to the choice of reflections for refinement.  $R$ -factors based on  $F^2$  are statistically about twice as large as those based on  $F$ , and  $R$ -factors based on ALL data will be even larger.

#### Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ( $\text{\AA}^2$ )

|    | $x$         | $y$          | $z$          | $U_{\text{iso}}^*/U_{\text{eq}}$ |
|----|-------------|--------------|--------------|----------------------------------|
| F1 | 0.0410 (3)  | -0.01635 (6) | 0.16839 (7)  | 0.0312 (2)                       |
| F2 | 0.2348 (3)  | 0.26707 (6)  | 0.36896 (7)  | 0.0285 (2)                       |
| O2 | 0.2287 (3)  | 0.09843 (7)  | 0.46658 (7)  | 0.0238 (2)                       |
| O3 | 0.4751 (3)  | -0.00746 (7) | 0.35958 (8)  | 0.0222 (2)                       |
| C1 | 0.0163 (4)  | 0.07830 (9)  | 0.17659 (9)  | 0.0194 (2)                       |
| C2 | -0.1413 (4) | 0.12763 (10) | 0.08679 (10) | 0.0228 (3)                       |
| C3 | -0.1734 (4) | 0.22519 (10) | 0.09441 (10) | 0.0234 (3)                       |
| C4 | -0.0482 (4) | 0.27250 (10) | 0.19005 (11) | 0.0230 (3)                       |
| C5 | 0.1044 (4)  | 0.22003 (9)  | 0.27793 (9)  | 0.0184 (2)                       |
| C6 | 0.1398 (3)  | 0.12160 (8)  | 0.27576 (9)  | 0.0160 (2)                       |

|      |            |             |             |             |
|------|------------|-------------|-------------|-------------|
| C7   | 0.2939 (3) | 0.06665 (8) | 0.37288 (9) | 0.0156 (2)  |
| H2   | -0.221 (7) | 0.0927 (16) | 0.0182 (18) | 0.038 (6)*  |
| H3   | -0.285 (6) | 0.2599 (15) | 0.0302 (17) | 0.035 (5)*  |
| H4   | -0.074 (6) | 0.3406 (16) | 0.1979 (18) | 0.035 (5)*  |
| H1O2 | 0.341 (11) | 0.062 (3)   | 0.526 (3)   | 0.098 (12)* |

*Atomic displacement parameters (Å<sup>2</sup>)*

|    | $U^{11}$   | $U^{22}$   | $U^{33}$   | $U^{12}$    | $U^{13}$    | $U^{23}$    |
|----|------------|------------|------------|-------------|-------------|-------------|
| F1 | 0.0518 (6) | 0.0183 (4) | 0.0219 (4) | 0.0019 (4)  | -0.0044 (4) | -0.0039 (3) |
| F2 | 0.0459 (6) | 0.0169 (4) | 0.0210 (4) | -0.0010 (4) | -0.0048 (4) | -0.0018 (3) |
| O2 | 0.0340 (6) | 0.0238 (5) | 0.0135 (4) | 0.0038 (4)  | 0.0014 (4)  | 0.0013 (3)  |
| O3 | 0.0269 (5) | 0.0179 (4) | 0.0216 (4) | 0.0056 (4)  | 0.0012 (4)  | 0.0030 (3)  |
| C1 | 0.0238 (6) | 0.0181 (5) | 0.0162 (5) | 0.0001 (4)  | 0.0014 (4)  | 0.0003 (4)  |
| C2 | 0.0242 (6) | 0.0289 (6) | 0.0150 (5) | -0.0002 (5) | -0.0006 (4) | 0.0019 (4)  |
| C3 | 0.0224 (6) | 0.0289 (6) | 0.0184 (5) | 0.0037 (5)  | -0.0001 (4) | 0.0078 (4)  |
| C4 | 0.0272 (6) | 0.0193 (6) | 0.0225 (6) | 0.0041 (5)  | 0.0016 (5)  | 0.0062 (4)  |
| C5 | 0.0210 (5) | 0.0174 (5) | 0.0166 (5) | 0.0004 (4)  | 0.0012 (4)  | 0.0011 (4)  |
| C6 | 0.0182 (5) | 0.0160 (5) | 0.0137 (4) | 0.0009 (4)  | 0.0014 (4)  | 0.0019 (3)  |
| C7 | 0.0174 (5) | 0.0148 (5) | 0.0148 (4) | -0.0006 (4) | 0.0020 (4)  | 0.0012 (3)  |

*Geometric parameters (Å, °)*

|             |             |             |              |
|-------------|-------------|-------------|--------------|
| F1—C1       | 1.3442 (15) | C2—H2       | 0.99 (2)     |
| F2—C5       | 1.3467 (14) | C3—C4       | 1.3892 (19)  |
| O2—C7       | 1.2794 (14) | C3—H3       | 0.98 (2)     |
| O2—H1O2     | 0.96 (4)    | C4—C5       | 1.3807 (17)  |
| O3—C7       | 1.2574 (15) | C4—H4       | 0.97 (2)     |
| C1—C2       | 1.3815 (17) | C5—C6       | 1.3965 (17)  |
| C1—C6       | 1.3976 (16) | C6—C7       | 1.4866 (15)  |
| C2—C3       | 1.387 (2)   |             |              |
| C7—O2—H1O2  | 113 (2)     | C5—C4—H4    | 119.3 (13)   |
| F1—C1—C2    | 117.86 (11) | C3—C4—H4    | 122.2 (13)   |
| F1—C1—C6    | 118.83 (11) | F2—C5—C4    | 117.84 (11)  |
| C2—C1—C6    | 123.29 (12) | F2—C5—C6    | 118.74 (10)  |
| C1—C2—C3    | 118.58 (12) | C4—C5—C6    | 123.38 (11)  |
| C1—C2—H2    | 119.4 (13)  | C5—C6—C1    | 115.44 (10)  |
| C3—C2—H2    | 122.0 (13)  | C5—C6—C7    | 122.18 (10)  |
| C2—C3—C4    | 120.79 (11) | C1—C6—C7    | 122.37 (11)  |
| C2—C3—H3    | 118.2 (13)  | O3—C7—O2    | 123.76 (11)  |
| C4—C3—H3    | 121.0 (13)  | O3—C7—C6    | 119.51 (10)  |
| C5—C4—C3    | 118.49 (12) | O2—C7—C6    | 116.72 (10)  |
| F1—C1—C2—C3 | 179.13 (13) | C4—C5—C6—C7 | -177.92 (12) |
| C6—C1—C2—C3 | 1.2 (2)     | F1—C1—C6—C5 | -179.87 (12) |
| C1—C2—C3—C4 | 0.3 (2)     | C2—C1—C6—C5 | -1.92 (19)   |
| C2—C3—C4—C5 | -0.9 (2)    | F1—C1—C6—C7 | -0.65 (19)   |

|             |              |             |              |
|-------------|--------------|-------------|--------------|
| C3—C4—C5—F2 | 178.01 (12)  | C2—C1—C6—C7 | 177.31 (12)  |
| C3—C4—C5—C6 | 0.0 (2)      | C5—C6—C7—O3 | -147.25 (13) |
| F2—C5—C6—C1 | -176.65 (11) | C1—C6—C7—O3 | 33.57 (18)   |
| C4—C5—C6—C1 | 1.31 (19)    | C5—C6—C7—O2 | 33.33 (17)   |
| F2—C5—C6—C7 | 4.12 (18)    | C1—C6—C7—O2 | -145.84 (13) |

*Hydrogen-bond geometry (Å, °)*

| <i>D</i> —H $\cdots$ <i>A</i>    | <i>D</i> —H | H $\cdots$ <i>A</i> | <i>D</i> $\cdots$ <i>A</i> | <i>D</i> —H $\cdots$ <i>A</i> |
|----------------------------------|-------------|---------------------|----------------------------|-------------------------------|
| O2—H1O2 $\cdots$ O3 <sup>i</sup> | 0.95 (4)    | 1.68 (4)            | 2.6318 (14)                | 174 (4)                       |
| C3—H3 $\cdots$ F2 <sup>ii</sup>  | 0.98 (2)    | 2.54 (2)            | 3.3428 (16)                | 138.7 (16)                    |

Symmetry codes: (i)  $-x+1, -y, -z+1$ ; (ii)  $x-1, -y+1/2, z-1/2$ .