2-(5-Fluoro-3-methylsulfanyl-1-benzofuran-2-yl)acetic acid

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The title compound, $C_{11}H_9FO_3S$, was prepared by alkaline hydrolysis of ethyl 2-(5-fluoro-3-methylsulfanyl-1-benzofuran-2-yl)acetate. In the crystal structure, the carboxyl groups are involved in intermolecular O—H···O hydrogen bonds, which link the molecules into centrosymmetric dimers. These dimers are further packed into stacks along the b axis by intermolecular C—H···O and C—H···F interactions.

Related literature

For the crystal structures of similar 2-(3-methylsulfanyl-1-benzofuran-2-yl) acetic acid derivatives, see: Choi *et al.* (2009*a*,*b*). For the pharmacological activity of benzofuran compounds, see: Howlett *et al.* (1999); Twyman & Allsop (1999).
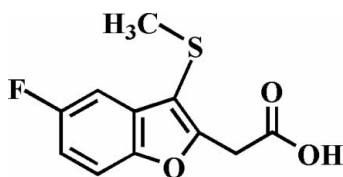
Experimental

Crystal data

$C_{11}H_9FO_3S$	Monoclinic, $P2_1/c$
$M_r = 240.24$	$a = 7.5179$ (4) Å
$b = 27.325$ (2) Å	Mo $K\alpha$ radiation
$c = 5.0582$ (3) Å	$\mu = 0.31$ mm^{-1}
$\beta = 90.478$ (1)°	$T = 173$ K
$V = 1039.05$ (11) Å^3	$0.40 \times 0.40 \times 0.20$ mm
$Z = 4$	

Data collection

Bruker SMART CCD diffractometer	5774 measured reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1999) $T_{min} = 0.885$, $T_{max} = 0.940$	2015 independent reflections
	1758 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.016$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.028$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.076$	
$S = 1.10$	
2015 reflections	$\Delta\rho_{max} = 0.26$ e Å^{-3}
150 parameters	$\Delta\rho_{min} = -0.21$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C6—H6···O3[i]	0.93	2.52	3.2896 (19)	141
C6—H6···O3[ii]	0.93	2.51	3.296 (2)	143
O2—H2···O3[iii]	0.84 (2)	1.85 (2)	2.6902 (17)	178 (2)
C11—H11B···F[iv]	0.96	2.69	3.572 (2)	153
C11—H11B···F[v]	0.96	2.67	3.361 (2)	130

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

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *DIAMOND* (Brandenburg, 1998); software used to prepare material for publication: *SHELXL97*.

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supplementary materials

2-(5-Fluoro-3-methylsulfanyl-1-benzofuran-2-yl)acetic acid

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Comment

The benzofuran ring systems have been attracted considerable interest in the view of their pharmacological properties (Howlett *et al.*, 1999; Twyman & Allsop, 1999). As a part of our ongoing studies on the synthesis and structures of 2-(3-methylsulfanyl-1-benzofuran-2-yl)acetic acid analogues, the crystal structure of 2-(5-bromo-3-methylsulfanyl-1-benzo-furan-2-yl)acetic acid (Choi *et al.*, 2009*a*) and 2-(5-isopropyl-3-methylsulfanyl-1-benzofuran-2-yl)acetic acid (Choi *et al.*, 2009*b*) have been described in the literature. Here we report the crystal structure of the title compound, 2-(5-fluoro-3-methyl-sulfanyl-1-benzofuran-2-yl)acetic acid (Fig. 1).

The benzofuran unit is essentially planar, with a mean deviation of 0.005 (1) Å from the least-squares plane defined by the nine constituent atoms. In the crystal structure, the carboxyl groups are involved in intermolecular O–H···O hydrogen bonds (Table 1 and Fig. 2), which link the molecules into centrosymmetric dimers. These dimers are further packed into stacks along the *b* axis by intermolecular C–H···O and C–H···F interactions; the first between an H atom of benzofuran ring and the C=O unit, with C6–H6···O3[i] and C6–H6···O3[ii], the second between a methyl H atom of methylsulfanyl group and the fluorine atom of the benzofuran ring, with C11–H11B···F[iv] and C11–H11B···F[v], respectively (Table 1 and Fig. 2).

Experimental

Ethyl 2-(5-fluoro-3-methylsulfanyl-1-benzofuran-2-yl)acetate (402 mg, 1.5 mmol) was added to a solution of potassium hydroxide (505 mg, 9.0 mmol) in water (20 ml) and methanol (20 ml), and the mixture was refluxed for 6h, then cooled. Water was added, and the solution was extracted with dichloromethane. The aqueous layer was acidified to pH 1 with concentrated hydrochloric acid and then extracted with chloroform, dried over magnesium sulfate, filtered and concentrated under vacuum. The residue was purified by column chromatography (ethyl acetate) to afford the title compound as a colorless solid [yield 84%, m.p. 438–439 K; R_f = 0.6 (ethyl acetate)]. Single crystals suitable for X-ray diffraction were prepared by evaporation of a solution of the title compound in benzene at room temperature.

Refinement

The H atom of O2 was positioned in a difference Fourier map and refined freely. The other H atoms were positioned geometrically and refined using a riding model, with C–H = 0.93 Å for the aryl, 0.97 Å for the methylene, and 0.96 Å for the methyl H atoms with Uiso(H) = 1.2Ueq(C) for the aryl and methylene H atoms, and 1.5Ueq(C) for methyl H atoms.
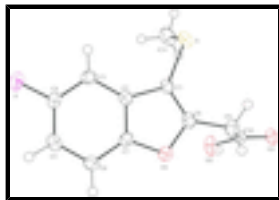
supplementary materials

Figures

Fig. 1. The molecular structure of the title compound with the atom numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are presented as a small cycles of arbitrary radius.
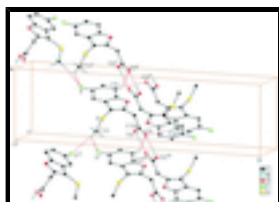

Fig. 2. The O–H···O hydrogen bonds, and C–H···O, and C–H···F interactions (dotted lines) in the title compound. [Symmetry code: (i) $1 + x$, y, $- 1 + z$; (ii) $1 - x$, $1 - y$, $1 - z$; (iii) $- x$, $1 - y$, $1 - z$; (iv) $x - 1$, $-y + 1/2$, $z + 1/2$; (v) $x - 1$, y, $z + 1$.]

2-(5-Fluoro-3-methylsulfanyl-1-benzofuran-2-yl)acetic acid

Crystal data

$C_{11}H_9FO_3S$	$F_{000} = 496$
$M_r = 240.24$	$D_x = 1.536$ Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Hall symbol: -P 2ybc	Cell parameters from 3920 reflections
$a = 7.5179$ (4) Å	$\theta = 2.2–27.5°$
$b = 27.325$ (2) Å	$\mu = 0.31$ mm^{-1}
$c = 5.0582$ (3) Å	$T = 173$ K
$\beta = 90.4780$ (10)°	Block, colourless
$V = 1039.05$ (11) Å^3	$0.40 \times 0.40 \times 0.20$ mm
$Z = 4$	

Data collection

Bruker SMART CCD diffractometer	2015 independent reflections
Radiation source: fine-focus sealed tube	1758 reflections with $I > 2\sigma(I)$
Monochromator: graphite	$R_{int} = 0.016$
Detector resolution: 10.0 pixels mm^{-1}	$\theta_{max} = 26.0°$
$T = 173$ K	$\theta_{min} = 2.8°$
φ and ω scans	$h = -8 \rightarrow 9$
Absorption correction: multi-scan (SADABS; Sheldrick, 1999)	$k = -33 \rightarrow 31$
$T_{min} = 0.885$, $T_{max} = 0.940$	$l = -5 \rightarrow 6$
5774 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.028$

$wR(F^2) = 0.076$

$S = 1.10$

2015 reflections

150 parameters

Primary atom site location: structure-invariant direct methods

Hydrogen site location: difference Fourier map

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0321P)^2 + 0.495P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max} = 0.26$ e Å^{-3}

$\Delta\rho_{min} = -0.21$ e Å^{-3}

Extinction correction: none

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds 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, convention-al R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\mathrm{sigma}(F^2)$ is used only for calculat-ing 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 (Å^2)

	x	y	z	$U_{iso}*/U_{eq}$
S	0.31784 (5)	0.316516 (15)	0.58563 (8)	0.02756 (13)
F	0.83216 (14)	0.28556 (4)	−0.2451 (2)	0.0378 (3)
O1	0.59504 (15)	0.43332 (4)	0.3745 (2)	0.0255 (3)
O2	0.19605 (18)	0.46681 (5)	0.3551 (2)	0.0343 (3)
H2	0.102 (3)	0.4823 (9)	0.316 (4)	0.047 (6)*
O3	0.09836 (15)	0.48144 (4)	0.7637 (2)	0.0268 (3)
C1	0.4579 (2)	0.36074 (6)	0.4469 (3)	0.0217 (3)
C2	0.58779 (19)	0.35365 (6)	0.2404 (3)	0.0211 (3)
C3	0.6420 (2)	0.31379 (6)	0.0878 (3)	0.0231 (3)
H3	0.5921	0.2829	0.1067	0.028*
C4	0.7740 (2)	0.32324 (6)	−0.0924 (3)	0.0251 (3)
C5	0.8516 (2)	0.36865 (6)	−0.1307 (3)	0.0277 (4)
H5	0.9394	0.3725	−0.2575	0.033*
C6	0.7982 (2)	0.40828 (6)	0.0203 (3)	0.0264 (3)
H6	0.8478	0.4392	−0.0006	0.032*
C7	0.6668 (2)	0.39915 (6)	0.2039 (3)	0.0224 (3)
C8	0.4683 (2)	0.40835 (6)	0.5179 (3)	0.0232 (3)
C9	0.3703 (2)	0.43787 (6)	0.7168 (3)	0.0277 (4)
H9A	0.4513	0.4620	0.7909	0.033*
H9B	0.3345	0.4164	0.8594	0.033*
C10	0.2076 (2)	0.46410 (5)	0.6137 (3)	0.0219 (3)
C11	0.1570 (2)	0.30916 (8)	0.3207 (3)	0.0372 (4)

H11A	0.0973	0.3397	0.2896	0.056*
H11B	0.0715	0.2847	0.3690	0.056*
H11C	0.2169	0.2991	0.1627	0.056*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S	0.0263 (2)	0.0334 (2)	0.0230 (2)	−0.00356 (16)	0.00305 (15)	0.00559 (16)
F	0.0415 (6)	0.0317 (5)	0.0406 (6)	0.0029 (4)	0.0146 (5)	−0.0114 (4)
O1	0.0268 (6)	0.0213 (5)	0.0285 (6)	0.0022 (4)	0.0046 (5)	−0.0023 (4)
O2	0.0339 (7)	0.0485 (8)	0.0207 (6)	0.0195 (6)	0.0010 (5)	−0.0011 (5)
O3	0.0251 (6)	0.0318 (6)	0.0234 (6)	0.0067 (5)	0.0057 (4)	0.0003 (4)
C1	0.0189 (7)	0.0249 (8)	0.0215 (7)	0.0035 (6)	0.0008 (6)	0.0025 (6)
C2	0.0174 (7)	0.0238 (8)	0.0219 (7)	0.0022 (6)	−0.0014 (6)	0.0025 (6)
C3	0.0226 (8)	0.0211 (7)	0.0257 (8)	0.0011 (6)	−0.0012 (6)	0.0008 (6)
C4	0.0237 (8)	0.0261 (8)	0.0254 (8)	0.0051 (6)	0.0009 (6)	−0.0048 (6)
C5	0.0216 (8)	0.0346 (9)	0.0269 (8)	−0.0005 (7)	0.0050 (6)	0.0007 (7)
C6	0.0241 (8)	0.0243 (8)	0.0308 (8)	−0.0033 (6)	0.0027 (6)	0.0011 (6)
C7	0.0216 (8)	0.0212 (7)	0.0244 (7)	0.0029 (6)	−0.0003 (6)	−0.0016 (6)
C8	0.0202 (8)	0.0275 (8)	0.0218 (7)	0.0045 (6)	0.0008 (6)	0.0017 (6)
C9	0.0286 (9)	0.0319 (9)	0.0224 (8)	0.0085 (7)	0.0005 (6)	−0.0028 (6)
C10	0.0236 (8)	0.0197 (7)	0.0225 (7)	−0.0001 (6)	0.0028 (6)	−0.0015 (6)
C11	0.0322 (10)	0.0500 (11)	0.0293 (9)	−0.0112 (8)	0.0006 (7)	−0.0013 (8)

Geometric parameters (Å, °)

S—C1	1.753 (2)	C3—H3	0.9300
S—C11	1.809 (2)	C4—C5	1.385 (2)
F—C4	1.361 (2)	C5—C6	1.386 (2)
O1—C8	1.382 (2)	C5—H5	0.9300
O1—C7	1.384 (2)	C6—C7	1.385 (2)
O2—C10	1.312 (2)	C6—H6	0.9300
O2—H2	0.84 (2)	C8—C9	1.489 (2)
O3—C10	1.219 (2)	C9—C10	1.507 (2)
C1—C8	1.352 (2)	C9—H9A	0.9700
C1—C2	1.449 (2)	C9—H9B	0.9700
C2—C7	1.391 (2)	C11—H11A	0.9600
C2—C3	1.398 (2)	C11—H11B	0.9600
C3—C4	1.378 (2)	C11—H11C	0.9600
C1—S—C11	100.36 (8)	O1—C7—C6	125.50 (14)
C8—O1—C7	105.54 (12)	O1—C7—C2	110.57 (13)
C10—O2—H2	107.9 (15)	C6—C7—C2	123.93 (14)
C8—C1—C2	106.38 (13)	C1—C8—O1	111.99 (13)
C8—C1—S	126.22 (12)	C1—C8—C9	132.27 (15)
C2—C1—S	127.38 (12)	O1—C8—C9	115.73 (14)
C7—C2—C3	119.76 (14)	C8—C9—C10	115.38 (13)
C7—C2—C1	105.51 (13)	C8—C9—H9A	108.4
C3—C2—C1	134.72 (14)	C10—C9—H9A	108.4

C4—C3—C2	115.75 (14)	C8—C9—H9B	108.4
C4—C3—H3	122.1	C10—C9—H9B	108.4
C2—C3—H3	122.1	H9A—C9—H9B	107.5
F—C4—C3	118.04 (14)	O3—C10—O2	123.98 (15)
F—C4—C5	117.43 (14)	O3—C10—C9	121.25 (14)
C3—C4—C5	124.53 (14)	O2—C10—C9	114.76 (13)
C4—C5—C6	119.90 (14)	S—C11—H11A	109.5
C4—C5—H5	120.0	S—C11—H11B	109.5
C6—C5—H5	120.0	H11A—C11—H11B	109.5
C7—C6—C5	116.12 (15)	S—C11—H11C	109.5
C7—C6—H6	121.9	H11A—C11—H11C	109.5
C5—C6—H6	121.9	H11B—C11—H11C	109.5
C11—S—C1—C8	107.19 (15)	C5—C6—C7—C2	−0.6 (2)
C11—S—C1—C2	−74.59 (15)	C3—C2—C7—O1	−179.70 (13)
C8—C1—C2—C7	−0.23 (17)	C1—C2—C7—O1	0.38 (17)
S—C1—C2—C7	−178.73 (12)	C3—C2—C7—C6	0.6 (2)
C8—C1—C2—C3	179.87 (17)	C1—C2—C7—C6	−179.33 (15)
S—C1—C2—C3	1.4 (3)	C2—C1—C8—O1	−0.01 (17)
C7—C2—C3—C4	0.0 (2)	S—C1—C8—O1	178.52 (11)
C1—C2—C3—C4	179.93 (16)	C2—C1—C8—C9	179.85 (16)
C2—C3—C4—F	179.70 (14)	S—C1—C8—C9	−1.6 (3)
C2—C3—C4—C5	−0.7 (2)	C7—O1—C8—C1	0.24 (17)
F—C4—C5—C6	−179.66 (14)	C7—O1—C8—C9	−179.65 (13)
C3—C4—C5—C6	0.7 (3)	C1—C8—C9—C10	−92.8 (2)
C4—C5—C6—C7	−0.1 (2)	O1—C8—C9—C10	87.07 (18)
C8—O1—C7—C6	179.32 (15)	C8—C9—C10—O3	165.74 (15)
C8—O1—C7—C2	−0.39 (16)	C8—C9—C10—O2	−14.8 (2)
C5—C6—C7—O1	179.77 (14)		

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C6—H6···O3[i]	0.93	2.52	3.2896 (19)	141
C6—H6···O3[ii]	0.93	2.51	3.296 (2)	143
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C11—H11B···F[iv]	0.96	2.69	3.572 (2)	153
C11—H11B···F[v]	0.96	2.67	3.361 (2)	130

Symmetry codes: (i) *x*+1, *y*, *z*−1; (ii) −*x*+1, −*y*+1, −*z*+1; (iii) −*x*, −*y*+1, −*z*+1; (iv) *x*−1, −*y*+1/2, *z*+1/2; (v) *x*−1, *y*, *z*+1.

Fig. 1

Fig. 2